Rijksinstituut voor Volksgezondheid
en Milieu
*Ministerie van Volksgezondheid,
Welzijn en Sport*

Interventiewaarden voor incidentbestrijding: interventiewaarden, stofdocumenten en handleiding

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Interventiewaarden voor incidentbestrijding: interventiewaarden, stofdocumenten en handleiding december 2020

Colofon

K. Mahieu (auteur), RIVM
L. Geraets (auteur), RIVM
P. Bos (auteur), RIVM

Contact: Peter M.J. Bos,
Projectcoördinator Nederlandse Interventiewaarden voor incidentbestrijding
(email: peter.bos@rivm.nl)

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Rijksinstituut voor Volksgezondheid en Milieu
Postbus 1 | 3720 BA Bilthoven
Nederland
www.rivm.nl

Inhoud

Kobalthydrocarbonyl
Koolmonoxide
Kwik
Magnesiumaluminiumfosfide
Magnesiumfosfide
Maleinezuuranhydride
Methacrylaldehyde
Methacrylonitril
Methanol
Methylamine
Methylbromide
Methylchloorformiaat
Methylchloride
Methyleenchloride
Methylethylketon
Methylhydrazine
Methylisocyanaat
Methyljodide
Methylmercaptaan
Methylmethacrylaat
Methylnonafluoro(iso) butylether
Methylsilicaat
Methyl-tert-butylether
Methyltrichloorsilaan
Methylvinylketon
Mierenzuur
Monochloorazijnzuur
Monochloorbenzeen
Natriumfosfide
Nikkelcarbonyl
Oleum
Osmiumtetroxide
Parathion
Pentaboraan
Perazijnzuur
Perchloorethyleen
Perchloormethylmercaptaan
Perfluorisobutyleen
Piperidine
Propaan
Propionaldehyde
Propionitril
Propyleenglycoldinitraat
Propyleenimine
Propyleenoxide
Propyltrichloorsilaan
Salpeterzuur (70%)
Sarin
Seleenhexafluoride
Seleenwaterstof
Silaan
Siliciumtetrachloride
Stibine
Stikstofdioxide
Stikstofmonoxide
Stikstoftrifluoride
Strontiumfosfide
Styreen
Sulfurylchloride
Sulfurylfluoride
Tetrachloorkoolstof
Tetrafluorethyleen
Tetrahydrofuraan
Tetranitromethaan
Thionylchloride
Titaantetrachloride
Tolueen
Tolueen-2,4-diisocyanaat
Tolueen-2,6-diisocyanaat
Traangas (CS)
1,1,1-Trichloorethaan
Trichloorethyleen
Trichloorsilaan
Trimethoxysilaan
Trimethylamine
1,2,3-Trimethylbenzeen
1,2,4-Trimethylbenzeen
1,3,5-Trimethylbenzeen
Trimethylchloorsilaan
Triuraniumoctaoxide
Uraniumdioxide
Uraniumhexafluoride
Vinylacetaat
Vinylchloride
Vinyltrichloorsilaan
VX
Waterstofperoxide 90%
Xylenen
Zinkfosfide
Zwavelchloride
Zwaveldioxide
Zwavelkoolstof
Zwavelmosterd
Zwaveltrioxide
Zwavelwaterstof
Zwavelzuur

Overzicht van stoffen met 'oude' interventiewaarden

Acetylchloride
Acetyleen
Allylbromide
Allylglycidylether
Amylmercaptanen
Boriumtrichloride
Broomchloormethaan
Broomcyanide
Butaandion
n-Butaanthiol
n-Butanol
1-Buteen
2-Buteen
n-Butylamine
sec-Butylamine
tert-Butylhydroperoxide
Chinon
Chloortoluenen
Chloortrifluormethaan
Chloraal
2-Chloropreen
Collodium
o-Cresol
Cumeenhydroperoxide
Cyclohexanon
Diallylamine
Dichloordifluormethaan
1,1-Dichloorethaan
Dichloormonofluormethaan
1,2-Dichloorpropaan
1,3-Dichloorpropeen
1,2-Dichloor-1,1,2,2-tetrafluorethaan
Diethylamine
Diethylsulfide
Difenyloxide
1,1-Difluorethyleen
Diisodecylftalaat
Dimethylether
2,4-Dinitroaniline
Etheen
Ether
Ethylacetaat
Ethylbromide
Ethylbroomacetaat
Ethylchloride
Ethyleenglycolmono-ethyleter
Ethyleenglycolmono-ethylether acetaat
Ethyleenglycolmono-methylether
Ethylformiaat
Fosforpentasulfide
Fosfortribromide
Gasolie
Heptaan
Hexachloorcyclopentadieen
Hexanol
Isobutaan
Isobutanol
Isobutylacetaat
Isobutylacrylaat
Isobutylamine
Isobutyleen
Isobutylisocyanaat
Isobutylmethacrylaat
Isoforon
Isopentaan
Isopropylacetaat
Isopropylalcohol
Isopropylamine
Isopropylchloride
Isopropylether
Isopropylnitraat
Kooldioxide
Koolwaterstof-oplosmiddelen
Lachgas
LPG
Methylacetaat
Methylacetyleen/propadieen gasmengsel
Methylacrylaat
Methylal
n-Methylethylamine
Methylformiaat
Methylisobutylcarbinol
a-Methylstyreen
Monochloordifluormethaan
Nicotine
Nitrobenzeen
Nitromethaan
2-Nitropropaan
Nitrosylchloride
Octaan
Ozon
n-Pentaan
Piperazine
n-Propanol
Propeen
Propionylchloride
Propionzuur
Propylacetaat
Propylamine
Propylbromide
1,2-Propyleenglycol
Propyleenglycolethylether
Propylmercaptaan
n-Propylnitraat
Pyridine
Terpentijn
Tetrahydrothiofeen
Tetramethyllood
Tintetrachloride
Triethylaluminium
Triethylamine
Trifluorazijnzuur
Trifluorbroommethaan
Valeriaanaldehyde
Vinylbromide
Vinylethylether
Vinyltrimethoxisilaan
Waterstof
Xylidine
Zwaveldichloride
Zwaveltetrafluoride

Voorwoord

Inleiding

De Nederlandse interventiewaarden voor incidentbestrijding worden afgeleid om de gezondheidsrisico's in te schatten van inhalatoire blootstelling aan gassen, dampen of aerosolen. Vanaf 2008 worden de Nederlandse interventiewaarden voor de incidentbestrijding herzien; hiervoor is de methodiek voor de afleiding van interventiewaarden aangepast (RIVM rapport, 2019-0055 (https://www.rivm.nl/bibliotheek/rapporten/2019-0055.pdf)). Dit heeft geleid tot kwalitatief beter onderbouwde interventiewaarden. Ook worden er stofdocumenten opgesteld, waarin, naast de interventiewaarden zelf, informatie is opgenomen die van belang kan zijn voor de operationele fase van een incident.

Het huidige rapport bevat de stofdocumenten van alle stoffen waarvoor nieuwe interventiewaarden zijn afgeleid. Ook is een korte Handleiding opgenomen waarin wordt toegelicht welke, voor de operationele fase belangrijke, informatie in het stofdocument is opgenomen en hoe deze kan worden gebruikt. Het rapport is voorzien van diverse doorklikmogelijkheden. Vanuit de inhoudsopgave kan worden doorgeklikt naar het stofdocument van een stof. Individuele informatieblokken of afzonderlijke termen van Deel A van het stofdocument zijn gelinkt aan de betreffende toelichting in de Handleiding. Onderaan iedere pagina staan links naar dit Voorwoord, de Handleiding en de Inhoudsopgave.

Dit rapport bevat ook een apart overzicht van de stoffen waarvoor de interventiewaarden nog niet zijn herzien en waarvoor nog oude interventiewaarden gelden. Uit praktische overwegingen is de inhoudsopgave in twee delen gesplitst: eerst de stoffen waarvoor nieuwe interventiewaarden zijn afgeleid en waarvoor een stofdocument is opgesteld, gevolgd door de stoffen met oude interventiewaarden. Voor een geïntegreerd overzicht van alle nieuwe en oude interventiewaarden wordt verwezen naar de complete Interventiewaarden lijst die kan worden gedownload van https://rvs.rivm.nl/normen/rampen-en-incidenten/interventiewaarden.

Dit document zal regelmatig worden aangepast en uitgebreid. De meest recente versie zal actief verspreid worden binnen het GAGS en AGS-netwerk. Suggesties voor verbetering kan worden gedownload van https://rvs.rivm.nl/normen/rampen-en incidenten/interventiewaarden en aanpassing zijn dan ook welkom en kunnen worden gestuurd naar Peter M.J. Bos, Projectcoördinator Nederlandse Interventiewaarden voor incidentbestrijding (email: peter.bos@rivm.nl). Ook onjuistheden die worden aangetroffen kunnen naar dit email-adres worden gestuurd.

Nieuwe interventiewaarden

De belangrijkste verschillen tussen de nieuwe en de oude interventiewaarden zijn:

- Nieuwe interventiewaarden worden afgeleid voor zes verschillende tijdsduren (van 10 min tot 8 uur), in plaats van alleen de standaard 1-uurs waarde.
- De nieuwe waarden zijn wetenschappelijk beter onderbouwd en alleen gebaseerd op gezondheidskundige effecten, en niet meer op geur en explosielimieten.
- Voor de stoffen waarvoor nieuwe waarden zijn afgeleid, zijn, waar mogelijk en van toepassing, ook aparte waarden afgeleid voor geurwaarneming en het kankerrisico bij een eenmalige blootstelling.

Het stofdocument

Dit rapport bevat de nieuwe stofdocumenten van alle stoffen waarvoor nieuwe interventiewaarden zijn afgeleid. Het stofdocument bestaat uit twee delen, Deel A en Deel B.

Deel A is het operationele deel van het stofdocument en is vooral bedoeld ter ondersteuning van de GAGS en AGS voor gebruik tijdens de repressieve fase van een incident. Het bevat de waarden voor de VRW, AGW en LBW voor alle afgeleide blootstellingsduren, waarden voor explosiegrenzen en het hinderniveau van geur (de LOA). Daarnaast bevat Deel A basisinformatie over de fysisch-chemische en (klinisch) toxicologische eigenschappen van de stof en een indicatie van de benodigde medische informatie bij blootstelling. Deel A is opgesteld in het Nederlands en omvat maximaal één pagina.

Deel B geeft beknopt de informatie en de verantwoording voor de afleiding van de interventiewaarden. Het geeft het toxicologische startpunt voor de afleiding van elk van de interventiewaarden en eventueel aanvullende (toxicologische) informatie die de afleiding ondersteunt. Ook worden de toegepaste onzekerheidsfactoren benoemd en de wijze van tijdschalen. Tevens wordt de afleiding gegeven van de LOA en, indien van toepassing, het mogelijk kankerrisico. Tot slot bevat Deel B een overzicht van andere bestaande interventiewaarden (AEGL, ERPG) en de IDLH-waarden die voor acute blootstellingen bij incidenten zijn afgeleid. Deel B wordt opgesteld in het Engels en omvat maximaal twee pagina's.

Voor meer informatie over het Stofdocument wordt verwezen naar Hoofdstuk 4 van RIVM rapport 2019-0055 *(Handreiking voor de afleiding van interventiewaarden voor incidentbestrijding)*.

Oude interventiewaarden
Wanneer de interventiewaarden voor een stof nog niet zijn herzien, gelden de interventiewaarden uit 2007, waarbij alleen 1-uurs waarden zijn afgeleid. Het kan zinvol zijn om een oude interventiewaarde te gebruiken voor een andere blootstellingsduur. Daarvoor is in het verleden, na overleg met het GAGS platform, besloten de waarde voor een andere duur dan de opgegeven 1 uur als volgt vast te stellen:

1. Voor een blootstelling korter dan 1 uur geldt dezelfde waarde als voor 1 uur blootstelling.
2. Voor een blootstelling van 1 uur geldt de opgegeven waarde.
3. Voor een blootstelling langer dan 1 uur kan volgens onderstaande systematiek een waarde uit de standaard reeks …- 500 – 200 – 100 – 50 – 20 – 10 – 5 – 2 – 1 – 0,5 – 0,2 – 0,1… worden gekozen. Voor de eenvoud en in lijn met de nieuwe methodiek worden alleen waarden voorgesteld voor 2, 4 en 8 uur: voor 2 uur één waarde lager uit de reeks, voor 4 uur twee waarden lager, en voor 8 uur drie waarden lager.

Voor deze lijst geldt nog het volgende:
- n.v.t.: Deze stoffen kunnen ernstige acute gezondheidsschade veroorzaken bij een blootstelling van één uur zonder dat daar een sensorische waarneming aan voorafgaat. Deze stoffen hebben dan ook geen VRW onder het niveau van de AGW.
- ?: Er waren onvoldoende gegevens om voor deze stof interventiewaarde vast te stellen.
- (getal): Getallen tussen haakjes zijn concentraties gebaseerd op percentages van de onderste explosiegrens (Lower Explosive Limit, LEL). Voor stoffen met explosiegevaar als het kritische effect voor de LBW of AGW is de LBW vastgesteld op 100% van de LEL, en de AGW op 10% van de LEL.

Gebruiksaanwijzing
De inhoudsopgave bestaat uit twee delen. In het eerste deel zijn de stoffen opgenomen waarvoor de interventiewaarden zijn herzien en waarvoor stofdocumenten zijn opgesteld. Een stofdocument voor een stof is te vinden door te klikken op de stofnaam in dit deel van de inhoudsopgave. Het tweede deel bevat de stoffen waarvoor de oude interventiewaarden nog gelden; deze interventiewaarden kunnen worden gevonden door op de stofnaam te klikken. Het kan dus voorkomen dat in beide delen van de inhoudsopgave moet worden gezocht om interventiewaarden voor een stof te kunnen vinden.

In beide delen van de inhoudsopgave is de volgorde van de stoffen in de inhoudsopgave is gelijk aan de volgorde in de overzichtslijst met interventiewaarden op naam. Stofnamen staan op alfabetische volgorde van de hoofdnaam, waarbij geen rekening wordt gehouden met cijfers of met specifieke voorvoegsels die een nadere duiding van de structuurformule geven, zoals *n-*, *sec-*, *tert-*, *cis-* en *trans-*, of *o-, m-* en *p-*. Indien een naam niet in de inhoudsopgave staat kan het zijn dat de stof onder een synonieme naam is opgenomen. Met de algemene zoekfunctie kan een stofdocument ook op CAS-nummer of op een synonieme naam worden gezocht.

In Deel A van de stofdocumenten zijn links aangebracht bij de hoofdkopjes van informatieblokken en bij individuele termen. Hiermee kan worden doorgeklikt naar achtergrondinformatie in de Handleiding die vooraan in dit rapport is opgenomen. In de Handleiding wordt toegelicht welke informatie in informatieblokken is opgenomen. Termen worden in de Handleiding gedefinieerd en/of uitgelegd en toegelicht. Ook wordt in de Handleiding toegelicht hoe de gegeven informatie in de praktijk kan worden toegepast. Om

vervolgens vanuit de handleiding terug te keren naar het stofdocument kan op een computer gebruik worden gemaakt van de ‘previous view’ functie in de menubalk (of via ‘ALT+left arrow’). Indien deze knop niet zichtbaar is in de menubalk kan deze in *Adobe Acrobat* zichtbaar worden gemaakt door in de menubalk op de rechter muisknop te klikken en dan bij ‘Show Page Navigation Tools’ ‘Previous view’ aan te vinken. Op een tablet kan in *Adobe Acrobat* teruggegaan worden naar de Inhoudsopgave (via de knop ‘Inhoudsopgave’ onderaan de pagina) en dan weer door te klikken naar het stofdocument.

Handleiding voor de toepassing van interventiewaarden voor incidentenbestrijding

Voor stoffen waarvoor nieuwe interventiewaarden zijn afgeleid zijn ook nieuwe stofdocumenten opgesteld. In deze beknopte handleiding wordt beschreven hoe de informatie in Deel A van de nieuwe stofdocumenten optimaal kan worden toegepast tijdens een operationele fase. Dit wordt gedaan aan de hand van de verschillende informatieblokken waaruit stofdocument Deel A is opgebouwd. Voor meer uitgebreide informatie wordt verwezen naar het RIVM rapport 2019-0055[1].

Basisinformatie
Als basisinformatie worden enkele identificatie- en gevaarskenmerken voor de stof gegeven. De identificatiekenmerken kunnen behulpzaam zijn om de stof te identificeren, maar kunnen ook gebruikt worden om aanvullende informatie voor de stof te zoeken in zoeksystemen. Deze kenmerken omvatten de stofnaam en enkele veel gebruikte synoniemen in het Engels en in het Nederlands, het CAS-nr en de structuurformule.
De vermelde gevaarskenmerken zijn:

- VN-nummer (of UN nummer): Een stofidentificatienummer bestaande uit een getal van vier cijfers dat een gevaarlijke stof identificeert tijdens het transport volgens de voorschriften van de Verenigde Naties

- GEVI-nummer: Het gevaarsidentificatienummer dat gebruikt wordt voor vervoer van gevaarlijke stoffen over de weg en het spoor. Het nummer bestaat uit twee of drie cijfers en wordt, indien van toepassing, voorafgegaan door de letter X (i.e. reageert op gevaarlijke wijze met water). Het eerste nummer geeft een indicatie van het hoofdgevaar, overeenkomend met de ADR -gevarenklassen. Als het tweede cijfer gelijk is aan het eerste geeft dat een versterking van het hoofdgevaar aan (bijvoorbeeld 3=brandbaar; 33=licht ontvlambaar).

- A/B-Status: De A- of B-status wordt afgeleid van een risico-index (berekend op basis van de dampspanning en de 1-uurs AGW), en wordt bepaald door de lengte van het benedenwinds gebied (aangeduid als het effectgebied) waarbinnen de alarmeringsgrenswaarde (AGW) wordt overschreden bij een gestandaardiseerde fictieve ontsnapping van de stof. B-stoffen veroorzaken onder deze standaardomstandigheden een groter effectgebied (zijn risicovoller) dan A-stoffen.

Interventiewaarden

- Interventiewaarden: De drie niveaus van interventiewaarden worden als volgt gedefinieerd:
  VRW: De voorlichtingsrichtwaarde is de luchtconcentratie die met grote waarschijnlijkheid door de blootgestelde bevolking als hinderlijk wordt waargenomen, of waarboven lichte gezondheidseffecten mogelijk zijn.

  AGW: De alarmeringsgrenswaarde is de luchtconcentratie waarboven onherstelbare of andere ernstige gezondheidseffecten kunnen optreden, of waarbij door blootstelling aan de stof personen minder goed in staat zijn zichzelf in veiligheid te brengen.

  LBW: De levensbedreigende waarde is de luchtconcentratie waarboven mogelijk sterfte of levensbedreigende aandoeningen kunnen ontstaan.

  Interventiewaarden worden afgeleid voor drie niveaus van gezondheidseffecten en voor zes blootstellingsduren. Dit maakt het mogelijk om de ernst van een situatie en dringendheid van handelen in te schatten aan de hand van twee trends: *verticaal* (de te verwachten gezondheidseffecten in relatie tot een toenemende concentratie) en *horizontaal* (de te verwachten gezondheidseffecten bij toenemende blootstellingsduur). Zie ter illustratie het voorbeeld van acrylnitril.

[1] https://www.rivm.nl/bibliotheek/rapporten/2019-0055.pdf

Interventiewaarden acrylnitril (mg/m³)		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarde	**VRW**	3,3	3,3	3,3	3,3	3,3	3,3
Alarmeringsgrenswaarde	**AGW**	650	240	130	67	36	19
Levensbedreigende	**LBW**	1300	440	220	110	58	30

Verticaal: Voor de dringendheid van handelen is de ratio tussen de LBW, AGW en VRW een belangrijke parameter. Hoe kleiner deze ratio, des te smaller de bandbreedte van handelen. **Opmerking: voor een stof kunnen deze ratio's variëren met de blootstellingsduur.** *(Vergelijk bijvoorbeeld de AGW/VRW ratio en de LBW/AGW ratio voor de verschillende blootstellingsduren in het voorbeeld van acrylnitril hierboven.)*

Horizontaal: De concentratie behorend bij de drie niveaus van interventiewaarden kan variëren over de tijd, deze variatie is vooral afhankelijk van de aard van het gezondheidseffect waarop de interventiewaarde is gebaseerd en de fysisch-chemische eigenschappen van een stof. Voor de meeste gezondheidseffecten geldt dat een interventiewaarde zal afnemen bij langere blootstellingsduur. Deze afname kan per stof verschillen en bepaalt mede de dringendheid van handelen, vooral als verwacht wordt dat het incident nog enige tijd kan voortduren. **Bijvoorbeeld: de luchtconcentratie tijdens een incident kan lager zijn dan een 30-min AGW maar bijvoorbeeld hoger dan een 1- of 2-uurs AGW of zelfs hoger dan een 2-uurs LBW.** *(Zie de tabel van acrylnitril hierboven voor bijvoorbeeld een luchtconcentratie van 150 mg/m³).*
Sommige effecten zijn echter vooral afhankelijk van de blootstellingsconcentratie en hiervoor geldt dat de interventiewaarde gelijk is voor meerdere tijdsduren. (*Zie de VRW voor acrylnitril in het voorbeeld hierboven*).
Indien verwacht wordt dat de **blootstelling langer zal duren dan 8 uur** wordt aanbevolen om contact op te nemen met RIVM/MOD omdat bij extrapolatie naar langere tijdsduren meerdere factoren een rol spelen.

Eén of meerdere asterisken (*) bij een interventiewaarde geven aan hoe de interventiewaarde zich verhoudt tot de Lower Explosive Limit (LEL). Indien een interventiewaarde hoger is dan 10%, 50% of 100% van de LEL wordt dit aangegeven door respectievelijk '*', '**' en '***' bij de betreffende interventiewaarde.

Indien **geen waarden** zijn afgeleid (aangegeven door '**NA**' (niet aanbevolen)) kan dit één van de volgende redenen hebben (de betreffende reden wordt vermeld in Deel B van het stofdocument):
- Er zijn geen geschikte gegevens beschikbaar om een getalswaarde af te leiden. Dit kan voor zowel VRW, AGW als LBW gelden. In deze gevallen kan niet worden uitgesloten dat er wél effecten kunnen optreden.
- Alleen voor de VRW: De beschikbare informatie geeft aan dat gezondheidseffecten behorend bij het niveau van de VRW niet optreden of pas beginnen op te treden bij een concentratie boven het niveau van de AGW. Soms geldt dit alleen bij een langere duur van blootstelling.
  Dit houdt in dat de betreffende stof geen waarschuwende toxicologische eigenschappen kent beneden de AGW. Dit vereist een verhoogde alertheid gedurende het verloop van het incident.

- Conversiefactor: De interventiewaarden worden uitgedrukt in mg/m³. Vaak wordt in het veld gebruik gemaakt van meetresultaten uitgedrukt in ppm. De interventiewaarden kunnen worden omgerekend naar waarden in ppm met de conversiefactor; de conversiefactor wordt berekend bij 20°C. Deze omrekening is alleen van toepassing op gassen en dampen; voor een aerosol kan de concentratie niet worden uitgedrukt in ppm.

- Explosiegrens: Lower Explosive Limit (LEL): Deze moet beschouwd worden in relatie tot interventiewaarden. Het explosiegevaar kan in enkele gevallen kritischer zijn dan het gezondheidsgevaar bij betreding van een effectgebied. Indien een interventiewaarde hoger is dan 10%, 50% of 100% van de LEL wordt dit aangegeven door respectievelijk '*', '**'en '***' bij de betreffende interventiewaarde.

- LOA: Level of distinct Odour Awarenes: De LOA is een schatting van de concentratie in lucht waarboven meer dan de helft van de blootgestelde bevolking een geur duidelijk waarneemt; de LOA is dus **geen geurdrempel**. (Indien de geurdrempel bekend is, kan deze worden teruggevonden in Deel B van een stofdocument, in het kader "Odour and derivation of the LOA value"). De geurwaarneming wordt niet als uitgangspunt gebruikt voor het afleiden van nieuwe interventiewaarden; een gerapporteerde geurwaarneming kan wel bijdragen aan een inschatting van de hoogte van de concentratie. Indien bekend, wordt bij de LOA de geurkarakteristiek beschreven.

Fysisch-chemische eigenschappen
De fysische-chemische eigenschappen zoals opgenomen in de stofdocumenten zijn primair overgenomen van de Nederlandse Chemiekaarten.

Overige informatie
Het stofdocument bevat ook informatie over de grenswaarden voor de werkplek:
- Nederlandse publieke grenswaarde voor de werkplek,
- Duitse MAK-waarde
- TLV-waarde

Deze waarden geven de maximale concentraties aan die op de werkplek in de lucht mogen voorkomen; deze gelden in principe voor een blootstellingsduur van 8 uur per dag gedurende 40 jaar. Deze waarden zullen dus over het algemeen lager zijn dan de interventiewaarden, waarbij het gaat om een eenmalige blootstelling.
In principe wordt alleen de acht uurs-waarde genoteerd, maar de STEL of Ceiling(plafond)waarde worden opgenomen als deze informatief zijn. Indien huidopname een belangrijke bijdrage aan de blootstelling kan leveren, wordt dit aangegeven met een H onder de betreffende waarde.

Toxicologische eigenschappen
- Effecten bij inhalatoire blootstelling:
  Dit tekstblok bevat een korte beschrijving van de te verwachten klachten/effecten bij eenmalige inhalatoire blootstelling aan oplopende concentraties in lucht, onderverdeeld op basis van de afgeleide Interventiewaarden. Hoewel de Interventiewaarden gebaseerd zijn op een belangrijk effect wordt hier aangegeven of, en zo ja, welke andere effecten te verwachten zijn bij overschrijding van een interventiewaarde.

- Toxiciteit bij eenmalige, inhalatoire blootstelling:
  In dit tekstblok staat een korte beschrijving van de mechanismen van toxiciteit en het doelorgaan bij kortdurende inhalatoire blootstelling. Indien van toepassing worden ook gevoelige bevolkingsgroepen vermeld.

- IARC-classificatie: (International Agency for Research on Cancer).
  IARC identificeert en classificeert omgevingsfactoren op basis van carcinogeniteit.
  Daarbij zijn 5 categorieën te onderscheiden:
  - 1 (carcinogenic to human)
  - 2A (probably carcinogenic to humans)
  - 2B (possibly carcinogenic to humans)
  - 3 (not classifiable as to carcinogenicity to humans)
  - 4 (probably not carcinogenic to humans)

  Indien een stof niet door IARC is geëvalueerd wordt vermeld: 'not evaluated'.
  De IARC-classificatie geeft vooral de sterkte van het bewijs voor carcinogeniteit aan en niet de carcinogene potentie. Voor een stof in categorie 1 is het bewijs dat de stof carcinogeen voor de mens is sterker dan voor een stof in categorie 2 of 3. De Carcinogene Risico Potentie (CRP) geeft wel de carcinogene potentie aan.

- CRP: Carcinogene Risico Potentie bij kortdurende blootstelling:
  De CRP geeft het blootstellingniveau aan waarboven, bij een eenmalige inhalatieblootstelling van één uur, verwacht wordt dat het risico op kanker groter is dan 1 op 10.000. Het berekenen van de CRP vanuit chronische dierexperimenten of epidemiologische data met een levenslange blootstelling vereist een groot aantal

aannames en extrapolaties en is daarom erg onzeker. De CRP moet dan ook niet gezien worden als een hard getal, maar als informatieve duiding. De CRP moet vooral geïnterpreteerd worden als een indicatie voor het risico op kanker in vergelijking met de interventiewaarden, ten behoeve van crisiscommunicatie.

Beknopte medische informatie
Dit blok biedt informatie voor de eerste praktische hulpverlening.
Bij voorkeur wordt echter het NVIC ingeschakeld.

Stofdocumenten met herziene interventiewaarden (nieuwe methodiek)

Stoffen waarvoor interventiewaarden zijn afgeleid volgens de nieuwe methodiek:
- kennen interventiewaarden voor zes verschillende tijdsduren (10, 30 en 60 min en 2, 4 en 8 uur),
- kennen interventiewaarden die wetenschappelijk beter zijn onderbouwd en alleen zijn gebaseerd op gezondheidskundige effecten, en niet meer op geur en explosielimieten,
- kennen aparte waarden voor geurwaarneming en het kankerrisico bij een eenmalige blootstelling.

Voor iedere stof is een stofdocument opgesteld, bestaande uit twee delen.

Deel A is het operationele deel van het stofdocument en is vooral bedoeld ter ondersteuning van de GAGS en AGS voor gebruik tijdens de repressieve fase van een incident. Het bevat de waarden voor de VRW, AGW en LBW voor alle afgeleide blootstellingsduren, waarden voor explosiegrenzen en het hinderniveau van geur (de LOA). Daarnaast bevat Deel A basisinformatie over de fysisch-chemische en (klinisch) toxicologische eigenschappen van de stof en een indicatie van de benodigde medische informatie bij blootstelling. Een toelichting op de informatie in Deel A wordt gegeven in de Handleiding (zie link onderaan de pagina). Deel A is opgesteld in het Nederlands.

Deel B geeft beknopt de informatie en de verantwoording voor de afleiding van de interventiewaarden. Het geeft het toxicologische startpunt en de onderbouwing voor de afleiding van elk van de interventiewaarden en eventueel aanvullende (toxicologische) informatie die de afleiding ondersteunt. Tevens wordt de afleiding gegeven van de LOA en, indien van toepassing, het mogelijk kankerrisico. Tot slot bevat Deel B een overzicht van andere bestaande interventiewaarden (AEGL, ERPG) en de IDLH-waarden die voor acute blootstellingen bij incidenten zijn afgeleid.
Deel B is opgesteld in het Engels.

Stofdocument deel A

CAS-nr: 75-07-0 **Aceetaldehyde** **CH_3CHO** **VN-nr: 1089**

GEVI: 33

Synoniemen: acetylwaterstof, ethanal, ethylideenoxide (Engels: acetaldehyde) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m³)**	82	82	82	82	82	82
Alarmeringsgrenswaarden	**AGW (mg/m³)**	910	630	500	400	320	210
Levensbedreigende waarden	**LBW (mg/m³)**	2800	1900	1500	1200	970	490

Datum vaststelling: 13-05-2009

Conversiefactor: 1 mg/m³ = 0,544 ppm; 1 ppm = 1,84 mg/m³

Explosiegrens: LEL = 4.0 vol% ≈ 73.000 mg/m³

Geur: Stekend, fruitig

LOA: 1,0 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp/lucht mengsel: 1,5

Molecuulmassa: 44,1 g/mol
Zuurgraad: Geen data
LogKow: 0,6
Wateroplosbaarheid: volledig
Verzadigde dampdruk: 1007 mbar

Overige informatie

Publieke grenswaarde: 37 mg/m³ (8-uur TGG)
TLV-TWA: 183 mg/m³
MAK: 91 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: oogirritatie, milde (bovenste) luchtwegirritatie, hoest

AGW → LBW: tranenvloed, irritatie van bovenste luchtwegen, benauwdheid, longoedeem, verhoogde hartslag, bewustzijnsdaling

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Aceetaldehyde veroorzaakt irritatie van de ogen en de bovenste luchtwegen.
- Aceetaldehyde kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- In hoge concentraties kan aceetaldehyde verlamming van de ademhalingsspieren veroorzaken.
- Aceetaldehyde is een genotoxische alkylerende verbinding met een beperkt vermogen om genmutaties te veroorzaken.
- Personen met astma zijn mogelijk gevoeliger voor de effecten van aceetaldehyde.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn

Oogcontact: bijtend, tranenvloed, roodheid en pijn, slecht zien, hoornvliesbeschadiging, ernstige brandwonden

Carcinogeniteit

IARC classificatie: 2B

CRP: 9900 mg/m³

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding; arts raadplegen bij aanhoudende klachten (ademhaling, bewustzijnsverlaging)

ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*:* geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 75-07-0 **Acetaldehyde** **CH_3CHO** **VN-nr: 1089**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 13-05-2009 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	82	82	82	82	82	82	Threshold for mild respiratory and eye irritation in humans
AGW	910	630	500	400	320	210	Histopathological changes in nasal epithelium in animals
LBW	2800	1900	1500	1200	970	490	Animal lethality

Derivation of the Dutch Intervention Values

VRW: In a human study, mild respiratory irritation was observed at a measured concentration of 134 ppm (246 mg/m^3) for 30 minutes. Subjects did not report eye irritation, like in another human study, but in the latter study only nominal concentrations were given. The concentration of 246 mg/m^3 for 30 minutes is chosen as the point of departure for VRW derivation. An uncertainty factor of 3 is applied to this concentration to account for intraspecies variability. A higher factor is not needed because little variation is expected for direct eye irritation effects. Also no time scaling is applied and the resulting value of 45 ppm (82 mg/m^3) is held constant across all time points.

AGW: In a subacute rat study, degeneration of the nasal epithelium was observed after exposure to 410 ppm (752 mg/m^3), 6 hours/day, 5 days/week for 4 weeks. This effect was not observed after a single exposure to 750 or 1500 ppm (1380 or 2750 mg/m^3) for 6 hours, although some nasal changes were observed following exposure to 1380 or 2750 mg/m^3 on 3 consecutive days (6-h/day). The concentration of 1500 ppm (2750 mg/m^3) for 6 hours is taken as the point of departure for AGW, this being the no effect level for sub-AGW damage to the nasal epithelium. A total uncertainty factor of 10 is applied, consisting of an interspecies factor of 3 and an intraspecies factor of 3. The intraspecies factor of 3 was considered sufficient to account for variability in human susceptibility to acetaldehyde. Default time-scaling was applied using $C^n \times t = k$ with default values n=1 for extrapolation to longer time periods and n=3 for extrapolation to shorter time periods. In contrast to the 10 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: LBW derivation is based on animal data. Studies in hamsters and rats provide the most reliable basis for the LBW. Rats being the more sensitive species in these studies are the preferred species. Using the Benchmark software of the US-EPA, log-probit modeling was done on the results from acute and subacute rat studies. This led to a $BMDL_{05}$ of 5,295 ppm (9710 mg/m^3) for a 4-hour exposure as point of departure. To this level a total uncertainty factor of 10 is applied, consisting of a factor of 3 for interspecies extrapolation and a factor of 3 for sensitive human subpopulations. Larger factors are considered not necessary given the typical irritative aldehyde toxic action by acetaldehyde. Time scaling was performed using $C^n \times t = k$ with default values n=1 and n=3 for extrapolation to longer time periods and n=3 for extrapolation to shorter time periods. In contrast to the 10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Irritation of eyes, skin, and respiratory tract are the primary effects of acute acetaldehyde inhalation. In rats, sensory irritation has been observed. In addition, erythema, coughing, pulmonary edema and narcosis may develop. At high concentrations (not specified) paralysis leading to death may occur. Prolonged exposure to high concentrations (unspecified) may injure the corneal epithelium, causing persistent lacrymation, photophobia, and foreign body sensation. Fatalities following inhalation are due to anesthesia when prompt, and to pulmonary edema when delayed. Asthmatic patients are considered a vulnerable group.
No inhalation studies were performed to determine the reprotoxic effects. The only data on reprotoxic effects

of acetaldehyde are from a 90-day hamster inhalation study where reduced gonad weights were observed in both sexes at ≥1340 ppm (2460 mg/m^3).

H319: causes serious eye irritation; H335: may cause respiratory irritation; H351: suspected of causing cancer.

Carcinogenicity and derivation of the CRP value

IARC classification: 2B (possibly carcinogenic to humans).

Derivation of the carcinogenic risk potency (CRP):

10^{-4} risk level after inhalation: 0.045 mg/m^3

CRP = (10^{-4} risk level * average life span in hours)/DRCF

= (0.045 * 613.200) /2.8 = 9900 mg/m^3

US-EPA (1991) provided aquantitative cancer risk estimation for inhalation of acetaldehyde based on incidences of nasal tumours as observed in the chronic rat study of Woutersen et al. (1986). A risk of 1 x 10^{-4} was calculated to be 0.045 mg/m^3 (virtually safe dose).

Odour and derivation of the LOA value

Odour: pungent, suffocating, and fruity odor

OT_{50}: 0.0018ppm (0.00275mg/m^3) [AEGL (2008); Nagata (2002)]

LOA = 11.8 * OT_{50} * 1.33 = 1.0 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is below the VRW, therefore subjects will be aware of the odour below the level where health effects may be expected.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **82**	*AEGL-1* 81	*ERPG-1* 18		*IDLH:* 3770 (10 min or 30 min)
AGW level **500**	*AEGL-2* 490	*ERPG-2* 370		
LBW level **1500**	*AEGL-3* 1500	*ERPG-3* 1800		

Stofdocument deel A

CAS-nr: 67-64-1 **Aceton** **CH_3-CO-CH_3** **VN-nr: 1090**

GEVI: 33

Synoniemen: dimethylketon, 2-propanon, DMK (Engels: dimethyl ketone) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	480	480	480	480	480	480
Alarmeringsgrenswaarden	AGW (mg/m³)	22.000*	12.000*	7.800*	5.200*	3.500	2.300
Levensbedreigende	LBW (mg/m³)	40.000**	21.000*	14.000*	9.200*	6.100*	4.100

Datum vaststelling: 13-05-2009

Conversiefactor: 1 mg/m³ = 0,414 ppm; 1 ppm = 2,42 mg/m³

Explosiegrens: LEL= 2,1% ≈ 50.000 mg/m³
* berekende interventiewaarde hoger dan 10% LEL
** berekende interventiewaarde hoger dan 50% LEL

Geur: Karakteristieke, fruitige geur

LOA: 390 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze vloeistof.

Brand: De damp is zwaarder dan lucht en verspreidt zich over de grond met kans op ontsteking op afstand.

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,2

Molecuulmassa: 58,1 g/mol
Zuurgraad: Geen data
LogKow: -0,2

Wateroplosbaarheid: volledig
Verzadigde dampdruk: 247 mbar

Overige informatie

Publieke grenswaarde:
1210 mg/m³ (8 uur)
MAK: 1200 mg/m³

TLV-TWA: 1810 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: Geen informatie

VRW → AGW: Lichte oog-, keel-, en neusirritatie, hoofdpijn, gevoel van zwakte

AGW → LBW: misselijkheid, braken, hoofdpijn, duizeligheid, verwardheid, bewustzijnsdaling

Boven LBW: coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Aceton veroorzaakt irritatie van ogen, neus en keel.
- Aceton veroorzaakt depressie van het CZS.

Effecten bij blootstelling aan vloeistof

Huidcontact: prikkeling, droge huid, ruwe huid

Oogcontact: roodheid en pijn, tranenvloed

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding; arts raadplegen bij aanhoudende klachten (m.n. bewustzijnsverlaging)

ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en arts raadplegen

Specifieke behandeling en materialen*:…*

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 67-64-1 **Acetone** **CH_3-CO-CH_3** **UN-nr: 1090**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2 h value added

AGW: AEGL value is adopted, 2 h value added

LBW: AEGL value is adopted, 2 h value added

Date: 13-05-2009 | AEGL document: Interim, 2005

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	480	480	480	480	480	480	NOAEL for slight irritation in humans
AGW	22,000*	12,000*	7,800*	5,200*	3,500	2,300	NOAEL for ataxia in rats
LBW	40,000**	21,000*	14,000*	9,200*	6,100*	4,100	No lethality in rats

* value higher than 10% of LEL; ** value higher than 50% of LEL

Derivation of the Dutch Intervention Values

VRW: The VRW derivation is based on observations in four studies with human volunteers exposed for 3-5 minutes, 2 hours, 6 hours and 7.5 hours. At 200 ppm (483 mg/m³), subjective symptoms (eye/throat irritation) were not reported more often than in controls. At 250 ppm (604 mg/m³) no irritative symptoms on mucous membranes or effects on the central nervous system (headache, fatigue, feeling of sickness, dizziness, intoxication) were observed in one study; in a second study, slight irritation and few complaints about subjective discomfort (feeling of tension, general weakness, heavy eyes, lacking in energy) were reported at 250 ppm (604 mg/m³), and these subjective symptoms were felt by most volunteers at 500 ppm (1210 mg/m³) and 1000 ppm (2420 mg/m³). Slight irritation at 300 ppm (725 mg/m³) and subjective irritation in the majority of exposed volunteers at 500 ppm (1210 mg/m³) were reported in a further study. Therefore, 200 ppm (480 mg/m³) was selected as point of departure to derive VRW values. However, the irritation effects at this concentration are probably influenced by the odour of acetone. Based on an extensive literature search by Arts *et al.* (2002), it was noted that subjective irritation is observed at acetone concentrations <1000 ppm (2420 mg/m³) and objective irritation is observed >10,000 ppm acetone (24200 mg/m³).

Because the concentration of the point of departure represents a NOAEL for local effects and effects at higher concentrations were weak, an intraspecies factor of 1 is applied. The value of 200 ppm (480 mg/m³) was used for all timepoints since accommodation to slight irritation occurs and the complaints about subjective discomfort at higher concentrations were reported not to increase during 6 hour or 7.5 hour exposure.

AGW: The AGW is based on the NOAEL for ataxia in rats following exposure to 6000 ppm (14,500 mg/m³) acetone for 4 hours. At the next higher concentration of 12,000 ppm (29,000 mg/m³) reversible ataxia was observed. Reversible ataxia also was observed in another study at exposure of rats to 12,600 ppm (30,500 mg/m³) for 3 hours, but a no-effect level was not determined in that study. An interspecies factor of 1 was used for the following reasons. First, toxicokinetic studies show that following inhalation the concentration of acetone in blood is similar or lower in humans than in rats. Furthermore, with respect to toxicodynamics, effects of substances such as acetone that are non-specific acute CNS-depressants in general do not show much variation between species. Finally, an interspecies factor of 3 would (together with an intraspecies factor of 4.2, see below) have resulted in AGW of 1150 mg/m³ for 4 hours and of 765 mg/m³ for 8 hours. These values are not supported by data from controlled human studies in which exposures up to 1000 - 1200 ppm (2420 – 2900 mg/m³) for up to 7.5 hours resulted in irritation and slight headaches but no more severe effects. Furthermore, available toxicokinetic data for humans show that an exposure to 480 ppm (1160 mg/m³) for 4 hours or 320 ppm (773 mg/m³) for 8 hours would lead to acetone concentration in blood below 50 mg/L. Such concentrations are still in the physiological range which can be observed in healthy fasting humans. With respect to an intraspecies factor, it is observed in humans that newborns consistently are the most sensitive age group for volatile anesthetics in general. No human data for acetone were available allowing for the derivation of a substance-specific intraspecies factor. However, in a study with rats of different ages it was observed that the lethal dose (LD_{50} oral) of acetone was 4.2-fold lower in newborns than in adults. It is assumed that intraspecies differences between humans are also covered by this range. Therefore, an intraspecies uncertainty factor of 4.2 was applied to account for sensitive individuals. The data were scaled across time using $C^n \times t = k$ with n = 1.7 as outlined below for LBW.
It is noted that the reliability of the derived n-value is limited, however the n-value is derived from the same study and is expected to be better than the default values for n.

LBW: The LBW is based on a study in rats in which no deaths of animals occurred at exposure to 12,600 ppm (30,500

mg/m^3) for 3 hours. In that study, also no deaths were observed in animals exposed to 19,000 (45,900 mg/m^3) and 25,300 ppm (61,100 mg/m^3), but since 1 of 6 animals died at 16,000 ppm (38,700 mg/m^3) in another study, the findings at 12,600 ppm (30,500 mg/m^3) exposure for 3 hours were taken as point of departure for the derivation of LBW values. An interspecies uncertainty factor of 1 was applied because the same toxic effects (CNS depression) which are relevant for AGW are also relevant in case of LBW. Also, an interspecies factor of 3 (together with an intraspecies factor of 4.2, see below) would result in a 4 hour LBW of 840 ppm (2030 mg/m^3) and an 8 hour LBW of 560 ppm (1350 mg/m^3). These values are not supported by data from a controlled human study in which no life-threatening effects were observed at exposures up to 2110 ppm (5100mg/m^3) for 8 hours and a number of other studies in which no severe effects on the central nervous system were observed at exposures up to 1000 - 1200 ppm (2420 – 2900 mg/m^3) for 6 - 7.5 hours. A substance specific intraspecies uncertainty factor of 4.2 (see derivation of AGW above) was applied to account for sensitive individuals. The experimentally derived exposure values were scaled across time using $C^n \times t = k$ with n = 1.7 that was derived by extrapolation from 4-hour and 8-hour LC_{50} data.
It is noted that the reliability of the derived n-value is limited, however the n-value is derived from the same study and is expected to be better than the default values for n.

Additional toxicological information (including relevant results of a general literature search, if any)

The acute toxicity of acetone is low and no reports were located in which exposure of humans to acetone resulted in death. Following exposure to acetone, the primary effects in humans are irritation and effects on the central nervous system (CNS).

An extensive literature search was presented by Arts *et al.* (2002): An analysis of human response to the irritancy of acetone vapours. Crit. Rev. Toxicol. 32, 43-66. It was noted that subjective irritation is observed at acetone concentrations <1000 ppm (2420 mg/m^3) and objective irritation is observed >10,000 ppm acetone (24200 mg/m^3) and that subjective irritation is influenced by odour.

In a developmental/reproductive toxicity study with mice and rats, no maternal or fetal toxicity was observed at 2000 ppm (4800 mg/m^3). At 6,600 ppm (16,000 mg/m^3) in mice and 11,000 ppm (27,000 mg/m^3) in rats, maternal and fetal weight were reduced and the incidence of late resorptions in mice was slightly increased (however, the mean number of live fetuses per litter was not decreased). In rats exposed to 11,000 ppm (27,000 mg/m^3), the percent of litters with at least one pup exhibiting malformations and the diversity of malformations was higher compared to controls, but the incidence of fetal malformations was not significantly increased.

H319: Causes serious eye irritation; H336: may cause drowsiness or dizziness.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified.

No carcinogenic risk potency (CRP) was derived.

Carcinogenicity studies are lacking.

Odour and derivation of the LOA value

Odour: sweetish, mildly pungent and fruity odor.

OT_{50}: 10.25 ppm (24.77 mg/m^3)[AEGL (2005); Wysocki et al. (1997)]
LOA = 11.8 * OT_{50} * 1.33 = 390 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is below the VRW, therefore subjects will be aware of the odour below the level where health effects may be expected.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **480**	*AEGL-1* 480	*ERPG-1* not derived		*IDLH*: 6,040 (30 minutes)
AGW level **7,800**	*AEGL-2* 7,700	*ERPG-2* not derived		
LBW level **14,000**	*AEGL-3* 14,000	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 75-86-5 **Acetoncyaanhydrine** $(CH_3)_2$–C(OH)–CN **VN-nr: 1541** **GEVI: 669**

Synoniemen: ACH, 2-cyano-2-propanol; 2-methylacetonitril; (Engels: acetone cyanohydrin) ***Status:*** geen

Interventiewaarden		10 min.	30	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	60	27	16	9,7	5,8	3,5
Alarmeringsgrenswaarden	AGW (mg/m³)	79	35	21	13	7,6	4,6
Levensbedreigende waarden	LBW (mg/m³)	360	160	96	58	35	21

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,28 ppm; 1 ppm=

Explosiegrens: LEL=2,2 vol% ≈ 78.000 mg/m³

Stof reageert heftig met oxidatiemiddelen, geconcentreerde zuren en sterke basen met kans op brand en explosie, waarbij stof ontleedt in cyaanwaterstof en aceton.

Geur: Een bittere amandelgeur als gevolg van het ontstaan van HCN bij het snel uiteenvallen van acetoncyaanhydrine. De stof zelf heeft geen geur. De geur kan niet als detectiemaat worden gehanteerd.

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot gele vloeistof

Brand: brandbaar

Molecuulmassa:	85,1 g/mol
Zuurgraad:	Geen data
LogKow:	-0,5
Wateroplosbaarheid:	Volledig
Verzadigde dampdruk:	1,00 mbar

Overige informatie

Publieke grenswaarde:
Niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	geen effecten te verwachten
VRW → AGW:	hoofdpijn, misselijkheid
AGW → LBW:	duizeligheid, verwardheid, braken, oogirritatie, amandel of bittere smaak, verlamming, snelle pols en rood worden van gezicht
Boven LBW:	depressie van CZS en ademhaling, hartritmestoornissen, hypotensie, convulsies, coma en sterfte; mogelijk voorafgegaan door korte periode van CZS stimulatie, hypertensie en hyperventilatie

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Acetoncyaanhydrine ontleedt zeer snel in aceton en cyaanwaterstof. De acute toxiciteit van aceton is vele malen lager dan de acute toxiciteit van cyaanwaterstof; de toxiciteit van acetoncyaanhydrine wordt bepaald door de vorming van cyaanwaterstof.
- Cyanide blokkeert de ademhalingsketen in de cel. Hierdoor wordt de energiehuishouding verstoord en kan lactaatacidose ontstaan.
- Primaire doelorganen zijn het centrale zenuwstelsel en het cardiovasculaire systeem.
- Sterfte is veelal het gevolg van ademhalingsdepressie.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn
Stof kan door de huid worden opgenomen.
Oogcontact: roodheid en pijn

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: 100% zuurstof, GEEN mond-op-mondbeademing, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: direct spoedeisende medische hulp en specifieke behandeling inzetten, ondertussen verontreinigde kleding uittrekken, *af*spoelen met veel water of douchen.

ogen: direct spoedeisende medische hulp inzetten, ondertussen *uit*spoelen met water (evt. contactlenzen verwijderen)

inslikken: mond laten spoelen (uitspugen!), specifieke behandeling (GEEN mond-op-mondbeademing, GEEN braken opwekken) en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**:*

De benodigde middelen (100% zuurstof, specifieke antidota zoals o.a. hydroxocobalamine, of 4-DMAP, beide evt. gevolgd door natriumthiosulfaat) moeten met gebruiksaanwijzing ter plekke beschikbaar zijn.

Neem contact op met het NVIC (Tel: +31 (0)30 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 75-86-5 **Acetone cyanohydrin** **$(CH_3)_2$–C(OH)–CN** **UN-nr: 1541**

Dutch Intervention Values (mg/m³)

VRW: Based on hydrogen cyanide values, in accordance with AEGL (except 10 min value for which time scaling was applied), 2h value added

AGW: Based on hydrogen cyanide values, same point of departure as for AEGL values but using different value for n, 2h value added

LBW: Based on hydrogen cyanide values, same point of departure as for AEGL values but using different value for n, 2h value added

Date 16-12-2010	AEGL document: final, 2005

Proposal for the Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	60	27	16	9,7	5,8	3,5	Analogy with hydrogen cyanide; no adverse effects in humans during occupational exposure
AGW	79	35	21	13	7,6	4,6	Analogy with hydrogen cyanide; slight CNS depression in monkeys
LBW	360	160	96	58	35	21	Analogy with hydrogen cyanide; Lethality rats

Derivation of the Dutch Intervention Values

VRW: The derivation of the VRW values was based upon the fact that acetone cyanohydrin decomposes spontaneously to hydrogen cyanide and acetone and that both local and systemic toxic effects of acetone cyanohydrin are due to free cyanide. Once absorbed, a dose of acetone cyanohydrin behaves in a manner identical to that of its molecular equivalent in absorbed free cyanide. It is appropriate to apply the intervention values (on a ppm basis) derived from hydrogen cyanide to acetone cyanohydrin.

Derivation of VRW values for HCN

Chronic exposure of 63 workers in a cyanide salt production plant to geometric mean concentrations up to approximately 1 ppm and possible excursions up to 6 ppm, hydrogen cyanide (exposure duration was considered to be 8h) during part of the year did not produce clear exposure related symptoms. The 8-h no effect mean geometric concentration of 1 ppm was used as point of departure for determining VRW levels for acetone cyanohydrin. This would correspond to 1 ppm (3.5 mg/m³) acetone cyanohydrin. This value was time scaled to the other shorter exposure durations using $C^n x t = k$ with default values of n=1.36 when extrapolating to shorter exposure durations (see LBW).

This derivation-procedure is supported by the fact that similar values would have been derived on the basis of available acetone cyanohydrin studies in rats (derivation basis would be exposure to 9.2 ppm (33 mg/m³ acetone cyanohydrin) for 6 hours/day, 5 days/weeks for 4 weeks, which did not result in red nasal discharge) using the default time scaling procedure and a total uncertainty factor of 10.

AGW: The AGW values were based on hydrogen cyanide values using the same approach as the VRW.

Derivation of AGW values for HCN

Exposure to 60 ppm (67.4 mg/m³) for 30 minutes was used as point of departure. An interspecies uncertainty factor of 2 was applied because the respiratory tract of humans and monkeys are more similar than that of humans and rodents, and because both species have shown to be relatively insensitive to the incapacitative and lethal effect of hydrogen cyanide. The detoxifying enzyme is available in all humans, including newborns. The default intraspecies uncertainty factor of 3 was applied. Time scaling was applied using C^n x t = k, with n=1.36 (see LBW). Selection of this point of departure is supported by 2 animal studies. Exposure of rats for 30 minutes to 55 ppm (61.8 mg/m³) resulted in changes in lung dynamics and lung phospholipids (not irreversible or long-lasting).

This derivation-procedure is supported by the fact that similar values would have been derived on the basis of available acetone cyanohydrin studies in rats (derivation basis would be exposure to 19.9 ppm (70 mg/m³ acetone cyanohydrin) for 6 hours/day, 5 days/week for 4 weeks, which caused signs of irritation, while the next higher concentration produced respiratory distress, prostration, convulsions and tremors) using the default time scaling procedure and an uncertainty factor of 10.

LBW: The LBW values were based on hydrogen cyanide values using the same approach as the VRW.

Derivation of LBW values for HCN

In contrast to AEGL, LBW values were based on a more recent rat lethality dataset (Sweeney et al., 2014/2015). Groups of 10 male rats were exposed nose-only to hydrogen cyanide for 2.33, 5, 10, 15 and 30 min at concentrations ranging from 141.6 to 3175 ppm (159-3566 mg/m^3). LC_{01}values and the related time scaling factor were calculated using Doseresp, resulting in the following LC_{01} values for a 10 min, 30 min, 1h, 2h, 4h and 8h exposure period, respectively: 344.4 – 153.6 – 92.3 – 55.46 – 33.32 – 20.02 mg/m^3. Short exposure durations (i.e. ≤5 min) were excluded for analyses, as these were considered less reliable than longer exposure durations.

Lethal concentrations are very similar for various species, and study data show that man and the monkey are less sensitive to the effects of HCN than are the rat and dog. Relative to body weights, humans have a much lower respiratory rate and cardiac output than rodents. These are primary determinants of systemic uptake of volatile substances. Thus at similar exposure levels, rodents will absorb substantially more cyanide than primates. Lower detoxifying enzyme activity levels in primates will not be significant in high, acute HCN exposure levels. Based on this information, an interspecies uncertainty factor of 1 was applied. The available data do not demonstrate a susceptible population. The detoxifying enzyme is available in all humans, including newborns. The default intraspecies uncertainty factor of 3 was applied, leading to a total uncertainty factor of 3.

This procedure is supported by the close similarity of acetone cyanohydrin and hydrogen cyanide regarding death in rats: In a study with hydrogen cyanide, 3 out of 10 rats died after the first exposure to 68 ppm hydrogen cyanide for 6h, while subsequent two exposures on the following days caused no additional deaths. This finding closely resembles a study with acetone cyanohydrin reporting death of 3 out of 20 animals after the first exposure to 60 ppm (212 mg/m^3) acetone cyanohydrin for 6h, while no additional deaths were found in the 19 subsequent exposures.

Additional toxicological information (including relevant results of a general literature search, if any)

No specific susceptible populations were identified. The detoxifying enzymes are present in all individuals, including newborns.

From two fertility studies with rats with repeated inhalation exposure demonstrated that exposure to 60 ppm acetone cyanohydrin did not result in any potential for reproductive toxicity in male rats, nor did demonstrate any adverse effects on the fertility in females.

H300: Fatal if swallowed; H310: Fatal in contact with skin; H330: Fatal if inhaled

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

10^{-4} risk level after inhalation: not applicable

No information regarding the carcinogenic potential of acetone cyanohydrin exposure was located in the available literature. Genotoxicity studies with cyanide salts were generally negative and no cancers were induced in rats in a two-year feeding study with HCN.

In test using different *Salmonella* strains, acetone cyanohydrin failed to yield a reproducible positive response. No mutagenic activity was observed *in vitro* using CHO gene mutation assay. No significant increase in the frequency of chromosome aberrations were observed in an *in vivo* the bone marrow test.

Odour and derivation of the LOA value

Acetone cyanohydrin itself has no smell. However, since it decomposes readily into cyanide and acetone it can have the characteristic bitter almond odour due to the presence of free hydrogen cyanide. The level of detection will therefore also depend on the level of decomposition of acetone cyanohydrin in the air. Detection of odour will provide no information on uncontrolled exposure concentrations.

OT_{50}: no data
LOA = not derived

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **16**	*AEGL-1* 7.0	*ERPG-1* -		*IDLH: not derived*
AGW level **21**	*AEGL-2* 25	*ERPG-2* -		
LBW level **96**	*AEGL-3* 53	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 75-05-8 **Acetonitril** **CH_3-CN** **VN-nr: 1648**

GEVI: 33

Synoniemen: ethaannitril, methylcyanide, cyanomethaan (Engels: acetonitrile) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	34	34	34	34	34	34
Alarmeringsgrenswaarden	AGW (mg/m³)	2.400	1.200	790	510	330	210
Levensbedreigende waarden	LBW (mg/m³)	3.500	1.800	1.100	740	480	310

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,585 ppm; 1 ppm = 1,71 mg/m³

Explosiegrens: LEL = 3 vol% ≈ 51.000 mg/m³

Geur: Aromatische geur

LOA: 1.130 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof **Brand:** zeer brandgevaarlijk.

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,04

Molecuulmassa:	41,1 g/mol
Zuurgraad:	Geen data
LogKow:	-0,3
Wateroplosbaarheid:	Volledig
Verzadigde dampdruk:	97 mbar

Overige informatie

Publieke grenswaarde:
34 mg/m³ (TGG: 8 uur)
MAK: 34 mg/m³
TLV-TWA: 34 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: mogelijk lichte irritatie

VRW → AGW: irritatie ogen en bovenste luchtwegen, hoofdpijn

AGW → LBW: effecten op de ongeboren vrucht, hoesten, zwelling/verkramping strottenhoofd, benauwdheid, pijn op de borst, misselijkheid, braken, duizeligheid, krachtsverlies, verwardheid

Boven LBW: convulsies, ademnood, ademstilstand, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Acetonitril wordt omgezet tot o.a. cyanide.
- Cyanide blokkeert de ademhalingsketen in de cel. Hierdoor wordt de energiehuishouding verstoord en kan lactaatacidose ontstaan.
- Primaire systemische doelorganen zijn het centrale zenuwstelsel en het cardiovasculaire systeem.
- Acetonitril veroorzaakt irritatie van de bovenste luchtwegen. In zeldzame gevallen treedt longoedeem op.
- Acetonitril kan embryotoxiciteit veroorzaken.
- Verschijnselen kunnen vertraagd optreden.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid ademnood, blauwe lippen of nagels, duizeligheid, slaperigheid, hoofdpijn, zwaktegevoel, krampen.

Oogcontact: roodheid, pijn, slecht zien.

Carcinogeniteit

IARC classificatie: niet geclassificeerd.

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting ***damp***

algemeen: 100% zuurstof, GEEN mond-op-mondbeademing, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: 100% zuurstof, GEEN mond-op-mondbeademing, verontreinigde kleding uittrekken, afspoelen met water, specifieke behandeling en onmiddellijk arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen) en dan naar oogarts brengen

inslikken: mond laten spoelen (uitspugen!), 100% zuurstof, GEEN mond-op-mondbeademing, GEEN braken opwekken, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen

Bij vergiftiging door deze stof is specifieke eerste hulp noodzakelijk; specifieke antidota (zoals 100% zuurstof en o.a. hydroxocobalamine en natriumthiosulfaat) moeten met gebruiksaanwijzing ter plekke beschikbaar zijn. Voor aanwijzingen over verdere behandeling zo nodig het NVIC (+31(0)30-274 88 88) bellen. ,

Stofdocument deel B

CAS-nr: 75-05-8 **Acetonitrile** **CH_3-CN** **UN-nr: 1648**

Basis for the Dutch Intervention Values

VRW: Same PoD as for AEGL, different modifying factor applied, 2h value added

AGW: Based on a different point of departure as for AEGL, 2h value added

LBW: Based on a different point of departure as for AEGL, 2h value added

Date: November 2015 | AEGL Document, Final, 2014

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	34	34	34	34	34	34	Slight chest tightness and cooling sensation in lungs in humans
AGW	2,400	1,200	790	510	330	210	Foetal death in rats
LBW	3,500	1,800	1,100	740	480	310	LC_{01} in the rat after a 4-hour exposure

Derivation of the Dutch Intervention Values

VRW: Slight chest tightness and cooling sensation in the lungs noted in one out of three human male volunteers exposed to 40 ppm (68 mg/m^3) acetonitrile for 4 hours was used as point of departure for VRW values. No interspecies uncertainty factor was applied, because the critical study was already performed in humans. No intraspecies factor was applied because the effects are considered to have occurred in a sensitive subject and no symptoms were reported in the two other subjects exposed to this same regimen. Also at a higher dosis of 80 ppm (140 mg/m^3) for 4 hours no effects were noted in these two subjects. A modifying factor of 2 was applied to account for the sparse database for effects relevant for the VRW. Time scaling was not applied. For shorter durations no human data exist for periods of less than 4-hours and time-scaling effects could result in values that would elicit effects above those as defined relevant for VRW.

AGW: In contrast to the AEGL-2, the no-effect level for maternal and fetal mortality in pregnant rats exposed to acetonitrile at 1,500 ppm (2,564 mg/m^3) for 6 h/day on gestational days 6-20 was used as the point of departure for deriving AGW values. Although the study involved repeated exposures, fetal death is considered relevant for AGW derivation, as fetal death can also occur during a narrow developmental window and does not necessarily require repeated exposures. This is in contrast to maternal death, which is not considered an acute effect, but a result of repeated exposure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Scaling the AGW values across time was done using the equation $C^n \times t = k$ and the empirically derived chemical-specific value of 1.6 for n (see LBW rationale). In contrast to the 10 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: In contrast to the AEGL-3, a calculated 4-hour rat LC_{01} of 8421 ppm (14,400 mg/m^3) was used as point of departure for derivation of LBW values. Although the mouse is the most sensitive species, rat data are selected because utilization of mouse data yields LBW values ranging from 12 to 113 ppm (21-190 mg/m^3), which are inconsistent with the available human data, and due to availability of species-specific time-scaling data for rats. This rat study is selected because the analytical methods appear sound and data reporting allowed for the calculation of an LC_{01}. Based on the available lethality data, the rat is considered less sensitive than other species. However, the rats dataset is the most robust dataset. Therefore an interspecies factor of 10 instead of the default 3 was used. Scaling the LBW values across time was done using the equation $C^n \times t = k$ and the empirically derived chemical-specific value of 1.6 for n. In contrast to the 10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Aliphatic nitriles like acetonitrile induce local irritation effects. In addition, aliphatic nitriles are readily absorbed from the lung and gastrointestinal tract, resulting in systemic toxicity. Most of the systemic toxicity of these nitriles is mediated through hepatic and extrahepatic cytochrome P450 catalyzed oxidation of the carbon

alpha to the cyano group producing a cyanohydrin and an aldehyde. The metabolically-liberated cyanide is then conjugated with thiosulfate to form thiocyanate and is excreted in the urine. The toxicity of acetonitrile is due to the metabolic liberation of cyanide and signs and symptoms are similar to those observed after cyanide exposure.

No information concerning potential human reproductive toxicity was located.

There was an increase in the number of abnormal fetuses in hamsters exposed to 5,000 or 8,000 ppm (8,500 or 14,000 mg/m^3) for 1 hour on day 8 of gestation. At these concentrations also maternal toxicity was observed, and one dam exposed to 5,000 ppm (8,500 mg/m^3) died. In rats exposure to 100-1200 ppm (170-2,100 mg/m^3) did not result in treatment related effects on reproductive indices or in increases in fetal malformations or variations. In another study in rats, maternal death, an increase in the mean percentage of nonsurviving implants and early embryonic resorptions, and a decrease in mean number of live fetuses per litter were observed after repeated exposure to 1,800 ppm (3,100 mg/m^3).

H302: Harmful if swallowed, H312: harmful in contact with skin, H332: harmful if inhaled, H319: causes serious eye irritation.

Carcinogenicity and derivation of the CRP value

There is no evidence of carcinogenic activity of acetonitrile in rats and mice.

IARC classification: Not classified.

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: sweet, ether-like odor

Odour threshold: 42 ppm (72 mg/m^3) [Ruth, 1986]

LOA = 11.8 * 72 * 1.33 = 1130 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is higher than the VRW, AGW and LBW values.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **34**	*AEGL-1* 22	*ERPG-1* Not derived		*IDLH:* 855 (30 minutes)
AGW level **790**	*AEGL-2* 84	*ERPG-2* Not derived		
LBW level **1,100**	*AEGL-3* 250	*ERPG-3* Not derived		

Stofdocument deel A

CAS-nr: 107-02-8 **Acroleine** **CH_2=CHCHO** **VN-nr: 1092** **GEVI: 663**

Synoniemen: acrylaldehyde, allylaldehyde, 2-propenal (Engels: acrolein) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,070	0,070	0,070	0,070	0,070	0,070
Alarmeringsgrenswaarden	AGW (mg/m³)	1,0	0,42	0,23	0,23	0,23	0,23
Levensbedreigende waarden	LBW (mg/m³)	15	5,8	3,3	1,8	1,1	0,63

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,429 ppm; 1 ppm = 2,33 mg/m³

Explosiegrens: LEL = 2,8 vol% ~ 65.000 mg/m³

Geur: Scherpe, bijtende geur

LOA: onvoldoende betrouwbare gegevens

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze vloeistof
Brand: Zeer brandgevaarlijk. Kans op ontsteking op afstand

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,27

Molecuulmassa:	56,1 g/mol
Zuurgraad:	geen data
LogKow:	0,9
Wateroplosbaarheid:	20,6 g/100 ml (goed)
Verzadigde dampdruk:	293 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: oogirritatie, tranenvloed

AGW → LBW: irritatie aan ogen en luchtwegen, benauwdheid, longoedeem

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Acroleine veroorzaakt irritatie aan ogen en luchtwegen.
- Acroleine kan longoedeem veroorzaken. De effecten hiervan kunnen vertraagd optreden en versterkt worden door lichamelijk inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, pijn, brandwonden

Oogcontact: bijtend, roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: 3

CRP: n.v.t.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**:* geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 107-02-8 **Acrolein** **CH_2=CHCHO** **VN-nr: 1092**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: November 2015 | AEGL document: Final, 2010

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.070	0.070	0.070	0.070	0.070	0.070	Eye irritation
AGW	1.0	0.42	0.23	0.23	0.23	0.23	Severe eye and airway irritation
LBW	15	5.8	3.3	1.8	1.1	0.63	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: The threshold for eye irritation and annoyance/discomfort in human subjects of 0.09 ppm (0.21 mg/m^3) was used to derive the VRW values. An intraspecies uncertainty factor of 3 was applied, which was considered sufficient because minor ocular contact irritation is unlikely to vary greatly between humans. The values were held constant across time because minor irritancy is generally a threshold effect and prolonged exposure is not likely to result in a greatly enhanced effect. These VRW values are considered protective because data suggested no irritation in humans exposed to 0.06 ppm (0.14 mg/m^3) acrolein for 5 minutes.

AGW: The AGW was based on severe eye irritation (in 3% of the subjects after 10 minutes and 18% of the subjects after 20 minutes) in healthy human subjects exposed to 0.3 ppm (0.70 mg/m^3) for 1 hour. Medium eye irritation was reported by 18% and 35% of the subjects after 10- and 20-min of exposure, respectively. The average eye irritation index slightly increased between 20 and 40 min of exposure and remained constant between 40 and 60 min of exposure. The eye blink reflex more than doubled in the first 10 min of exposure and remained constant thereafter. Subjects experiencing more severe eye irritation generally also showed a higher increase in eye blink reflex. The one-hour exposure to 0.3 ppm also induced a 10-15% decrease in respiratory rate (60% of subjects after 20 minutes), moderate (19%) to severe (4%) nose irritation after 20 minutes and the onset of moderate to severe throat irritation in few subjects. The 1-hour exposure to 0.3 ppm (0.70 mg/m^3) was seen as cut off point for severe eye- and airway irritation and used as point of departure for the derivation of the AGW. An intraspecies uncertainty factor of 3 was applied, which was considered sufficient because irritation is not expected to vary greatly between individuals. Further, 0.09 ppm (0.21 mg/m^3) was reported as threshold concentration for eye irritation by in the same study. Application of a higher uncertainty factor would yield AGW values below this threshold level. Because the study showed progressive effects during the first 40 minutes of exposure, the value was back-extrapolated to the 10- and 30-minute time points using the relationship $C^n \times t = k$ where n = 1.2 (derived from lethality data in rats exposed to acrolein from 1 to 4 hours). The value was held constant for the 2-, 4-, and 8-hr AGW values since irritation is generally a threshold effect and prolonged exposure is not likely to result in a greatly enhanced effect. This is supported by the observation that the severity of the eye irritation did not further increase between 40- and 60-min of exposure to 0.3 ppm.

LBW: The 10-min, 30 min, 1 hour and 2 hour LBW values were based on the highest concentration causing no mortality in the rat after a 1-hour exposure (14 ppm; 33 mg/m^3). The 4-hour and 8-hour LBW values were based on the highest concentration causing no mortality in the rat after a 4-hour exposure (4.8 ppm; 11.2 mg/m^3). An intraspecies uncertainty factor of 3 was applied, which is considered sufficient due to the steepness of the concentration response curve. An interspecies uncertainty factor of 3 will also be applied (total uncertainty factor = 10). Although an interspecies uncertainty factor of 10 might normally be applied due to limited data, LBW values calculated utilizing a total uncertainty factor of 30 would yield values that are inconsistent with the total data base. For example, LBW values for acrolein would range from 2.1-0.09 ppm (4.9 to 0.21 mg/m^3), and only ocular, nasal, or throat irritation and decreased respiratory rates were observed in humans exposed to 0.09-0.6 ppm (0.21 to 1.4 mg/m^3) acrolein for up to 40 minutes). LBW values were extrapolated

using the relationship $C^n \times t = k$, where n = 1.2, derived from lethality data in rats exposed to acrolein from 1 to 4 hours.
A recent update of literature provided two studies on the effects of acroleine on normo and hypertensive rats (Haradin, 2014 and Perez, 2013). Exposure to acroleine led to cardiac arrhythmias. Using this as PoD for the LBW would result in less conservative, but comparable LBWs. No adjustments were made.

Additional toxicological information (including relevant results of a general literature search, if any)

No information concerning effects in young, elderly, or asthmatic individuals was available.

Information concerning human mortality from acrolein exposure is limited and anecdotal, containing no verifiable concentration and time parameters. Nonlethal case reports and experimental studies with healthy human volunteers suggest that low concentrations of acrolein are irritating to the eyes, nose, and throat, and cause a decrease in respiratory rate. At higher concentrations, coughing, pulmonary edema (may be delayed in onset), bronchitis, or tracheobronchitis may occur.

Nonlethal animal studies indicate that the respiratory system is the target for acrolein toxicity and that acrolein is a potent irritant at relatively low concentrations and short exposure durations. Irritancy was demonstrated by respiratory rate decreases in rodents, signs of irritation such as gasping and dyspnea, and decreased immunoreactivity of sensory nerve fibers in rodents. At higher concentrations and/or longer exposure times, respiratory system histopathology and pulmonary edema were evident. Data also suggest that exposure to acrolein may suppress pulmonary antibacterial defenses.

There is no evidence that inhaled acrolein is a reproductive/developmental toxicant.

H300: Fatal is swallowed; H311: Toxic in contact with skin; H314: Causes severe skin burns and eye damage; H330: Fatal if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to carcinogenicity to humans)

No carcinogenic risk potency (CRP) was derived.

Carcinogenicity studies regarding human exposure to acrolein were not available. There is no evidence that inhaled acrolein is a carcinogen in experimental animals.

Odour and derivation of the LOA value

Odour: Acrid, pungent odour

No LOA was derived due to lack of reliable data.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **0.070**	*AEGL-1* 0.070	*ERPG-1* 0.12		*IDLH:* 4.7 (30 minutes)
AGW level **0.23**	*AEGL-2* 0.23	*ERPG-2* 0.35		
LBW level **3.3**	*AEGL-3* 3.3	*ERPG-3* 3.5		

Stofdocument deel A

CAS-nr: 107-13-1 **Acrylnitril** **CH_2=CH-CN** **VN-nr: 1093**

GEVI: 336

Synoniemen: acrylonitril, 2-propeennitril, vinylcyanide (Engels: acrylonitrile) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	3,3	3,3	3,3	3,3	3,3	3,3
Alarmeringsgrenswaarden	AGW (mg/m³)	650	240	130	67	36	19
Levensbedreigende waarden	LBW (mg/m³)	1300	440	220	110	58	30

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,453 ppm; 1 ppm = 2,21 mg/m³

Explosiegrens: LEL = 2,8 vol% ≈ 62.000 mg/m³

Geur: scherp, ui- en knoflookachtig

LOA: 323 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot lichtgele vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,1

Molecuulmassa:	53,1 g/mol
Zuurgraad:	Geen data
LogKow:	-0,9
Wateroplosbaarheid:	7,3 g/100 ml (matig)
Verzadigde dampdruk:	124 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen klachten

VRW → AGW: rode en geïrriteerde brandende ogen, lichte tranenvloed, pijn in keel en neus, niezen, hoesten, hoofdpijn

AGW → LBW: pijn op de borst en pijn bij (door)ademen, piepende ademhaling, benauwdheid, misselijkheid, braken, duizeligheid, krachtsverlies, verwardheid

Boven LBW: convulsies, ademnood, ademstilstand, coma, overlijden

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Acrylnitril wordt omgezet tot o.a. cyanide en 2-cyano-ethyleenoxide.
- Cyanide blokkeert de ademhalingsketen in de cel. Hierdoor wordt de energiehuishouding verstoord en kan lactaatacidose ontstaan.
- Acrylnitril werkt irriterend op de luchtwegen; mogelijk veroorzaakt door cyanide.
- Primaire systemische doelorganen zijn het centrale zenuwstelsel en het cardiovasculaire systeem.
- Acrylnitril kan hematologische effecten veroorzaken, mogelijk veroorzaakt door adduct-vorming van acrylnitril of 2-cyano-ethyleenoxide met hemoglobine. Methemoglobinevorming en hemolyse zijn een mogelijk gevolg hiervan.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, pijn, blaren, brandwonden. De stof wordt door de huid opgenomen!

Oogcontact: bijtend, roodheid, pijn, ernstige brandwonden

Carcinogeniteit

IARC classificatie: 2B
CRP: 329 mg/m³

Beknopte medische informatie

Ontsmetting damp

algemeen: DIRECT 100% ZUURSTOF TOEDIENEN!, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: PAS OP: HUIDOPNAME! DIRECT 100% ZUURSTOF TOEDIENEN! (GEEN mond-op-mondbeademing), specifieke behandeling en direct spoedeisende medische hulp inzetten, ondertussen verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: DIRECT 100% ZUURSTOF TOEDIENEN!, mond laten spoelen (uitspugen!), GEEN braken opwekken, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen:

De benodigde middelen (specifieke antidota zoals 100% zuurstof en o.a. N-acetylcysteïne, hydroxocobalamine en natriumthiosulfaat) moeten met gebruiksaanwijzing ter plekke beschikbaar zijn.

Voor aanwijzingen over verdere behandeling zo nodig het NVIC (tel: +31 (0)30 –274 8888) bellen.

Stofdocument deel B

CAS-nr: 107-13-1 **Acrylonitrile** **CH_2=CH-CN** **UN-nr: 1093**

Basis for the Dutch Intervention Values

VRW: AEGL endpoint is adopted but used for all timepoints, 2h value added

AGW: Different point of departure than AEGL values, 2h value added

LBW: Different point of departure than AEGL, 2h value added

Date: November 2015 | AEGL document: Final, 2014

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	3.3	3.3	3.3	3.3	3.3	3.3	No effect level in human volunteers
AGW	650	240	130	67	36	19	Slight ocular and nasal irritation in rats
LBW	1300	440	220	110	58	30	Lethality threshold in rats

Derivation of the Dutch Intervention Values

VRW: The VRW values are developed based upon results from a controlled experiment with 6 male human volunteers exposed by inhalation to 2.3 ppm (5 mg/m³) and 4.6 ppm (10 mg/m³) acrylonitrile for 8 hours. Exposure to the highest concentration (4.6 ppm/10 mg/m³) for 8 hours did not result in any symptoms of exposure. This finding is consistent with a report stating that workers routinely exposed to approximately 5 ppm (11 mg/m³) acrylonitrile experienced mild effects (initial conjunctival irritation) to which some degree of accommodation occurred. Data indicate that at higher concentrations during occupational exposure (16 to 100 ppm (35-221 mg/m³) for 20-45 minutes) more severe effects like nasal and ocular irritation, discomfort of the chest, nervousness, irritability and headaches were reported. A 3-fold reduction (an appropriate adjustment for mild irritation effects) of the lower limit of this range is equivalent to the 4.6 ppm (10 mg/m³) which is in line with the no-effect concentration of the study in human volunteers. Therefore, the point of departure for the derivation of the VRW is the 8 hour exposure to 4.6 ppm (10 mg/m³) acrylonitrile, based on data from healthy volunteers and workers. As the data are partly obtained in workers and because some accommodation occurred an intraspecies uncertainty factor of 3 was applied. The VRW values are not time scaled, because the effect is ocular irritation for which it is not to be expected that effects vary over time. This is supported by data in humans. The VRW values where held constant at 1.5 ppm (3.3 mg/m³) for all timepoints.
This approach deviates from the AEGL-1 derivation, where values above 30 minutes were not recommended, because these would result in levels higher than the AEGL-2.

AGW: The AGW values are based upon data from rats (16/group) showing slight transient effects (ocular and nasal irritation) following a 2-hour exposure by inhalation to 305 ppm (674 mg/m³) acrylonitrile. At the next highest concentration (595 ppm, 1300 mg/m³) effects were indicated as marked. All effects resolved within 12 hours post exposure. Point of departure was 305 ppm (674 mg/m³) exposure for 2 hours. An interspecies uncertainty factor of 3 and an intraspecies uncertainty factor of 3 was applied because the effects associated with acute irritation effects are not likely to vary greatly among individuals and because metabolism may be of limited relevance regarding such effects. An overall uncertainty factor of 10 was applied. Application of higher or additional uncertainty factors would also result in AGW values unacceptably similar to VRW values that were based upon human exposure data. Time scaling was performed using the equation $C^n \times t = k$ with n = 1.1 based on ten Berge (1986). This approach deviates from the AEGL which uses reprotoxic effects (decreases in fetal body weight) for derivation of AEGL-2 levels. Fetal body weight effects are not considered relevant for AGW.
This approach deviates from the AEGL-2 derivation, where the AEGL-2 levels were calculated using the change in fetal body weight in a developmental study as point of departure.

LBW: In contrast to the AEGL-3, the LBW values were derived from a rat lethality study (Dudley and Neal, 1942) from which 10 and 30 minute, 1-, 2-, 4-, and 8-hour LC_{01} values (12660, 4370, 2233, 1141, 583, 298 mg/m³) were calculated. Although the dog appears to be the most sensitive species, the overall database for rats is more robust thereby justifying use of the rat data. The LC_{01} values were

points of departure for derivation of LBW-values. An interspecies factor of 3 was considered sufficient to account for possible toxicodynamic/metabolism differences, because PBPK models demonstrated that predicted concentrations of acrylonitrile and the metabolite 2-cyanoethylene oxide in blood and brain were similar in rats and humans exposed by inhalation. For effects resulting from a single acute exposure, an intraspecies uncertainty factor of 3 would seem sufficient for accounting for variability in metabolism-mediated effects. Additional uncertainty factor application would result in incompatible LBW and AGW values. The 10-minute, 30-minute, 1-hour, 2-hour and 8-hour LBW values were derived based upon their respective LC_{01} values.

Additional toxicological information (including relevant results of a general literature search, if any)

Generally, the toxic effects following acute inhalation exposure to acrylonitrile appear to be irritation of the respiratory tract and toxic effects which appear to be related to the metabolism of acrylonitrile to cyanide. Acrylonitrile-induced neurological effects in laboratory animals appear to involve the parent compound and the cyanide metabolite. The pivotal role of cyanide has been clearly demonstrated. Acrylonitrile-induced convulsions are likely the result of cyanide resulting from acrylonitrile metabolism, although recent work suggests that only the early seizures are cyanide-mediated and that severe clonic convulsions preceding death may be due to parent compound. The mechanism by which acrylonitrile causes irritation is unknown. Nasal tissue damage in rats may be related to metabolism of acrylonitrile by this tissue. Hematologic effects may be due to acrylonitrile hemoglobin adducts and 2-cyanoethylene oxide hemoglobin adducts, while GSH depletion in red blood cells may result in the oxidation of hemoglobin to methemoglobin.

Acrylonitrile toxicity appears to be directly related to its metabolism. Two major metabolism pathways have been described; conjugation with glutathione and epoxidation by microsomal cytochrome P4502E1 which forms 2-cyanoethylene oxide. Metabolites from both pathways are subject to additional biotransformation. The glutathione conjugate may form a mercapturic acid which is excreted in urine. 2-Cyanoethylene oxide is further metabolized via conjugation with glutathione (catalysis with cytosolic GST or nonenzymatically) resulting in additional conjugates and via hydrolysis by microsomal epoxide hydrolase (EH). The secondary metabolites of 2-cyanoethylene oxide may also be further metabolized. Cyanide may be generated via the EH pathway and by one of the GSH conjugation products. Cyanide, in turn, is detoxified to thiocyanate via rhodanese mediated reactions with thiosulfate.

A developmental inhalation toxicity study in rats showed a statistically increased incidence of malformations (short tail, short trunk, missing ribs, delayed ossification of skull bones, omphalocele and hemivertebrae) in rats exposed to 80 ppm (180 mg/m^3) acrylonitrile for 6 hrs/day on gestation days 6 through 15. There was no evidence of teratogenicity or embryotoxicity in rats exposed to 40 ppm (90 mg/m^3). In another developmental inhalation toxicity study in rats evaluation of external, visceral and skeletal variation in the fetuses revealed no acrylonitrile related effects at exposures up to 100 ppm (220 mg/m^3) for 6 hrs/day on gestation days 6 to 20. Another study found nonlethal effect on fetal development that included decreases in fetal body weight without fetal malformations (25-100 ppm; 55-221 mg/m^3) and nonlethal fetal malformations (40 and 80 ppm; 88 and 176 mg/m^3). A two generation reproductive toxicity study revealed weight decreases in the F_1 offspring of the 90-ppm (198 mg/m^3) group.

H350: May cause cancer, H301: Toxic if swallowed, H331: Toxic by inhalation, H318: Causes serious eye damage, H335: May cause respiratory irritation, H315: Causes skin irritation, H317: May cause allergic skin reaction

Carcinogenicity and derivation of the CRP value

IARC classification: 2B (possibly carcinogenic to humans)

IARC downgraded acrylonitrile from a category 2A to a category 2B (1999). This status change was based upon the lack of carcinogenic evidence from the more recent epidemiological studies. The data regarding potential carcinogenicity in humans is considered to be inadequate and no evidence of a causal association exists. This decision supports the conclusion that acrylonitrile is probably not carcinogenic to man.

Derivation of the carcinogenic risk potency (CRP):
10^{-4} risk level after inhalation: 1,5*10^{-3} mg/m^3 [EPA, 1984]
CRP = (1,5*10^{-3} mg/m^3 * 613,200) /2.8 = 329 mg/m^3

Odour and derivation of the LOA value

Odour: Sharp, onion-garlic

OT_{50}: 20.5 mg/m^3 [Nagata, 2003; corrected value derived from 9.3 ppm]

LOA = 11.8 * OT_{50} * 1.33 = 323 mg/m^3

(The concentration Level leading to distinct Odour Awareness (l=3) is calculated using the formula: l = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

Note, the AEGL document states a LOA of 145 ppm (320 mg/m3)

The LOA lies above the AGW, VRW and LBW

The CRP values lie above the AGW, VRW and LBW values.	values.

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)***				
VRW level **3.3**	*AEGL-1* NR	*ERPG-1* 22		*IDLH:* 188 (30 minutes)
AGW level **130**	*AEGL-2* 3.8	*ERPG-2* 77		
LBW level **220**	*AEGL-3* 62	*ERPG-3* 166		

Stofdocument deel A

CAS-nr: 79-10-7 **Acrylzuur** $CH_2=CH-CO_2H$ **VN-nr: 2218** **GEVI: 839**

Synoniemen: (2-)propeenzuur, etheencarbonzuur, AA (Eng.: acrylic acid) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	4,5	4,5	4,5	4,5	4,5	4,5
Alarmeringsgrenswaarden	AGW (mg/m³)	200	200	140	94	64	43
Levensbedreigende waarden	LBW (mg/m³)	1500	800	540	370	250	170
Datum vaststelling: 28-11-2008			Conversiefactor: 1 mg/m³ = 0,33 ppm; 1 ppm = 3,00 mg/m³				

Explosiegrens: LEL 2,4% ≈ 72.000 mg/m³

Geur: scherpe, stekende geur (walgingwekkend)

LOA: 0,60 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: heldere, kleurloze vloeistof

Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp/lucht mengsel: 1,01

Molecuulmassa: 72,1 g/mol
Zuurgraad: Geen data
LogKow: 0,3
Wateroplosbaarheid: volledig
Verzadigde dampdruk: 4,3 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: 30 mg/m³
TLV-TWA: 6,0 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: lichte oogirritatie

AGW → LBW: ernstige oog- en luchtwegirritiatie, benauwdheid, longoedeem

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Sterk irriterend voor slijmvliezen van ogen en luchtwegen.
- Blootstelling aan acrylzuur kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijk inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, bij hoge concentraties brandwonden, stof wordt via huid ook opgenomen.

Oogcontact: bijtend, roodheid en pijn, ernstige brandwonden, verlies van gezichtsvermogen

Carcinogeniteit

IARC classificatie: 3
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen, arts raadplegen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!) GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**:…*

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 79-10-7 **Acrylic acid** **CH_2=CH-CO_2H** **VN-nr: 2218**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 28-11-2008 | AEGL, interim 2004

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	4.5	4.5	4.5	4.5	4.5	4.5	Irritation in humans
AGW	200	200	140	94	64	43	Nasal epithelium damage and threshold for involuntary eyelid closure
LBW	1500	800	540	370	250	170	Animal lethality

Derivation of the Dutch Intervention Values

VRW: VRW values are based on irritation in humans. Eye irritation was experienced after occupational exposure to 4.5 - 23 ppm (13.5 – 69 mg/m^3) for 30 minutes (personal air sampling). For VRW derivation, the lower bound of 4.5 ppm (13.5 mg/m^3) was used. An uncertainty factor of 3 was applied for intraspecies variability. For local effects, the toxicokinetic differences between individuals are usually much smaller when compared to systemic effects. Therefore, a reduced uncertainty factor of 3 was considered sufficient. Since very slight irritative effects depend primarily on the actual exposure concentration and not much on exposure time, it was considered adequate to use the same exposure concentration for all exposure durations between 10 minutes and 8 hours. The VRW values are supported by a study in mice in which repeated exposure to 5 ppm (15 mg/m^3) for 6 hours/day for 2 weeks induced no histopathological alterations in the nasal passage.

AGW: In studies in monkeys, rabbits, rats and mice, histopathological alteration of the nasal mucosa consistently was a more sensitive toxicological endpoint than the appearance of clinical signs of irritation. It was therefore considered appropriate to use a single inhalation exposure studies in monkeys and rats as key studies for the derivation of AGW values. Exposure to 75 ppm (225 mg/m^3) acrylic acid for 6 hours resulted in severe histopathological changes of the nasal epithelium (olfactory epithelial cell degeneration, sustentacular cell necrosis), while exposure for 3 hours resulted in less severe changes and a lesser percentage of the olfactory epithelium was affected. The histological damage after the 6-hour exposure was considered as severe and probably irreversible, while the moderate changes after the 3-hour exposure were considered reversible. Therefore, AGW values were derived from the 3-hour exposure to 75 ppm (225 mg/m^3). This point of departure was supported by the observation that 77 ppm (231 mg/m^3) was the NOAEL for blepharospasm in rabbits. A total uncertainty factor of 3 was used. An uncertainty factor of 1 was applied for interspecies variability: because the deposited concentration of acrylic acid on the olfactory epithelium is about two- to threefold higher in rats than in humans and single inhalation exposure of monkeys resulted in similar olfactory lesions compared to rats. An uncertainty factor of 3 was applied for intraspecies variability (see VRW for rationale). Time scaling using the equation C^n x t = k was done with n = 1.8, which was derived from lethality data. The time-scaled 10-minute AGW value would be 370 mg/m^3. Since 77 pm (231 mg/m^3) was a no effect level for blepharospasm in rabbits, the 10-min AGW value was set equal to the 30-min value to keep the AGW values below a level which might cause blepharospasm in humans.

LBW: A rat lethality study, in which a large number of rats was exposed for various time periods (30 minutes, 1 hour and 2 hours), was considered the most relevant study for deriving LBW values. Although the study employed exposure to acrylic acid aerosols, its results are considered relevant also for vapour exposure. Using Probit analysis (Ten Berge software), maximum likelihood estimates for a 1-hour LC_{50} of 3850 ppm (11,550 mg/m^3) and for a 1-hour LC_{01} of 1806 ppm (5,416 mg/m^3 = Point of Departure) were calculated from the aerosol data. Time scaling was done by using the equation C^n x t = k with n=1.8, derived from the probit analyses. A total uncertainty factor of 10 was applied to the 1-hour LC_{01}. An uncertainty factor of 3 was applied for interspecies variability based on the intrinsic irritant effect of acrylic acid, which is not expected to vary greatly among species or among individuals. The intraspecies uncertainty factor was set at 3 for the same reasons.

Additional toxicological information (including relevant results of a general literature search, if any)

The physical state, to which a subject is exposed to, is relevant for the toxicity of acrylic acid. Animal acute

toxicity data indicate that aerosols are more toxic than acrylic acid in vapour form. Acrylic acid is highly water soluble and thus is solubilized in the mucus covering the epithelia of the upper respiratory airways, e.g. in rats it is completely absorbed in the mucus of the nasal turbinates. Irritation is caused most likely by acrylic acid itself and there is no evidence in the literature that the effects observed after exposure to acrylic acid are caused by a metabolite.
No developmental toxic effects of acrylic acid were found in several inhalation studies.

H302: Harmful if swallowed; H312: Harmful in contact with skin; H314: Causes severe skin burns and eye damage; H332: Harmful if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to carcinogenic to humans)

Odour and derivation of the LOA value

Pungent odour

OT_{50}: 0.013 ppm (0.039 mg/m^3) [AEGL (2004); Hellman and Small (1974)]
LOA = 11.8 * OT_{50} * 1.33 = 0,60 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is below the VRW for all points in time.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **4.5**	*AEGL-1* 4.5	*ERPG-1* 3.0		*IDLH:* not established
AGW level **140**	*AEGL-2* 140	*ERPG-2* 150		
LBW level **540**	*AEGL-3* 540	*ERPG-3* 750		

Stofdocument deel A

CAS-nr: 107-18-6 **Allylalcohol** **CH_2=CH-CH_2OH** **VN-nr: 1098** **GEVI: 663**

Synoniemen: 2-propenol-1; propenylalcohol; vinylcarbinol (Engels: Allyl alcohol) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m³)**	5,0	5,0	5,0	5,0	5,0	5,0
Alarmeringsgrenswaarden	**AGW (mg/m³)**	10	10	10	10	10	10
Levensbedreigende waarden	**LBW (mg/m³)**	88	61	48	24	24	24

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,414 ppm; 1 ppm = 2,42 mg/m³

Explosiegrens: LEL = 2,5 vol% ≈ 60.000 mg/m³

Geur: doordringende mosterdgeur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze heldere vloeistof

Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-luchtmengsel: 1,02

Molecuulmassa:	58,1 g/mol
Zuurgraad:	geen data
LogKow:	0,2
Wateroplosbaarheid:	volledig
Verzadigde dampdruk:	24 mbar

Overige informatie

Publieke grenswaarde: 4,8 mg/m³ (huid)
MAK: geen data
TLV-TWA: 1,21 mg/m³ (huid)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: lichte tot matige oog- en neus irritatie

AGW → LBW: matige tot ernstige oogirritatie (necrose); irritatie luchtwegen, kortademigheid, ademnood, longoedeem, lever- en nierfunctiestoornissen.

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Allylalcoholdamp is irriterend voor de huid, ogen en slijmvliezen. Oogcontact kan verbranding van de cornea veroorzaken. Direct huidcontact kan in eerste- en tweedegraads brandwonden resulteren en epidermale necrose veroorzaken.
- Blootstelling aan allylalcohol kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Allylalcohol veroorzaakt ook effecten op het zenuwstelsel, lever en nieren.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, pijn, blaarvorming, brandwonden

Oogcontact: bijtend, roodheid, pijn, slecht zien, lichtgevoeligheid

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende hulp inzetten.

Specifieke behandeling en materialen:

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 107-18-6 **Allyl alcohol** **CH_2=CH-CH_2OH** **VN-nr: 1098**

Basis for the Dutch Intervention Values

VRW: Different point of departure, different uncertainty factors, 2 h value added

AGW: Different point of departure, different uncertainty factors, no time scaling, 2 h value added

LBW: Different point of departure, different uncertainty factor, different time scaling, 2 h value added

Date: November 2015 | AEGL document: Final 2014

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	5.0	5.0	5.0	5.0	5.0	5.0	Light to moderate irritation (nose) humans
AGW	10	10	10	10	10	10	Threshold of severe irritation to eyes and respiratory tract in humans
LBW	88	61	48	24	24	24	Threshold of Lethality in animals (3 species)

Derivation of the Dutch Intervention Values

VRW: In contrast to the AEGL effects observed in a human volunteer study were used as point of departure. Exposure to a concentration of 6.25 ppm (15 mg/m^3) for 5 minutes resulted in slight or moderate nose irritation in 3/6 and 1/6 volunteers, respectively. This endpoint was used for the derivation of the VRW. The default intraspecies uncertainty factor of 3 was used. The same value was applied across the 10- and 30- minutes and 1, 2, 4 and 8 hour exposure times, because mild irritancy generally does not vary greatly over time, and it is not expected that prolonged exposure will result in an enhanced effect. The VRW values are supported by experimental animal data showing that repeated exposure of male rats (7 hours/day; 5 days/week; 12 weeks) to concentrations of up to 20 ppm (48 mg/m^3) did not induce any effect (clinical or after microscopic examination) apart from a reduced body weight gain.

AGW: In contrast to the AEGL, the basis for the derivation of the AGW was the same human volunteer study as for derivation of the VRW. At 12.5 ppm (30 mg/m^3) for 5 minutes, moderate or greater nose irritation was reported by 4 of 7 volunteers and 1 out of 7 volunteers reported slight eye irritation. At 25 ppm (60 mg/m^3) for 5 minutes, severe eye irritation and moderate nose irritation was reported by 5/5 subjects. The 12.5 ppm (30 mg/m^3) was used as point of departure for the derivation of the AGW. The default intraspecies uncertainty factor of 3 was applied. The same value was applied across the 10- and 30- minute, and the 1, 2, 4 and 8 hour exposure times, because mild irritancy generally does not vary greatly over time, and because it is not expected that prolonged exposure will result in an enhanced effect. The AGW values are supported by experimental animal data showing that repeated exposure of male rats (7 hours/day; 5 days/week; 12 weeks) to concentrations of up to 20 ppm (48 mg/m^3) did not induce any effect (clinical or after microscopic examination) apart from a reduced body weight gain.

LBW: The concentration of 200 ppm (484 mg/m^3) for 1 hour that produced no mortality in groups of 10 mice, rats and rabbits was chosen as point of departure for the LBW. Several lethality studies suggest little difference among species in response to allyl alcohol exposure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling to 10- and 30-min LBW values was performed using the concentration-time relationship given by the equation $C^n \times t = k$, using the default value n = 3. Repeated exposure of rats (7 hours/day; 5 days/week for 12 weeks) to 100 ppm (242 mg/m^3) did not result in deaths during the first few days of exposure. This indicates that time scaling to longer exposure times, using a default of n = 1 may be too conservative. Therefore, a modifying factor of 2 is applied to the 1-hour LBW to derive a 2-, 4- and 8-hour LBW of 10 ppm (24 mg/m^3) instead of the usual time scaling using the default of 1 to extrapolate to longer durations.

Additional toxicological information (including relevant results of a general literature search, if any)

Allyl alcohol is a potent sensory irritant. Signs of intoxication following inhalation exposure to allyl alcohol include lacrimation, pulmonary oedema and congestion, inflammation, haemorrhage, and degeneration of the liver and kidney. Data from a study of Li et al. (2012) shows that mortality in rats occurs at a concentration of

50 ppm (121 mg/m^3) for 8 hours. The results support the data from the study of Kirkpatrick (2008).

It is likely that to exert its toxicological effects, metabolism of allyl alcohol to the reactive metabolite acrolein is deemed necessary.

The dose response curve of allyl alcohol is steep, as can be observed in a human volunteer study, in which eye irritation was reported in one individual only at 6.25 ppm and 12.5 ppm (15.1 and 30.3 mg/m^3, resp.) and in all 5 individuals at 25 ppm (60.5 mg/m^3).

Allyl alcohol is a hepatotoxicant

No information on reproductive or developmental toxicity in animals exposed to allyl alcohol via inhalation are found. Oral exposure studies reported various results. One study showed no evidence of reproductive toxicity. Two other studies reported a decrease in pup viability index in offspring of rats exposed to 40 mg/kg/day before mating and through lactation day 3 and litter loss at a concentration of 35 mg/kg/day and 50 mg/kg/day on gestation day 9-19. Maternal toxicity was also observed at these two studies.

H331: Toxic if inhaled, H311: Toxic in contact with skin, H301: Toxic if swallowed, H319: Causes serious eye irritation, H315: Causes skin irritation, H335: May cause respiratory irritation.

Carcinogenicity and derivation of the CRP value
IARC classification: not classified No carcinogenic risk potency (CRP) was derived. It is noted that some metabolites are recognized carcinogens: IARC has classified glycidaldehyde as a possible human carcinogen (2B) and acrolein as a category 3 carcinogen (not classifiable as to carcino-genicity to humans).

Odour and derivation of the LOA value
Odour: pungent, mustard-like odour Odour threshold: 1.4 ppm or 3.4 mg/m^3 [AIHA, 1989] A LOA could not be determined due to inadequate reference data for n-butanol.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **5.0**	*AEGL-1* 0.22	*ERPG-1* -		*IDLH:* 48 (30 minutes)
AGW level **10**	*AEGL-2* 4.1	*ERPG-2* -		
LBW level **48**	*AEGL-3* 31	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 107-11-9 **Allylamine** $CH_2=CHCH_2NH_2$ **VN-nr: 2334**

GEVI: 663

Synoniemen: 2-propeen-1-amine, 2-propenylamine (Engels: allylamine) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	1,0	1,0	1,0	1,0	1,0	1,0
Alarmeringsgrenswaarden	AGW (mg/m³)	7,9	7,9	7,9	7,9	7,2	4,8
Levensbedreigende waarden	LBW (mg/m³)	1500	430	200	89	40	18

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,421 ppm; 1 ppm = 2,38 mg/m³

Explosiegrens: LEL = 2,2 vol% ≈ 52.000 mg/m³

Geur: scherpe, ammoniakachtige geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot lichtgele vloeistof

Brand: zeer brandgevaarlijk, kans op ontsteking op afstand

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,3

Molecuulmassa: 57,1 g/mol
Zuurgraad: geen data

LogKow: 0,0

Wateroplosbaarheid: volledig
Verzadigde dampdruk: 257 mbar

Overige informatie

Publieke grenswaarde:
niet afgeleid.

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	mogelijk lichte irritatie
VRW → AGW:	irritatie aan ogen, neus en luchtwegen, keelpijn, hoesten
AGW → LBW:	toenemende mate van irritatie, cardiovasculaire toxiciteit, onregelmatige ademhaling, benauwdheid, longoedeem, longbloedingen
Boven LBW:	ademnood, convulsies, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Allylamine werkt primair irriterend op de ogen, neus, huid en luchtwegen.
- Bij hogere concentraties kan allylamine effecten op het centrale zenuwstelsel en het cardiovasculaire systeem veroorzaken.
- De cardiovasculaire effecten zijn waarschijnlijk het gevolg van omzetting van allylamine in acroleine, waterstofperoxide en ammonia.
- Allylamine kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, pijn

Oogcontact: bijtend, roodheid, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen).

Ontsmetting vloeistof

huid: eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen: geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 107-11-9 **Allylamine** **$CH_2=CHCH_2NH_2$** **UN-nr: 2334**

Basis for the Dutch Intervention Values

VRW: AEGL-value is adopted, 2h value added

AGW: AEGL-value is adopted but using different uncertainty factors for 4- and 8-hour values, 2h value added

LBW: Same point of departure as for AEGL values but using different uncertainty factors and difference in time scaling, 2h value added

Date: November 2015 | AEGL document: Final, 2005

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	1.0	1.0	1.0	1.0	1.0	1.0	Eye and nose irritation in humans
AGW	7.9	7.9	7.9	7.9	7.2	4.8	Eye and nose irritation 10-min, 30-min, 60-min, 2h values; threshold for cardio-toxicity (4h and 8h values)
LBW	1500	430	200	89	40	18	Lethality in animals

Derivation of the Dutch Intervention Values

VRW: VRW values were based on a study in which 35 young adult human volunteers were exposed for 5 minutes to 2.5, 5, 10 or 14 ppm (5.9, 11.9, 23.8, or 33.3 mg/m³) allylamine, which caused dose-related increases in the incidence of slight or moderate eye irritation, nose irritation, and pulmonary discomfort, but not CNS effects. The VRW point of departure was 1.25 ppm (3.0 mg/m³), which was obtained by applying a modifying factor of 2 to the lowest effect level of 2.5 ppm (5.9 mg/m³). The modifying factor was used because exposure was for only 5 minutes and it is unclear whether "moderate" irritation and discomfort is comparable to "notable" irritation or discomfort, which exceeds the scope of the VRW. An intraspecies uncertainty factor of 3 was applied because allylamine is acting as a contact irritant, and the severity of its effects is not expected to vary greatly among humans. Also, use of a greater uncertainty factor would yield a concentration below 0.2 ppm (0.48 mg/m³), which was a no-effect level for workers exposed for up to 4 hours. The same VRW value was used for 10 minutes to 8 hours because mild sensory irritation and discomfort do not generally vary greatly with time.

AGW: AGW values for the 10-, 30-, and 60-minute and 2-hour time points were derived from the human 5-minute exposure study that was used to derive VRW values, but using 10 ppm (23.8 mg/m³) as the point of departure. Exposure to 10 ppm (23.8 mg/m³) caused slight or moderate eye and nose irritation and pulmonary discomfort and was used as threshold for "intolerable" irritation that occurred at 14 ppm (33.3 mg/m³). The same value was adopted for all time-points because the degree of irritation and discomfort was not expected to increase in time beyond the scope of AGW. An intraspecies uncertainty factor of 3 was used because allylamine is acting as a contact irritant, and the severity of its effects is not expected to vary greatly among humans.
AGW values for the 4- and 8-hour time points were derived from a rat study indicating cardiotoxicity of allylamine in rats because cardiotoxicity was considered to be a more sensitive end point for these time points. The threshold for cardiovascular lesions in this study was exposure to 40 ppm (95 mg/m³) for 16 hours; exposure to 60 ppm for 14 hours induced myofibril fragment damage, perivascular oedema and cellular infiltration. Time scaling was performed using $C^n \times t = k$ and n = 1.7, which was calculated from the rat cardiotoxicity data. An interspecies uncertainty factor of 3 was applied because the mechanism of toxicity is similar among several species. An intraspecies uncertainty factor of 10 was used because the variability of the cardiotoxic response to allylamine among humans is undefined and potentially sensitive populations exist (diabetics, persons with congestive heart failure).

LBW: The derivation of LBW values was based on lethality data from a rat study in which animals were exposed to four different concentrations for each of three time points (1, 4 and 8 hours). Rats that died had stomachs distended with air, fluid-filled lungs, alveolar haemorrhage, and pulmonary oedema. The data were analysed using the Ten Berge DoseResp software (version 2006) to calculate the value of n (0.874) and the LC_{01} value for each time point. The 10-min, 30-min, 1-, 2-, 4- and 8-hour LC_{01} values were 240, 4335, 1961, 887, 401 and 182 mg/m³, respectively. An overall uncertainty factor of 10 was applied to these LC_{01} values: 3 to account for interspecies variability and 3 for human variability (the steep dose-response (the approximate 2-fold increase in concentration caused mortality to increase from 0 to 100%) indicates that the threshold for lethality due to direct destruction of lung tissue is not likely to vary greatly among humans).

Additional toxicological information (including relevant results of a general literature search, if any)

In addition to being a severe respiratory, eye, and skin irritant, allylamine is cardiotoxic when administered at high doses orally, by inhalation, or by injection. It has been used to induce cardiac and vascular lesions in laboratory animals to model human cardiovascular disease. Allylamine cardiotoxicity is proposed to be related to its metabolism to acrolein and hydrogen peroxide in cardiac and vascular tissues. Several studies indicate that allylamine absorption through the skin can cause acute lethality. Allylamine is an irritant to the skin of experimental animals and can cause skin corrosion (necrosis).

Rats dying from exposure to allylamine had stomachs distended with air, fluid-filled lungs with haemorrhage in the alveolar spaces, and pulmonary oedema. Allylamine inhalation caused cardiotoxicity in rats in several single- and multiple exposure studies. Cardiovascular lesions were not found following inhalation exposure in species other than rats, but were induced in a variety of animal species by the oral, parenteral, and intravenous routes. In mice exposed to allylamine clinical signs, in order of appearance, were: naso-oral irritation, ear flushing, irregular respiration, cyanosis, delirium, convulsions, coma, and death.

No *in vivo* studies on the developmental or reproductive effects of allylamine or information on the developmental or reproductive effects of allylamine in humans were located.

H301: Toxic if swallowed; H311: Toxic in contact with skin; H331: Toxic if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

No studies on the carcinogenicity or genotoxicity of allylamine in humans were located (nor of its proposed metabolite, acrolein).

Odour and derivation of the LOA value

Odour: very sharp, ammonia-like odour

The calculated LOA for allylamine of 58 ppm exceeds a concentration (i.e. 14 ppm) found to be intolerable by humans. Therefore, the calculated LOA conflicts with human empirical data, as did the OT_{50}, and neither the LOA nor the OT_{50} are considered valid. Therefore, no LOA was derived due to lack of reliable data.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **1.0**	*AEGL-1* 1.00	*ERPG-1* not derived		*IDLH:* not derived
AGW level **7.9**	*AEGL-2* 7.8	*ERPG-2* not derived		
LBW level **200**	*AEGL-3* 43	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 107-05-1 **Allylchloride** **C_3H_5Cl** **VN-nr: 1100** **GEVI: 336**

Synoniemen: 3-chloorpropeen, 3-chloorpropyleen (Engels: Allyl chloride) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m³)**	8,8	8,8	8,8	8,8	8,8	8,8
Alarmeringsgrenswaarden	**AGW (mg/m³)**	6.700	1.100	330	110	33	11
Levensbedreigende waarden	**LBW (mg/m³)**	20.000*	3.200	1.000	320	100	32

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,314 ppm; 1 ppm = 3,18 mg/m³

Explosiegrens: LEL= 3,2 vol% ≈ 100.000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

Geur: scherpe, knoflook-achtige geur

LOA: 150 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,6

Molecuulmassa:	76,5 g/mol
Zuurgraad:	geen data
LogKow:	2,1
Wateroplosbaarheid:	0,36 g/100 ml (slecht)
Verzadigde dampdruk:	395 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 3,2 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen klachten

VRW → AGW: irritatie neus en luchtwegen, oogirritatie, tranenvloed, hoesten, benauwdheid, duizeligheid, hoofdpijn

AGW → LBW: benauwdheid, longoedeem, bewustzijnsdaling, lever- en nierfunctiestoornissen

Boven LBW: ademnood, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Allylchloride werkt irriterend tot bijtend op ogen, neus en luchtwegen.
- Blootstelling aan allylchloride kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Allylchloride kan schade toebrengen aan de lever, nieren en het centrale zenuwstelsel.
- Sterfte door blootstelling aan allylchloride is waarschijnlijk het gevolg van ademhalingsfalen.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn, bijtend, ernstige brandwonden. De inwerking van allychloride op de huid kan leiden tot een hevige, diepe pijn en openbaart zich soms pas na enkele uren.

Oogcontact: damp: roodheid en pijn, bijtend. Vloeistof: bijtend, corneabeschadiging, verlies van gezichtsvermogen.

Carcinogeniteit

IARC classificatie: 3

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: PAS OP: HUIDOPNAME! verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen

Neem contact op met het NVIC (Tel: +31 (0)30 - 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 107-05-1 **Allyl chloride** **C_3H_5Cl** **UN-nr: 1100**

Basis for the Dutch Intervention Values

VRW: AEGL values are adopted; 2h value added

AGW: Based on a different point of departure than used for derivation of the AEGL values

LBW: Based on a different point of departure than used for derivation of the AEGL values

Date: 16-12-2010 AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	8.8	8.8	8.8	8.8	8.8	8.8	Threshold for irritation in humans
AGW	6,700	1,100	330	110	33	11	One third of LBW
LBW	20,000*	3,200	1,000	320	100	32	Animal lethality

* value higher than 10% of LEL

Derivation of the Dutch Intervention Values

VRW: The VRW values are based on the sensory response experienced by an unknown number of unconditioned personnel during or following five minutes of exposure to allyl chloride. Exposure to 3-6 ppm (9.5-19 mg/m³) did not cause respiratory, eye, or nose irritation. Nasal irritation and pulmonary discomfort occurred between 6 and 25 ppm (19 and 80 mg/m³) in half of those tested and noticeable irritation of the sensory organs for most people occurred at concentrations ranging from 25-100 ppm (80 – 318 mg/m³). An estimate of the threshold of irritation was calculated by dividing 25 ppm (80 mg/m³) by a factor 3 to yield 8.3 ppm (26.4 mg/m³). This was point of departure for the VRW levels.
An intraspecies uncertainty factor of 3 was applied instead of the default value of 10 because allyl chloride is a direct acting irritant and it would protect sensitive populations, those experiencing noticeable irritation below 25 ppm (80 mg/m³). An uncertainty factor of 10 would result in VRW values that are lower than concentrations humans have been exposed to with no irritation or physiological changes. In two studies it was shown that humans did not report irritation after being exposed to 3-6 ppm of allyl chloride for 1-5 minutes. An occupational study found that workers exposed to 0.5-36 ppm allyl chloride for 6 months had normal liver enzyme activity levels.
An interspecies factor of 1 was applied because human data were used. The VRW value was held constant across all exposure time points. That approach was considered appropriate because mild irritant effects generally do not vary greatly over time.

AGW: Although some studies did report AGW type effects, these observations were in conflict with the lethality data used for the derivation of the LBW values. Therefore, the AGW values were derived by dividing the LBW values by 3.

In contrast to the AGW values, the AEGL-2 values were based on exposure data showing no incapacitating or irreversible effects at 300 ppm (955 mg/m³) in female rats after 6-hr exposure. At the next highest concentration, 500 ppm (1590 mg/m³), moderate eye closure and redness, lethargy, and reversible acute renal tubular degeneration were observed. An interspecies factor of 3 was used because allyl chloride is a direct acting irritant, and data from the more sensitive sex and species (female rat) were used as the point of departure. An intraspecies uncertainty factor of 3 was applied because human data suggested that allyl chloride is a direct-acting irritant and described effects similar to those seen in rats, guinea pigs, and mice. Time scaling was performed using the equation $C^n \times t = k$, using the default values of n =1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively. The 10 minute AEGL-2 value was set equal to the 30 minute AEGL-2 value. The thus derived AEGL-2 values ranged from 220 mg/m³ for 10 and 30 minutes exposure and 70 mg/m³ for 8 hours exposure. It is noted that using this point of departure and the chemical specific value of n of 0.6 (see derivation LBW values) would result in values ranging from 37,000 mg/m³ for

10 minutes exposure to 58 mg/m^3 for 8 hours of exposure. These values are higher than the derived LBW values.

LBW: The LBW values are based on a rat lethality study, where 4 or 5 rats per group were exposed to (target) concentrations ranging from 1000 to 100,000 mg/m^3 for 15 to 540 minutes. In total 28 exposure-time combinations were tested. The target concentrations were considered to be sufficiently reliable for the following reasons: a) the relatively high vapour pressure of allyl chloride, and b) similar values were reported for the target and actual concentrations in a second study , where similar techniques as applied In the key study were applied to generate the exposure. The complete dataset was analyzed using DoseResp (Wil ten Berge, 2006) to derive the animal probit function. With the probit function the LC_{01} values have been determined to obtain the LBW values for the exposure durations of interest. The derived LC_{01} values for the 10-, 30-min, and 1-, 2-, 4-, and 8-hr durations are 200,200- 32,110- 10,120- 3189- 1005- and 317 mg/m^3. The probit analysis yielded an n-value of 0.60. An interspecies factor of 3 is considered appropriate, because allyl chloride is a direct acting irritant and human data described effects similar to those seen in rats, guinea pigs, and mice. An intraspecies uncertainty factor of 3 was applied. Although data on sensitive populations are lacking for allyl chloride, as a direct-acting irritant for acute exposures, the mode of action is not expected to differ among individuals.

In contrast to the LBW values, the derivation of the AEGL-3 values was based on another (6-hr) rat lethality study, which derived a higher LC_{50} value for the 6-hr duration. The experimental concentration of 800 ppm (2500 mg/m^3) was selected as the point of departure as this was the highest concentration at which no lethality was observed. The same uncertainty factors and time-scaling approach were used as described above for the derivation of the AEGL-2 values (using default values for n). The resulting AEGL-3 values ranged from 570 mg/m^3 for 10 and 30 minute exposure and 190 mg/m^3 for 8 hours exposure.

A reason to prefer the study selected for deriving the LBW over the study selected for deriving the AEGL-3 was that the former study included a mortality range from 0 to 100% and several concentration and time combinations. In the study selected for deriving the AEGL-3, the results in rats consisted primarily of 0 and 10% mortality and one group (females) with 100% mortality. Furthermore, a second reason for not choosing the study selected for deriving the AEGL-3 was the uncertainty in the lethality response in this study caused by variable observation periods. In most exposure groups, already after 24 hours the first five animals were sacrificed, whereas the remaining animals were sacrificed after a longer observation period. Hence, it is unknown whether the sacrificed animals at 24 hours post-exposure would have lived until 168 hours post-exposure, which according to the current standards is still too short.

Additional toxicological information (including relevant results of a general literature search, if any)

The main target organs and tissues for inhalation exposure to allyl chloride are the respiratory tract and eyes. The health endpoints are irritation to the eyes and respiratory tract, but also damage to the liver and kidneys and central nervous system effects may result from allyl chloride exposure. Symptoms of high exposure are drowsiness, lacrimation, salivation, weakness, apnoea, pulmonary haemorrhage, pulmonary oedema and pneumonia. Lethality likely results from respiratory failure.

Allyl chloride does not appear to be reprotoxic.

H302: Harmful if swallowed; H312: Harmful in contact with skin; H315: Causes skin irritation; H319: Causes serious eye irritaion; H332: Harmful if inhaled; H335: May cause respiratory irritaion; H341: Suspected of causing genetic defects; H351: Suspected of causing cancer; H373: May cause damage to organs through prolonged or repeated exposure.

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to carcinogenicity to humans)

No carcinogenic risk potency (CRP) was derived.

There are no studies found addressing potential carcinogenicity of allyl chloride after inhalation exposure. There are no human carcinogenicity data.

Odour and derivation of the LOA value

Odour: Pungent garlic-like odour

OT_{50}: 9.5 mg/m^3 [Torkelson et al., 1959; AEGL]

LOA = 11.8 * OT_{50} * 1.33 = 150 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

	The LOA is higher than the VRW values, the 2-8 hr AGW values, and the 4-8 hr LBW values.

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)***				
VRW level **8.8**	*AEGL-1* 8.9	*ERPG-1* 9.5		*IDLH:* 800 (30 minutes)
AGW level **330**	*AEGL-2* 170	*ERPG-2* 130		
LBW level **1000**	*AEGL-3* 450	*ERPG-3* 950		

Stofdocument deel A

CAS-nr: 20859-73-8 **Aluminiumfosfide** **AIP** **VN-nr: 1397**

GEVI: X462

Synoniemen: - (Engels: aluminum phosphide) ***Status:*** B-stof

Interventiewaarden		10	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m³)**	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	**AGW (mg/m³)**	29	9,6	4,8	2,4	1,2	0,60
Levensbedreigende waarden	**LBW (mg/m³)**	52	17	8,7	4,3	2,2	1,1

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,414 ppm; 1 ppm = 2,41mg/m³

Explosiegrens: geen data

Kans op explosie door vorming van fosfine met vocht uit de lucht.

Geur: geen informatie

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: donkergrijze of donkergele kristallen

Brand: Niet brandbaar. Echter, kan spontaan ontbranden door vorming van fosfine met vocht uit lucht.

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa: 58,0 g/mol
Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: reactie
Verzadigde dampdruk: geen data

Overige informatie

Publieke grenswaarde:
niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

(gebaseerd op vrijkomen fosfine)

*Onder **AGW***: irritatie aan ogen, huid, neus en luchtwegen, hoofdpijn, misselijkheid, braken, zwakte, paresthesie, duizeligheid, tremor

AGW → LBW: benauwdheid, longoedeem, bewustzijnsdaling, hartritmestoornissen, nier- en leverfunctiestoornissen

Boven LBW: convulsies, cardiovasculaire collaps, myocardinfarct, ademnood, coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Aluminiumfosfide kan bij contact met vocht uit de lucht of luchtwegen omgezet worden in fosfine. De toxiciteit van aluminiumfosfide wordt bepaald door de vorming van fosfine.
- Fosfine verstoort door effecten op de celademhaling de zuurstofopname en energievoorziening van de cel.
- Fosfine werkt irriterend op de ogen, huid en luchtwegen.
- Hoge blootstelling kan tot longoedeem leiden. Dit kan pas na enkele uren optreden en wordt versterkt door lichamelijke inspanning.
- Kinderen zijn mogelijk gevoeliger voor toxiciteit door fosfine.

Effecten bij blootstelling aan vaste stof

Huidcontact: roodheid
Oogcontact: roodheid, pijn

Carcinogeniteit

IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
ogen: spoelen met water (evt. contactlenzen verwijderen).

Ontsmetting vaste stof

huid: verontreinigde kleding uittrekken, afspoelen met water.
ogen: spoelen met water (evt. contactlenzen verwijderen).
inslikken: mond laten spoelen (uitspugen!), rust, GEEN mond-op-mondbeademing, actieve kool (carbomix) toedienen, en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 20859-73-8 **Aluminum phosphide** **AIP** **UN-nr: 1397**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 24-09-2009 AEGL document: Final 2008

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	(insufficient data)
AGW	29	9.6	4.8	2.4	1.2	0.60	Irritation nasal mucosa rats (phosphine)
LBW	52	17	8.7	4.3	2.2	1.1	Lethality rats (phosphine)

Derivation of the Dutch Intervention Values

VRW: No data are available for aluminum phosphide. As toxicity of aluminum phosphide is due to phosphine, which is formed due to reaction of aluminum phosphide with moisture, data on phosphine could be used to derive intervention values. However, no appropriate data were available for derivation of VRW values for phosphine. Therefore VRW values are not recommended. This does not imply that exposure below AGW is without adverse effects.

AGW: Since no appropriate data exist for aluminum phosphide, AGW values for phosphine will be used (on ppm-basis) to derive AGW values for aluminum phosphide. The use of phosphine as a surrogate for aluminum phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because one mole of phosphine is produced for every mole of aluminum phosphide, no molar adjustment factor was needed.

Derivation of AGW values for phosphine

The phosphine AGW values were based on red mucoid nasal discharge in rats exposed to 10 ppm (14 mg/m3) phosphine for 6 hours, corresponding to 24.1 mg/m^3 aluminum phosphide. Since this endpoint is less severe than effects defined by AGW, the resulting values should be protective.
The default uncertainty factor of 3 was applied to account for interspecies variability. An uncertainty factor of 10 was applied to account for intraspecies variability since the human data suggest that children may be more sensitive than adults when exposed to presumably similar phosphine concentrations. For example, in two reports, exposed children died, but exposed adults survived. Time scaling was performed using the equation $C^n \times t = k$, and an n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine).

LBW: Since no appropriate data exist for aluminum phosphide, LBW values for phosphine will be used (on ppm-basis) to derive LBW values for aluminum phosphide. The use of phosphine as a surrogate for aluminum phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because one mole of phosphine is produced for every mole of aluminum phosphide, no molar adjustment factor was needed.

Derivation of LBW values for phosphine

The highest concentration yielding no deaths in rats (18 ppm = 25 mg/m^3) for 6 hours was used as point of departure for the calculation of the LBW values, corresponding to 43.38 mg/m^3 aluminum phosphide. The default uncertainty factor of 3 for interspecies and an intraspecies factor of 10 were applied for reasons provided above. Time scaling was performed using the equation $C^n \times t = k$ and a chemical specific n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine). These values are considered protective since workers were repeatedly exposed for “brief” periods of time to phosphine concentrations up to 35 ppm (49 mg/m^3) with no life-threatening effects and workers exposed to >50 ppm (>70 mg/m^3) for 2-5 minutes experienced only odour.

Additional toxicological information (including relevant results of a general literature search, if any)

When aluminum phosphide reacts with moisture, phosphine gas will be formed. Phosphine is considered to induce acute toxic effects following oral and inhalation exposure. Children are thought to be more vulnerable to phosphine exposure. Common clinical signs after exposure to phosphine are headache, vomiting, coughing, shortness of breath, paresthesia, weakness, tremors and jaundice. Pulmonary congestion, pleural effusion, and congestive heart failure may be observed upon post-mortem examination.

In vitro, phosphine reacts with cytochrome c and cytochrome c oxidase, thereby inhibiting mitochondrial oxygen uptake. In vitro studies have also shown that phosphine can react with the heme moiety of hemoglobin in the presence of oxygen. Cell death and loss of cell membrane integrity accounted for the increased liver enzymes, bronchiolytic effects, cloudy swelling of renal tubular epithelia, and hemorrhagic myocardial lesions.

No reproductive or developmental data were found.

H300: Fatal if swallowed; H311:Toxic in contact with skin; H330: Fatal if inhaled

Carcinogenicity and derivation of the CRP value

IARC classification: not evaluated.

No carcinogenic risk potency (CRP) was derived.

No data concerning carcinogenicity of aluminum phosphide are available.

Fumigation workers exposed long-term to phosphine have a higher incidence of both stable and less stable chromosomal aberrations. Molecular analysis of these lesions suggests that the breakpoints are near proto-oncogenes involved in non-Hodgkin's lymphoma, possibly contributing to the increased incidence of lymphomas in pesticide workers.

Odour and derivation of the LOA value

Odour: no information.

Pure phosphine is odourless at concentrations up to 200 ppm. Technical-grade phosphine has a garlic-like odour (may be due to impurities).

For phosphine, no LOA was derived due to lack of reliable data. Ruth (1986) reported an odour range of 0.028-3.6 mg/m^3 for phosphine.

Other standards and guidelines *(1h values in mg/m^3, unless otherwise indicated)*

VRW level **NR**	*AEGL-1* NR	*ERPG-1* not derived		*IDLH:* not derived
AGW level **4.8**	*AEGL-2* 4.7	*ERPG-2* not derived		
LBW level **8.7**	*AEGL-3* 8.5	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 7664-41-7 **Ammoniak** NH_3 **VN-nr: 1005** **GEVI: 268**

Synoniemen: ammoniak watervrij (Engels: ammonia) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	21	21	21	21	21	21
Alarmeringsgrenswaarden	AGW (mg/m³)	200	200	140	99	99	99
Levensbedreigende waarden	LBW (mg/m³)	1900	1100	780	550	390	280

Datum vaststelling: 13-05-2009

Conversiefactor: 1 mg/m³ = 1,41 ppm; 1 ppm = 0,707 mg/m³

Explosiegrens: LEL = 15 vol% ≈ 110.000 mg/m³

Geur: stekend, intens irriterend

LOA: 1,7 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas

Brand: kan brandbaar damp/lucht mengsel vormen

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa: 17,0 g/mol

Zuurgraad: 11,6

LogKow: 0,23

Wateroplosbaarheid: 52 g/100 ml (goed)

Verzadigde dampdruk: 8600 mbar (20 °C)

Overige informatie

Publieke grenswaarde: 14 mg/m³ (8 uur)

MAK: 14 mg/m³

TLV-TWA: 18 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: mogelijk lichte irritatie

VRW → AGW: irritatie ogen, keel en neus, hoesten, hyperventilatie

AGW → LBW: glottisoedeem, benauwdheid, longoedeem

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Ammoniak kan een type I inhalatoire intoxicatie veroorzaken.
- Contact met vocht leidt tot vorming van ammonium hydroxide (corrosief) en warmteproductie.
- Na inademing van hoge concentraties kan glottisoedeem en longoedeem ontstaan, waarbij de verschijnselen pas na enkele uren kunnen optreden en worden versterkt door lichamelijk inspanning.
- Blootstelling aan hoge concentraties kan overlijden veroorzaken.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, pijn, blaren, wonden (vanwege bevriezing)

Oogcontact: irritatie, tranenvloed, cornea-beschadiging, verlies gezichtsvermogen, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: aan de huid vastgevroren kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen, arts raadplegen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas)

Specifieke behandeling en materialen:.

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 7664-41-7 **Ammonia** **NH_3** **UN-nr: 1005**

Basis for the Dutch Intervention Values

VRW: AEGL Values are adopted, 2h value added

AGW: Different point of departure as for AEGL, 2h value added

LBW: AEGL Values are adopted, 2h value added

Date: 13-05-2009 | AEGL document: Final, 2006

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	21	21	21	21	21	21	Faint or no irritation in humans
AGW	200	200	140	99	99	99	Irritation eyes, nose, throat
LBW	1900	1100	780	550	390	280	Lethality

Derivation of the Dutch Intervention Values

VRW: Humans experience either faint or no irritation after exposure to ammonia at 30 ppm (21 mg/m^3) for 10 minutes. Therefore, 30 ppm (21 mg/m^3) was used to derive VRW values. An interspecies uncertainty factor was not applied to these data because the VRW is based on human data. An intraspecies uncertainty factor of 1 was selected because ammonia is efficiently scrubbed in the upper respiratory tract, and if irritation occurs, it would be confined to the nasal cavity (and possibly the eyes). Nonatopic and atopic subjects, including asthmatics, responded similarly in a nasal airway resistance test when volunteers were exposed head-only to 100 ppm (71 mg/m^3) of ammonia for up to 30 seconds; therefore, asthmatic individuals are not expected to respond differently from non-asthmatic individuals. No time-scaling was applied, because any effects that occur are not expected to become more severe with duration of exposure because adaptation occurs during prolonged exposure. This is supported by observations that humans reported similar intensity of response after exposure to 50 ppm (35 mg/m^3) for 10 minutes to 2 hours.

AGW: The AGW values were based on a human volunteer study with 8 non-expert individuals (unfamiliar with effects of ammonia or laboratory studies) and 8 expert individuals (familiar with the effects of ammonia) exposed to 50, 80, 110 and 140 ppm (35, 57, 78, 99 mg/m^3) ammonia for up to 2 hours. Exposure to 140 ppm (99 mg/m^3) for 2 hours was used as point of departure for deriving the AGW values. The expert individuals perceived no general discomfort after the highest exposure for 2 hours. Four out of 8 non-expert individuals exposed to 140 ppm (99 mg/m^3) perceived their general discomfort to range from “distinctly perceptible” to “unbearable” after 1 h.
An interspecies uncertainty factor is not applied to these data because the intervention values are based on human data. An intraspecies uncertainty factor of 1 was selected because ammonia is a contact irritant, it is efficiently scrubbed in the upper respiratory tract, and any perceived irritation is not expected to be greater than that of the most sensitive non-expert subject. The range of responses for this group is considered comparable to the range of responses that would be encountered in the population including asthmatics. The value of 140 ppm (99 mg/m^3) was adopted as the 4- and 8-hour values, because the maximum severity rating for irritation in one study in humans changed very little between 30 minutes and 2 hours and is not expected to change for exposures up to 8 hours. Time scaling to 30 minutes and 1 hour was performed using the equation $C^n \times t = k$, using an n-value of 2 (based on rat lethality data for ammonia). The 30-minute value was also adopted as the 10-min AGW value because time scaling would yield a 10-minute value that might impair escape. The intervention values are supported by other studies showing that exposures up to 100 ppm (71 mg/m3) were tolerated by human subjects for 2 to 6 hours without causing serious effects. The data of two additional human studies showed no serious irreversible effects after exposure to 336 or 500 ppm (248 or 350 mg/m^3), respectively.

LBW: The LC_{01} values for lethality after 1 hour exposure of 3317 and 3374 ppm (2346 and 2386 mg/m^3) derived from two different studies in mice were used as point of departure for the LBW values. The mouse is unusually sensitive to exposure to respiratory irritants, including ammonia; therefore, an interspecies uncertainty factor of 1 was applied. The default uncertainty factor of 3 was applied to account for intraspecies variability. Applying a total uncertainty factor of 3 to the 1 hour LC_{01} values

of 3317 or 3374 ppm (2346 or 2386 mg/m^3) results in a 1 hour LBW value of 1100 ppm (778 mg/m^3). This value was scaled across time using the equation $C^n \times t = k$, using an n-value of 2 (based on rat lethality data for ammonia).
The LBW value for 8 hours is supported by studies in rats, rabbits, guinea pigs, dogs, and monkeys showing that daily 8-hour exposures to 1101 ppm (779 mg/m^3) for 6 weeks caused no deaths. The only effects observed were nonspecific inflammation (rats and guinea pigs), lacrimation (dogs and rabbits), and dyspnea (dogs and rabbits).

Additional toxicological information (including relevant results of a general literature search, if any)

Tracheobronchial and pulmonary effects may occur at a lower concentration in elderly people.

Death in humans exposed to ammonia is associated with damage to the lower respiratory tract. Scientific data show that effects caused by ammonia on the lower respiratory tract would be lethal without prompt medical attention. Therefore, concentrations of ammonia that exceed the scrubbing capacity of the upper respiratory tract and cause coughing, which indicate lower respiratory effects, have potentially serious effects. (AHLS, 2006)

Ammonia produces effects immediately upon contact with moist mucous membranes of the eyes, mouth, and respiratory tract via the formation of ammonium hydroxide (a corrosive alkali) or the production of heat. Because of its irritant properties, individuals coming into contact with ammonia vapor (or gas) will try to escape as quickly as possible.

No reproductive or developmental data are available.

H331: Toxic if inhaled; H314: Causes severe skin burns and eye damage.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: Sharp and intensely irritating.

Odour threshold: 0.106 mg/m^3
[RIVM report 609200001]

LOA = 11.8 * OT_{50} * 1.33 = 1.7 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is lower than the VRW values. The odour threshold for ammonia is lower than its irritancy effect and serves as a warning of its presence.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **21**	*AEGL-1* 21	*ERPG-1* 18		*IDLH:* 210 (30 minutes)
AGW level **140**	*AEGL-2* 110	*ERPG-2* 110		
LBW level **780**	*AEGL-3* 780	*ERPG-3* 530		

Stofdocument deel A

CAS-nr: 62-53-3 **Aniline** $C_6H_5NH_2$ **VN-nr: 1547**

GEVI: 60

Synoniemen: aminobenzeen, benzeenamine, fenylamine (Eng.: Aniline) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	190	62	31	15	7,7	3,9
Alarmeringsgrenswaarden	AGW (mg/m³)	280	93	46	23	12	5,8
Levensbedreigende waarden	LBW (mg/m³)	460	150	77	39	19	9,7
Datum vaststelling: 28-11-2008			Conversiefactor: 1 mg/m³ = 0,258 ppm; 1 ppm = 3,87 mg/m³				

Explosiegrens: LEL = 1,3 vol% ≈ 50.000 mg/m³

Geur: typerende geur, aromatisch amino-achtige stekende geur.

LOA: 36 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos olieachtige vloeistof, wordt bruin aan de lucht

Brand: brandbaar

Relatieve dichtheid bij 20°C van verzadigd damp/luchtmengsel: 1,0

Molecuulmassa:	93,1 g/mol
Zuurgraad:	Geen data
LogKow:	0,9
Wateroplosbaarheid:	3,4 g/100ml (matig oplos-baar)
Verzadigde dampdruk:	0,4 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: 7,8 mg/m³

TLV-TWA: 7,8 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: hoofdpijn, duizeligheid

AGW → LBW: effecten mogelijk gerelateerd aan zuurstof tekort (hoofdpijn, zwakte, duizeligheid, cyanose, ataxie, slaperigheid, ademnood en tachycardie)

Boven LBW: coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Aniline veroorzaakt methemoglobinemie en de daarmee samenhangende symptomen van zuurstof tekort: hoofdpijn, zwakte, duizeligheid, cyanose, ataxie, ademnood en tachycardie.
- Zwangere vrouwen lopen extra risico i.v.m. foetale methemoglobinemie.
- Bij hoge concentraties kunnen schade aan lever, nieren en perifeer zenuwstelsel ontstaan.
- De stof is sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact.

Effecten bij blootstelling aan vloeistof

Huidcontact: prikkeling, hoofdpijn, misselijkheid, braken, blauwe lippen of nagels, blauwe huid, duizeligheid

Oogcontact: roodheid en pijn, permanente oogbeschadiging mogelijk bij extreme blootstelling

Carcinogeniteit

IARC classificatie: 3

CRP: 13.797 mg/m³ (blootstelling 1 uur)

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, en direct arts raadplegen.

ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en direct arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar (oog)arts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen: 100% zuurstof, specifieke antidota zoals o.a. methyleen– of toluïdineblauw

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 62-53-3 **Aniline** **$C_6H_5NH_2$** **UN-nr: 1547**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added.

AGW: AEGL value is adopted, 2h value added.

LBW: AEGL value is adopted, 2h value added.

Date:28-11-2008 | AEGL document, Final 2000 +update 2007

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	190	62	31	15	7.7	3.9	Increased methaemoglobin levels (20%)
AGW	280	93	46	23	12	5.8	Increased methaemoglobin levels (40%)
LBW	460	150	77	39	19	9.7	Increased methaemoglobin levels (80%)

Derivation of the Dutch Intervention Values

VRW: The concentration of 100 ppm (390 mg/m^3) for 8 h in a study with rats was used as the basis for the VRW. This exposure resulted in a methaemoglobin level of 22% but no hypoxic signs in rats. A review of the literature revealed that methaemoglobin levels of 15-20% in humans results in clinical cyanosis, but no sign of clinical hypoxia. Although inhalation data for comparison purposes are not available, oral ingestion data suggest that humans may be considerably more sensitive to methaemoglobin-forming chemicals than rats. An uncertainty factor of 10 was used for interspecies extrapolation. An intraspecies uncertainty factor of 10 was applied to account for the difference in sensitivity between humans. The overall uncertainty factor of 100 is considered sufficient to also protect infants who are more susceptible than adults. The data were scaled across time using $C^n \times t = k$ with n=1 because rat data showed that the relationship between concentration of aniline and methaemoglobin formation at a fixed time (8 h) is linear. Although an n value of 1 is not the most conservative when scaling to shorter time periods, it is believed that the total uncertainty factor of 100 is protective of human health. In contrast to the AEGL-1, time-scaling was also applied to derive the 10-minute VRW value.

AGW: An 8-h exposure at 150 ppm (580 mg/m^3) to rats resulted in elevation of methaemoglobin to 41% with no reported clinical signs. A review of the literature revealed that methaemoglobin levels of 30-45% in humans are associated with fatigue, lethargy, exertional dyspnoea, and headache. These signs or symptoms were considered the threshold for disabling effects. The 8-h exposure at 150 ppm (580 mg/m^3) was chosen as the basis for the AGW calculations. An overall uncertainty factor of 100 was used for both inter- and intraspecies extrapolation (see VRW). Based on the linear relationship between methaemoglobin formation and aniline concentration, the data were scaled to the relevant time periods using the relationship $C^n \times t = k$ and n=1. In contrast to the AEGL-2, time-scaling was also applied to derive the 10-minute AGW-value.

LBW: The LBW is based on methaemoglobin concentrations expected to represent a threshold for lethality in humans rather than on animal mortality data. Methaemoglobin levels were measured in rats exposed for 8 hours to concentrations of up to 150 ppm (580 mg/m^3) that resulted in a methaemoglobin level of 41%. Based on linear extrapolation of these data a methaemoglobin level between 70% and 80% was associated with an 8-hour exposure to an aniline concentration of 250 ppm (970 mg/m^3) which was chosen as the POD for the LBW. An overall uncertainty factor of 100 was used covering both for inter- and intraspecies extrapolation (see VRW). Time scaling was performed using $C^n \times t = k$ with n=1 because of the linear relationship between methaemoglobin formation and aniline concentration. In contrast to the AEGL-3, time-scaling was also applied to derive the 10-minute LBW-value.

The 1-h LBW value of 77 mg/m^3 (20 ppm) is considered safe for sensitive individuals. Human data reported that a concentration of 100 to 160 ppm (390-620 mg/m^3) was the maximum concentration that could be inhaled for 1 hour without serious disturbance, without correction for intraspecies differences. The 4-hour LBW of 19 mg/m^3 (5.0 ppm) is supported by a 4-hour rat lethality study with no deaths observed at exposure to 360 ppm (1400 mg/m^3) in combination with an overall uncertainty factor of 100.

Additional toxicological information (including relevant results of a general literature search, if any)

The formation of methaemoglobin and associated hypoxia, after exposure to aniline is responsible for the health effects such as headaches, dizziness, shortness of breath, cyanosis, ataxia, and death.

Oral exposure data in rats and humans show that humans may be more sensitive to methaemoglobin formation than rats are. Oral administration of aniline at 40 mg/kg to rats produced a maximum increase of 16.6% in methaemoglobin, whereas oral administration of aniline at 0.9 mg/kg to a human volunteer produced a maximum increase of 16.1%.

Differences in sensitivity to aniline among human subpopulations are known to occur, but the extent of the differences in the general population (excluding rare inherited disorders) is unknown. Infants are more sensitive to methaemoglobin-generating chemicals than adults as they have reduced levels of nicotine adenine dinucleotide (NADH, the cofactor (electron donor) for methaemoglobin reductase) and a high concentration of foetal hemoglobin in their erythrocytes (foetal haemoglobin is more oxidizable than adult haemoglobin). The foetus may be more susceptible to formation of methaemoglobin after aniline exposure. Therefore, the substance may be a developmental toxicant. Logically, pregnant women are considered a vulnerable group during accidents with this substance.

H301: Toxic if swallowed, H311: Toxic in contact with skin, H331: Toxic if inhaled, H317: May cause an allergic skin reaction, H318: Causes serious eye damage, H341: Suspected of causing genetic defects, H351: Suspected of causing cancer, H372: Ccauses damage to organs through prolonged or repeated exposure

Carcinogenicity and derivation of the CRP value

IARC classification: 3

Derivation of the carcinogenic risk potency (CRP):

10^{-4} risk level after inhalation: 6.3 *10^{-2} mg/m^3 [CIIT, 1982]

CRP = (10^{-4} risk level * average life span in hours)/DRCF

= (6.3 *10^{-2} * 613.200) /2.8 = 13,797 mg/m^3

Based on the chronic oral administration of aniline hydrochloride to CD-F rats where spleen tumors were observed.

Odour and derivation of the LOA value

Odour: Typical and pungent odour.

OT_{50}: 2.25 mg/m^3 [Van Doorn and Ruijten, 2002]
LOA = 36.1 mg/m^3

Aniline odour can be detected at the 30 min VRW level, as well as the 30 min and 1hr AGW levels and 30 min to 2 hr LBW levels. During relatively long exposures at relatively low concentrations (significant) adverse health effects may occur without odor detection.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **31**	*AEGL-1* 30	*ERPG-1* NR		*IDLH:* 390 (30 min)
AGW level **46**	*AEGL-2* 46	*ERPG-2* NR		
LBW level **77**	*AEGL-3* 76	*ERPG-3* NR		

Stofdocument deel A

CAS-nr: 7784-42-1 **Arsine** AsH_3 **VN-nr: 2188**

GEVI: geen

Synoniemen: arseenwaterstof, hydrogeenarsenide, waterstofarsenide (Engels: arsine) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	7,2	2,9	1,6	0,91	0,51	0,29
Levensbedreigende waarden	LBW (mg/m³)	22	8,7	4,9	2,7	1,5	0,86

Datum vaststelling: 13-05-2009

Conversiefactor: 1 mg/m³ = 0,309 ppm; 1 ppm = 3,24 mg/m³

Explosiegrens: LEL = 3,9 vol% ≈ 130.000 mg/m³

Geur: knoflookachtige geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloos gas

Brand: Zeer brandgevaarlijk. Kans op ontsteking op afstand

Relatieve dichtheid gas: 2,7

Molecuulmassa:	77,9 g/mol
Zuurgraad:	geen data
LogKow:	geen data
Wateroplosbaarheid:	0,07 g/100 ml (niet)
Verzadigde dampdruk:	10300 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 0,16 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***	geen informatie
AGW → LBW:	buikpijn, misselijkheid, spierpijn, hoofdpijn, duizeligheid, zwaktegevoel, bewustzijnsdaling, hemolyse, nierfunctiestoornissen
Boven LBW:	coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Arsine kan hemolyse veroorzaken; hemolytische effecten kunnen progressief zijn en enkele dagen na blootstelling aanhouden.
- Secundair aan hemolyse kan nierschade en uiteindelijk nierfalen ontstaan.
- Effecten kunnen vertraagd optreden.
- **Let op:** steile concentratie-respons curve

Klachten bij blootstelling aan vloeistof

Huidcontact: bevriezing door snel verdampen, pijn, roodheid, brandwonden.

Oogcontact: bevriezing door snel verdampen, pijn, roodheid, slecht zien.

Carcinogeniteit

IARC classificatie: 1 (arseen en arseenverbindingen)

CRP: niet afgeleid. (geen informatie beschikbaar over carcinogeniteit van arsine)

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust, halfzittende houding, specifieke behandeling en direct spoedeisende medische hulp inzetten.

ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen).

Ontsmetting vloeistof

huid: n.v.t. (gas), *maar in geval van bevriezingswonden*: aan de huid vastgevroren kleding NIET lostrekken, spoelen met veel water / kleding verwijderen en onmiddellijk arts raadplegen.

ogen: n.v.t. (gas), maar in geval van bevriezingswonden: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen. Blijven spoelen tijdens vervoer.

inslikken: n.v.t.

***Specifieke behandeling en materialen**:* Bij vergiftiging door deze stof is specifieke eerste hulp noodzakelijk.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7784-42-1 **Arsine** **AsH_3** **UN-nr: 2188**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: Same point of departure as for AEGL value but using different uncertainty factors and value for n, 2h value added

LBW: Same point of departure as for AEGL value but using different uncertainty factors and value for n, 2h value added

Date: 13-05-2009 | AEGL document: Final, 2000

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	-
AGW	7.2	2.9	1.6	0.91	0.51	0.29	Threshold of haemolytic effects in animals
LBW	22	8.7	4.9	2.7	1.5	0.86	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: Because of the extreme toxicity of arsine and the steep dose-response indicated by the available data, the derivation of VRW values for arsine was considered inappropriate. The available human and animal toxicity data indicate that there is little margin between exposures that produce little or no toxicity and those that result in lethality and, therefore, do not justify the derivation of a safe exposure level that meets the VRW definition. This is further supported by reports of toxicity in humans and animals at concentrations similar to or below odor detection levels (0.5-1ppm; 1.6-3.2 mg/m³) and where haemolysis, the mechanism of toxicity, may rapidly progress to renal failure. The decision also was based on the known toxicity of arsine, the latency in development and expression of toxicity even after removal from exposure, and the possible progression of haemolysis to life-threatening renal failure. The continuum of arsine-induced toxicity does not appear to include effects consistent with the VRW definition.

AGW: The 1-h no-observed-effect level (NOEL) of 5 ppm (16 mg/m³) for reversible alterations in hematologic parameters in mice exposed to arsine was used to derive the AGW values. Mice exposed to arsine concentration of 11 ppm (36 mg/m³) or higher showed a decreased haematocrit and erythrocyte number. Lethality was observed in mice exposed to 26 ppm (84 mg/m³). The use of what might appear to be a conservative NOEL in the derivation of AGW values is justified by the documented latency in the expression of severe toxicity in humans even after removal from exposure and the potential for haemolysis to rapidly progress to life-threatening renal failure. Furthermore, the choice of the LOAEL for haematological changes to derive the AGW values from would result in values that are less than 2-fold smaller than the LBW values. Considering the steep exposure-response curve (exposure to 26 ppm (84 mg/m³) resulted in 100% lethality, whereas exposure to 15 ppm (49 mg/m³) only resulted in severe but reversible haematologic changes) this was not considered appropriate. An uncertainty factor of 10 was applied to account for interspecies extrapolation (3) and intraspecies variability (3). As mice appeared to be the most sensitive species, an interspecies uncertainty factor of 3 was considered sufficient. Time-scaling was performed using and n-value of 1.2 using the $C^n \times t = k$ equation. The n-value of 1.2 was based on rat lethality data.

LBW: The most definitive data set for deriving LBW values provides exposure response data for mice exposed to arsine for 1 h at concentrations of 0, 5, 9, 11, 15, 26 ppm (0, 16, 29, 36, 49, or 84 mg/m³). Although the 26 ppm (84 mg/m³) exposure resulted in 100% mortality within 4 d post-exposure, the 15 ppm (49 mg/m³) exposure produced significant, haematologic changes. Therefore, these data affirm the steep exposure-response curve for arsine and provide a basis for a lethality threshold. Due to the steep concentration-response curve for arsine, the 15 ppm (49 mg/m³) exposure (where there was no lethality) was considered an estimate of the lethality threshold. An uncertainty factor of 10 was applied to account for interspecies extrapolation (3) and intraspecies variability (3). As mice appeared to be the most sensitive species, an interspecies uncertainty factor of 3 was considered sufficient. Time-scaling was performed using an n-value of 1.2 using the $C^n \times t = k$ equation. The n-value of 1.2 was based on rat lethality data.

Additional toxicological information (including relevant results of a general literature search, if any)

Exposure to arsine causes intravascular haemolysis resulting in anemia and acute oliguric renal failure, which can be lethal. However, the underlying mechanism by which arsine causes these effects is not fully understood.

Case reports are available regarding lethal effects of acute exposure to arsine in humans. However, no definitive quantitative exposure data accompany these reports. Signs and symptoms varied depending on the exposure situation but usually included abdominal and muscle pain, nausea and diarrhea, haematuria, and oliguria. There may be a 1- to 24-h delay between exposure and onset of signs and symptoms of poisoning. Haematologic parameters appear to be progressively affected for several days after the exposure. Delayed lethality, common in arsine poisoning, varied considerably. Studies in experimental animals show a steep dose-response curve for arsine.

No definitive, quantitative data were available regarding the potential reproductive and developmental toxicity of arsine in humans. From a study in rats it was concluded that there were no significant arsine-related development effects in the presence of mild maternal toxicity.

H330: Fatal if inhaled; H373: May cause damage to organs.

Carcinogenicity and derivation of the CRP value

IARC classification: 1 (carcinogenic to human) (arsenic and arsenic compounds)

No carcinogenic risk potency (CRP) was derived.

Some forms of inorganic arsenics are considered human carcinogens. However, there are no data available regarding the carcinogenic potential of arsine or its conversion to carcinogenic forms. The extreme acute toxicity of the gas precludes the relevance of carcinogenic potential after acute exposure.

Odour and derivation of the LOA value

Odour: garlic-like odour

No LOA was derived due to lack of reliable data.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **NR**	*AEGL-1* NR	*ERPG-1* NR	*IDLH:* not derived
AGW level **1.6**	*AEGL-2* 0.5	*ERPG-2* 1.6	
LBW level **4.9**	*AEGL-3* 1.6	*ERPG-3* 4.9	

Stofdocument deel A

CAS-nr: 64-19-7 **Azijnzuur** **CH_3-COOH** **VN-nr: 2789**

GEVI: 83

Synoniemen: Ethaanzuur, ijsazijn, methaancarbonzuur (Engels: acetic acid) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	25	25	25	25	25	25
Alarmeringsgrenswaarden	AGW (mg/m³)	410	290	230	180	140	94
Levensbedreigende waarden	LBW (mg/m³)	2500	1700	1400	1100	870	430

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,399 ppm; 1 ppm =2,50 mg/m³

Explosiegrens: LEL = 4,0 vol% ≈ 100 000 mg/m³
(boven 39°C damp met lucht explosief)

Geur: stekende geur

LOA: 2,0 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,02

Molecuulmassa: 60,1 g/mol

Zuurgraad: 2,4 bij 6 g/100ml
LogKow: -0,20
Wateroplosbaarheid: volledig
Verzadigde dampdruk: 16 mbar

Overige informatie

Publieke grenswaarde:
25 mg/m³
MAK: 25 mg/m³
TLV-TWA: 25 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	lichte neusirritatie
VRW → AGW:	irritatie slijmvliezen, pijn achter borstbeen
AGW → LBW:	bijtend, keelpijn en hoesten, tranen, branderig gevoel, benauwdheid
Boven LBW:	larynx- en glottisoedeem, ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Azijnzuur werkt irriterend tot bijtend op de ogen, de huid en de luchtwegen.
- Blootstelling aan azijnzuur kan longontsteking, longoedeem en een astmatische reactie veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- In ernstige gevallen kans op verstikking door zwellingen in de keel.
- Personen met astma en allergische rhinitis zijn mogelijk gevoeliger voor de effecten van azijnzuur.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, ernstige brandwonden

Oogcontact: bijtend, roodheid en pijn, hoornvliesbeschadiging; ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding, direct spoedeisende medische hulp inzetten
Ontsmetting vloeistof
huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, spoelen met veel water / kleding verwijderen, direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*
Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 64-19-7 **Acetic Acid** **CH_3-COOH** **UN-nr.: 2789**

Basis for the Dutch Intervention Values

VRW: Based on additional information to that described in ERPG-document, other time-points added

AGW: Based on the information as described in the ERPG-document, but different values are derived, other time-points added

LBW: Based on formic acid values, other time-points added

Date: 31-10-2017 | ERPG, 2011

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	25	25	25	25	25	25	Nasal irritation in human volunteers
AGW	410	290	230	180	140	94	Olfactory epithelium degeneration in mice
LBW	2500	1700	1400	1100	870	430	Analogy with formic acid; threshold for mortality in animals

Derivation of the Dutch Intervention Values

VRW: The VRW is based on a human study evaluating the acute irritation during controlled exposure to acetic acid vapor (See additional information for further details). Twelve healthy volunteers (6 women and 6 men) were exposed for two hours to acetic acid in a 20 m^3 dynamic exposure chamber to average concentrations of 5.1 ppm (12.8 mg/m^3) and 10 ppm (25 mg/m^3). No effects were reported at 12.8 mg/m^3. Symptoms were rated at 3, 60 and 118 minutes. No change in rating was observed during the exposure period. At 25 mg/m^3, marginal ratings for nasal irritation (discomfort in the nose: burning, irritated, or runny nose) were reported. For the VRW derivation 25 mg/m^3 was selected as point of departure. Since the effects observed were only marginal. No further uncertainty factor was considered necessary. Time scaling was not applied as the study results indicate that the effects are not time-dependent.

AGW: The AGW is based on a study with male mice exposed to acetic acid for 6 hours to 500 ppm (1250 mg/m^3) acetic acid and 2-day recovery period. Results showed that 2 out the 3 mice had very slight degeneration of the olfactory epithelium. These effects consisted of a flattening of the sustentacular cells, loss of mature neurons and an increase in the number of basal cell in the most anterior portions of the olfactory epithelium. The third mouse had a more severe lesion of the olfactory epithelium, described as slight degeneration of the olfactory epithelium. Another group of 4 mice was exposed 6 hours per day to 1250 mg/m^3 for 5 consecutive days or 563 mg/m^3 for 9 days. One mouse showed very slight degeneration of the olfactory epithelium and the remaining three mice showed slight degeneration. No lesions in the lacrimal glands were reported in both groups. For the AGW derivation, 1250 mg/m^3, was selected as PoD. Application of an uncertainty factor of 10 (3x3) would provide an AGW value of 130 mg/m^3 (50 ppm). Workers appear to be able to perform their jobs at this concentration but do experience a burning sensation in their eyes and respiratory tract. Time scaling was applied using the equation Cn × t = k with the default values of n = 1 and n = 3 when extrapolating to longer and shorter time points, respectively.

LBW: The LBW is based on data from formic acid because no adequate data for acetic acid was found that could serve as PoD for the LBW. In the ERPG document on formic acid, it is stated in the rationale for ERPG-3 that “The types of effects and the lethal concentrations in rats appear to be similar to that of acetic acid.” The ERPG-3 values for acetic acid and formic acid expressed as ppm are similar. The same reasoning is applied for the intervention values and the LBW values for acetic acid are set to similar values (expressed as ppm) as for formic acid.

Rationale for LBW values for formic acid

The key study for acute inhalation toxicity as described in the publically available REACH registration dossier on ECHAs website was used as PoD for derivation of LBW values. In this study Sprague-Dawley rats, 10 per sex/concentration, were exposed to analytical formic acid concentrations of 3380, 7290, 8370, 11100, 14700 mg/m^3 for 4 hours (see section additional toxicological information

below for more details). The mortality data were used to calculate a 4-hour LC_{01} value of 3465 ppm for formic acid, which equals 8662 mg/m^3 for acetic acid. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the equation Cn × t = k with the default values of n=1 and n=3 when extrapolating to longer and shorter time points, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Additional study used for VRW (Ernstgård *et al*., 2006)[2]*:* Six female and six male healthy volunteers were exposed to 0 ppm (control exposure), 5 (12.5 mg/m^3) and 10 ppm (25 mg/m^3) acetic acid vapour for 2 hours at rest in a balanced order. Subjective ratings of nasal irritation and smell increased significantly with exposure level. Except for smell, all average ratings at 10 ppm were at the lower end of the 0–100mm visual analogue scale, and did not exceed the verbal expression “somewhat” (26 mm). No effects on pulmonary function, nasal swelling, nasal airway resistance or plasma inflammatory markers (C-reactive protein, and interleukin-6), measured before and after exposure, were seen. There was a non-significant tendency to increased blinking frequency, as measured continuously during exposure, after exposure to 10 ppm acetic acid. Overall, only mild irritation effects were observed at 10 ppm.

Additional study used for LBW: In the publically available REACH registration dossier on ECHAs website a key acute inhalation study for formic acid was described (*https://echa.europa.eu/registration-dossier/-/registered-dossier/15127/7/3/3*). According to the summary of the registrant, the study was performed according to OECD TG 403. In this study Sprague-Dawley rats, 10 per sex/concentration, were exposed, whole body, to analytical vapour concentrations of 3380, 7290, 8370, 11100, 14700 mg/m^3 for 4 hours. Mortality rates for males and females were 0/10, 2/10, 8/10, 10/10, 10/10 and 0/0 and 1/10, 8/10, 10/10, 10/10, respectively. Clinical signs included closed lids, snout wiping, discharge from nose and eye, corrosion of nose and eyes, salivation, corneal opacity, loss of pain reflex, dyspnea, respiration sounds, flatulence, apathy, hunched posture, unsteady gait in all concentration groups. Symptoms persisted until termination at 14 days after treatment, except for the animals at 3380 mg/m^3, which were free of symptoms. Body weights were concentration dependently depressed. Gross pathology of the dead animals showed hyperemic heart dilatation, inflated lung. There were no histopathological findings in the sacrificed animals.

Acetic acid induces irritation of the conjunctival mucosa, oropharynx, trachea, and principal bronchi. Acetic acid can also induce eye and skin burns, skin sensitization, pharyngeal edema, and chronic bronchitis.

Susceptible populations include individuals with chronic respiratory, skin or eye disease, asthmatics and individuals with seasonal allergic rhinitis.

Acetic acid is not embryotoxic or teratogenic in animals.

H314: Causes severe burns and eye damage.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: pungent

OT: 0.025 mg/m^3 [AIHA, 1989]
LOA = 11.8 * OT * 1.33 = 0.4 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies below the VRW, AGW and LBW values.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)[3]

VRW level **25**	*AEGL-1* -	*ERPG-1* 12		*IDLH:* 120 (30 min)
AGW level **230**	*AEGL-2* -	*ERPG-2* 86		
LBW level **1400**	*AEGL-3* -	*ERPG-3* 610		

[2] Ernstgard, L., et al. (2006). "Acute effects of exposure to vapours of acetic acid in humans." Toxicology Letters 165(1): 22-30.
[3] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 108-24-7 **Azijnzuuranhydride** $(CH_3CO)_2O$ **VN-nr: 1715**

GEVI: 83

Synoniemen: acetyloxide, azijnzuuroxide (Engels: acetic anhydride) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	2,1	2,1	2,1	2,1	2,1	2,1
Alarmeringsgrenswaarden	AGW (mg/m³)	34	23	19	15	12	7,6
Levensbedreigende waarden	LBW (mg/m³)	290	200	160	120	99	65

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,235 ppm; 1 ppm = 4,247 mg/m³

Explosiegrens: LEL = 2,0 vol% ≈ 84 939 mg/m³ (boven 49°C damp met lucht explosief)

Geur: stekende geur

LOA: 8,0 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,01

Molecuulmassa: 102,1 g/mol

Zuurgraad: ≈ 3 bij 1g/100ml

LogKow: -0,3

Wateroplosbaarheid: reactie

Verzadigde dampdruk: 5,1 mbar

Overige informatie

Publieke grenswaarde:
Niet afgeleid
MAK: 21 mg/m³
TLV-TWA: 4,3 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte irritatie van neus

VRW → AGW: irritatie slijmvliezen, pijn achter borstbeen

AGW → LBW: keelpijn en hoest, tranen, branderig gevoel, benauwdheid

Boven LBW: larynx- en glottisoedeem, ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Azijnzuuranhydride werkt irriterend tot bijtend op de ogen, de huid en de luchtwegen.
- Blootstelling aan azijnzuuranhydride kan longontsteking, longoedeem en een astmatische reactie veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- In ernstige gevallen kans op verstikking door zwellingen in de keel.
- Personen met verminderende longfunctie en (chronische) obstructieve luchtwegaandoening zijn mogelijk gevoeliger voor de effecten van azijnzuuranhydride.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, prikkeling, roodheid, blaren, pijn, brandwonden
Oogcontact: tranenvloed, bijtend, hoornvliesbeschadiging, ernstige brandwonden, verlies van gezichtsvermogen

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding, direct spoedeisende medische hulp inzetten
Ontsmetting vloeistof
huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, spoelen met veel water / kleding verwijderen, direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, direct spoedeisende medische hulp inzetten.
Specifieke behandeling en materialen*: geen*.
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 108-24-7 **Acetic anhydride** **$(CH_3CO)_2O$** **UN-nr: 1715**

Basis for the Dutch Intervention Values

VRW: Based on information as described in ERPG-document, other time-points added

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added.

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added.

Date: 31-10-2017 ERPG, 2008

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	2.1	2.1	2.1	2.1	2.1	2.1	Mild respiratory irritation
AGW	34	23	19	15	12	7.6	Reversible irritation of the eye and respiratory tract
LBW	290	200	160	120	99	65	Threshold for rat lethality

Derivation of the Dutch Intervention Values

VRW: In the absence of suitable single exposure data, the VRW is based on data from a subchronic inhalation study. Rats (10/sex/concentration) were exposed to concentrations of 0.98, 4.96 and 20 ppm (4.2, 21 and 85 mg/m^3, respectively) for 6 hours per day, 5 days per week for 13 weeks. One third of each group was retained for a 13-week recovery period. At 85 mg/m^3, rats had partially closed eyes after the first two exposures, followed by noisy breathing (indicative of mild effects on the respiratory tract) which progressively diminished in the recovery period. Because noisy breathing was only occasionally observed at 21 mg/m^3, this was selected as a PoD for the VRW derivation. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was not applied as respiratory irritation is considered to be concentration-dependent rather than exposure duration-dependent.

AGW: In the absence of suitable single exposure data, the AGW is based on data from a subacute inhalation study as described in the ERPG document. Rats (5/sex/concentration) were exposed to concentrations of 24, 103 (males)/104 (females), and 407 (males only) ppm (corresponding to 102, 437/442 and 1729 mg/m^3, respectively) for 6 hours/day, 5 days/week for various periods of time: for 2 weeks for the 102 mg/m^3 group, only for 6 days (exposure was terminated due to treatment-related effects) for the 437/442 mg/m^3 group and for 1 day for the 1729 mg/m^3 group (due to mortality within 24 hours). Females were not treated with 1729 mg/m^3 due to the mortality observed in males. Rats exposed to 437 and 1729 mg/m^3 showed lachrymation, gasping, noisy respiration and half-closed eyes. At 1729 mg/m^3, severe degenerative changes were seen in nasal passages, larynx, trachea and lungs. At 437 and 102 mg/m^3, less severe degenerative changes were seen in nasal passages, larynx, trachea and lungs. At 102 mg/m^3, half-closed eyes in females was the only clinical abnormality seen during the first day of exposure and there were no clinical signs in males and no effects on bodyweight after the first exposure. For these reasons, 24 ppm (102 mg/m^3) was selected as the PoD for the AGW derivation. These findings are supported by a 13-week study (see VRW) which showed that at 85 mg/m^3, rats had partially closed eyes after the first two exposures, followed by noisy breathing. All changes regressed in this study during the recovery period, indicating the effects were reversible. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter time points, respectively.

LBW: In the absence of suitable single exposure data, the LBW is based on the same subacute inhalation toxicity study in rats as used for the AGW. Rats were exposed to 24, 103 (males)/104 (females), and 407 (males only) ppm (102, 437/442 and 1729 mg/m^3, respectively) for 6 hours/day for 1 day to 2 weeks. For exposure details see AGW rationale. At 1729 mg/m^3, 2/5 males died within 24 hours after one treatment and the remaining 3 males were killed due to clinical conditions (all had gasping respiration and 2 were lethargic). Females were not exposed to these concentrations due to severity of effects observed in male rats. No animals (males or females) died after repeated exposure to 102

mg/m^3 for 2 weeks or to 437 mg/m^3 for 6 days. The concentration of 1729 mg/m^3 in a 6-hour sub-acute inhalation toxicity study with rats was used as PoD for the derivation of the LBW. This exposure level is considered an assumed LC_{50} as 2 out of 5 male rats died. A modifying factor was applied to extrapolate this value to an LC_{01} value. Given the steep concentration-response curve a MF of 2 was considered sufficient. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter time points, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Susceptible populations include individuals with impaired pulmonary function, especially those with obstructive airway disease.

The available data indicate that acetic anhydride is not teratogenic or toxic for reproduction after inhalation.

H332: harmful if inhaled; H314: Causes severe burns and eye damage; H302: harmful if swallowed.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

Derivation of the carcinogenic risk potency (CRP):

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: pungent

OT: 0.56 mg/m^3 [Ruth, 1986]

LOA = 11.8 * 0.56 * 1.33 = 7.8 mg/m^3

(The concentration Level leading to distinct Odour Awareness (l=3) is calculated using the formula: l = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies below the AGW and LBW values, and above the VRW.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)[4]

VRW level **2.1**	*AEGL-1* -	*ERPG-1* 2.1		*IDLH: -*
AGW level **19**	*AEGL-2* -	*ERPG-2* 63		
LBW level **160**	*AEGL-3* -	*ERPG-3* 420		

[4] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG

Stofdocument deel A

CAS-nr: 151-56-4 **Aziridine** **CH_2-CH_2(-N-)H, cycl** **VN-nr: 1185 (gestabiliseerd)**

GEVI: 663

Synoniemen: ethyleenimine (Engels: Ethylenimine) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	25	10	5,7	3,2	1,8	1,0
Levensbedreigende waarden	LBW (mg/m³)	68	27	15	8,5	4,8	2,7

Datum vaststelling: 13-05-2009

Conversiefactor: 1 mg/m³ = 0,558 ppm; 1 ppm = 1,79 mg/m³

Explosiegrens: LEL= 3,3 vol% ≈ 59.000 mg/m³

Geur: stekende ammoniakgeur

LOA: 19,6 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze vloeistof
Brand: Zeer brandgevaarlijk. Kans op explosie door contact met zuren of kooldioxide.

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,1

Molecuulmassa: 43,07 g/mol
Zuurgraad: Geen data
LogKow: -0,3
Wateroplosbaarheid: Volledig
Verzadigde dampdruk: 215 mbar

Overige informatie

Publieke grenswaarde: 0,0009 mg/m³ (8 uur)

MAK: niet afgeleid

TLV-TWA: 0,90 mg/m³ huid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: mogelijk oog- en bovenste luchtwegirritatie

AGW → LBW: onderste luchtwegirritatie, hoesten, benauwdheid, longoedeem

Boven LBW: ademnood, convulsies, sterfte.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Aziridine veroorzaakt irritatie van de ogen en bovenste en onderste luchtwegen.
- Aziridine kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Het optreden van nierschade na blootstelling aan aziridine is beschreven.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, blaren, ernstige brandwonden.
De stof kan door de huid worden opgenomen!

Oogcontact: bijtend, roodheid en pijn, hoornvliesbeschadiging, ernstige brandwonden.

Carcinogeniteit

IARC classificatie: 2B
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp:

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

Ontsmetting vloeistof:

huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken, niet laten drinken, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen: geen

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 151-56-4 **Ethylenimine** **CH_2-CH_2(-N-)H, cycl** **UN-nr: 1185 (stabilised)**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same point of departure as for AEGL-2, different value for n, 2h value added

LBW: Same point of departure as for AEGL-3, different value for n, 2h value added

Date: 13-05-2009 | AEGL document: Final, 2010

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	(no data available)
AGW	25	10	5.7	3.2	1.8	1.0	Threshold of respiratory difficulty
LBW	68	27	15	8.5	4.8	2.7	LC_{01} value for lethality animals

Derivation of the Dutch Intervention Values

VRW: Data were not available for deriving VRW values for ethylenimine; therefore, no values are recommended. The absence of VRW values does not imply that exposures below the AGW are without adverse health effects.

AGW: The AGW was based on extreme respiratory difficulty in rats and guinea pigs exposed to 25 ppm (45 mg/m^3) for more than 3 hours. The next lowest concentration of 10 ppm (18 mg/m^3), which caused no respiratory difficulty in guinea pigs during 4 hour exposure, was used to derive AGW values. Data from the rat study were not used, since no NOEL was available. A total uncertainty factor of 10 was applied, consisting of an interspecies factor of 3 and an intraspecies factor of 3. An interspecies uncertainty factor of 3 was applied because ethylenimine is a very reactive direct-acting alkylating agent, and the AGW effects would most likely be confined to the respiratory tract. Respiratory tract damage appears to be due to a direct effect of an alkylating agent on the respiratory epithelium, and this mechanism is not expected to be much different among species. An intraspecies uncertainty factor of 3 was applied because the effects caused by a very reactive alkylating agent such as ethylenmine are not expected to vary considerably among individuals. AGW values were time-scaled using the relationship $C^n \times t = k$, where n = 1.2 (the same as for LBW).

LBW: The LBW was based on rat lethality data. The LC_{01} value for an 8-hour exposure was 15 ppm (27 mg/m^3). A total uncertainty factor of 10 was applied, consisting of an interspecies factor of 3 and an intraspecies factor of 3. An interspecies uncertainty factor of 3 was applied, based on the same rationale described for AGW derivation. Additionally, LC_{50} values for three test animal species were within a factor of 2 of each other. An intraspecies uncertainty factor of 3 was applied based on the same rationale described for AGW derivation. LBW values were time-scaled using the relationship $C^n \times t = k$, where n = 1.2 (derived from rat lethality data).

Additional toxicological information (including relevant results of a general literature search, if any)

Toxicity due to exposure to ethylenimine is generally delayed and includes irritation to contact organs (skin, eyes, oral cavity, and upper and lower respiratory tract), systemic toxicity, and death depending upon the concentration. At extremely high concentrations, however, irritation to contact organs may occur during or soon after exposure. The time course of irritation caused by ethylenimine is different from that caused by primary irritants such as ammonia, which causes an immediate response upon exposure regardless of concentration.

No data were found on the developmental/reproductive toxicity of ethylenimine.

H300: Fatal if swallowed; H310: Fatal in contact with skin; H314: Causes severe skin burns and eye damage; H330: Fatal if inhaled; H340: May cause genetic defects; H350: May cause cancer.

Carcinogenicity and derivation of the CRP value
IARC classification: 2B (possibly carcinogenic to humans) No carcinogenic risk potency (CRP) was derived Ethylenimine is clastogenic in cultured human cells. An unconfirmed report noted that no evidence of carcinogenicity was found among 144 ethylenimine workers after 40 years of experience. No other information on the potential carcinogenicity of ethylenimine in humans was described in the available literature.

Odour and derivation of the LOA value
Odour: ammonia-like odour OT_{50}: 0.698 ppm (1.25 mg/m^3) [AEGL (2010); van Doorn (2002)] LOA = 11.8 * 1.25 * 1.33 = 19.6 mg/m^3 (The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: $I = 2.33 * \log (C/OT_{50}) + 0.5$. A correction factor of 1.33 is applied to this value) The LOA is reached at the level of the AGW (10 min) and the LBW (10 min and 30 min). Odour will not serve as a specific warning to the presence of ethylenimine, because its odour is similar to that of ammonia.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* Not derived		*IDLH:* 179 mg/m^3 (30 minutes).
AGW level **5.7**	*AEGL-2* 8.2	*ERPG-2* Not derived		
LBW level **15**	*AEGL-3* 18	*ERPG-3* Not derived		

Stofdocument deel A

CAS-nr: 71-43-2 **Benzeen** **C_6H_6-cyclisch** **VN-nr: 1114**

GEVI: 33

Synoniemen: Benzol, cyclohexatrieen, fenylhydride (Engels: Benzene) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	410	240	170	120	60	30
Alarmeringsgrenswaarden	AGW (mg/m³)	6.400*	3.700	2.600	1.800	1.300	650
Levensbedreigende waarden	LBW (mg/m³)	32.000**	18.000*	13.000*	9.100*	6.400*	3.200

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,308 ppm; 1 ppm = 3,249 mg/m³

Explosiegrens: 1,2 vol% ≈ 39000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

** berekende interventiewaarde hoger dan 50% LEL

Geur: typerende, zoete, aromatische geur

LOA: 24 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: heldere, kleurloze vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,2

Molecuulmassa:	78,1 g/mol
Zuurgraad:	Geen data
LogKow:	2,1
Wateroplosbaarheid:	0,18 g/100 ml (matig)
Verzadigde dampdruk:	100 mbar

Overige informatie

Publieke grenswaarde: 3,25 mg/m³ (8 uur) H

MAK: niet afgeleid

TLV-TWA: 1,6 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte oogirritatie

VRW → AGW: irritatie van huid, ogen, neus en keel, lichte benauwdheid, hoofdpijn, misselijkheid, braken, vermoeidheid duizeligheid

AGW → LBW: ernstige irritatie van luchtwegen,benauwdheid, euforie, verwardheid, bewustzijnsdaling, longoedeem

Boven LBW: convulsies, coma, ademnood, ademstilstand, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Blootstelling aan benzeen kan leiden tot irritatie aan ogen en luchtwegen en stoornissen van het centrale zenuwstelsel (CZS), welke bij hoge concentraties tot ademnood en overlijden kunnen leiden.
- Bij hoge concentraties kan kortdurende CZS excitatie worden gevolgd door depressie van het CZS.
- De respiratoire effecten (ademstilstand) voorafgaand aan sterfte zijn zeer waarschijnlijk een secundaire response op depressie van het ademhalingscentrum in de hersenen.
- Blootstelling aan benzeen kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: droge huid, roodheid

Oogcontact: roodheid en pijn

Carcinogeniteit

IARC classificatie: 1

CRP: 2.800 mg/m³

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, direct spoedeisende medische hulp inzetten

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken, direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 71-43-2 **Benzene** **C_6H_6-cyclic** **UN-nr: 1114**

Basis for the Dutch Intervention Values

VRW: AEGL value adopted, 2h value added

AGW: AEGL value adopted, 2h value added

LBW: AEGL value adopted, 2h value added

Date: 06-10-2016 | AEGL interim 2009

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	410	240	170	120	60	30	CNS effects in humans
AGW	6,400*	3,700	2,600	1,800	1,300	650	CNS effects in rats
LBW	32,000**	18,000*	13,000*	9,100*	6,400*	3,200	Threshold for lethality in rats

* value higher than 10% of LEL; ** value higher than 50% of LEL

Derivation of the Dutch Intervention Values

VRW: The VRW is based on the results of a human volunteer study showing CNS effects. In total 23 volunteers inhaled benzene at levels between 47 and 110 ppm (153 and 357 mg/m³) through a facemask for periods up to 2h (sometimes up to 3h). It was reported that the volunteers had no subjective troubles (volunteers probably did not complain, no active questionnaire involved). The 2h NOEL of 110 ppm (357 mg/m³) for CNS effects was used as point of departure for the VRW.
The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. In contrast to toluene and xylene, benzene does not reach a steady state in blood before 4 hours. Therefore, for benzene time-scaling should continue over the whole intervention values time frame, instead of flatlining as is done for other substances acting on the CNS. Though the available data are insufficient to derive a substance specific value for n, the data on deep narcosis in cats show that the default value of 3 to extrapolate to shorter durations is too high. Therefore, a n-value of 2 is used for extrapolation to shorter durations and an n-value of 1 is used for extrapolation to longer durations.

AGW: CNS effects were used as basis for the AGW. Haematotoxicity is not considered suitable endpoint for the derivation of the AGW values as some of the effects (reduced numbers of circulating cells and possible unilineage progenitor cells) are reversible. For the haematological effects which are irreversible (effects on the pluripotent stem cell), no data are available showing effects on the pluripotent stem cell after a single dose. Furthermore, the database also shows that repeated exposure rather than a single high exposure is needed to induce the severe and irreversible critical effect on pluripotent stem cell reduction.
The AGW is based on a NOAEL for CNS effects in rats. Groups of 8 rats were exposed via whole body inhalation to benzene concentrations of 250, 500, 800, 1500, 2000, 4000 and 5940 ppm (corresponding to 812, 1624, 2599, 4873, 6497, 12995, 19297 mg/m³; exposure levels were estimated from figures in paper) applied to each of the exposure concentrations of 1, 2, 3 or 4 hours. Increased locomotor activity was observed at 12995 mg/m³ for 4h, whereas decreased locomotor activity was observed at 19297 mg/m³ for 4h. Increased activity is not considered an AGW-endpoint but clear decreases in neurobehavioral function are an AGW-endpoint. The 4h exposure to 12995 mg/m³ was therefore considered the highest level causing no AGW-effects and was used as point of departure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Although the basis for the AGW are CNS-effects, steady state blood levels for benzene are not attained until 4 hours. Therefore, for benzene time scaling should be performed over the whole intervention values time frame (see VRW). Time scaling was done using the equation $C^n \times t = k$, with n=1 and n=2 to extrapolate to longer and shorter time points, respectively (see VRW).

LBW: The LBW is based on the same acute rat inhalation study as is used for AGW-derivation. Groups of 8 rats were exposed via whole body inhalation to benzene in concentrations of 250, 500, 800, 1500, 2000, 4000 and 5940 ppm (corresponding to 812, 1624, 2599, 4873, 6497, 12995, 19297 mg/m³; exposure levels were estimated from figures in paper) applied to each of the exposure

concentrations of 1, 2, 3 or 4 hours. An exposure of 4h to the highest concentration (19297 mg/m^3) did not result in mortality and was considered a NOEL. This is supported by data from two mice studies that found no mortality at 4890 ppm (15888 mg/m^3) for 7h or at 5020 ppm (16310 mg/m^3) for 8h. An interspecies uncertainty factor of 1 is used. The use of a higher uncertainty factor for interspecies differences would result in LBW values which are in conflict with human data. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was done using the equation $C^n \times t = k$, with n=1 and n=2 (see VRW) to extrapolate to longer and shorter time points, respectively. The resulting LBW values are in agreement with the limited quantitative human experiences from occupational and accidental exposures.

Additional toxicological information (including relevant results of a general literature search, if any)

The mechanism of toxicity of benzene should be viewed separately for acute CNS effects and bone marrow toxicity. The mechanism of CNS effects of benzene shares many characteristics with halothane. The concentration of benzene in the brain is probably the pivotal factor for CNS effects. Most likely, the concentration of benzene in the brain lipid phase determines its CNS depressing effects. The CNS effect is a continuum from very slight dizziness to narcosis to paralysis of the respiratory center. The mortality data indicate a small range in concentration between 0 and 100% mortality. The mechanism of haematotoxicity via bone marrow toxicity of benzene is much more complex and is still a subject of extensive research. In general, it is expected that some sort of repeated exposure is required to induce these effects. However, little is known about the actual occurrence of haematological effects after single exposure within the 10-min to 8 hour timeframe of the intervention values.

The data on reproductive and developmental toxicity of benzene inhalation in humans and animals are inconclusive and are expected to require a repeated exposure pattern.

H304: may be fatal if swallowed and enters airways, H315: Causes skin irritation, H319: Causes serious eye irritation, H340: May cause genetic defects, H350: may cause cancer, H372: Causes damage to organs

Carcinogenicity and derivation of the CRP value

IARC classification: 1 (carcinogenic to humans)

Derivation of the carcinogenic risk potency (CRP):

10^{-4} risk level after inhalation: 0.013 mg/m^3 [AEGL 2009]

CRP = (10^{-4} risk level * average life span in hours)/DRCF

= (0.013 * 613,200) /2.8 = 2,800 mg/m^3

Benzene has a prominent carcinogenic effect on the haematopoetic system.

Odour and derivation of the LOA value

Odour: characteristic, sweet odour

OT_{50}: 1.53 mg/m^3 [AEGL, 2009]

LOA = 11.8 * OT_{50} * 1.33 = 24 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is lower than all VRW, AGW and LBW values.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **170**	*AEGL-1* 170	*ERPG-1* 160		*IDLH:* 1,600 (30 min)
AGW level **2,600**	*AEGL-2* 2,600	*ERPG-2* 490		
LBW level **13,000**	*AEGL-3* 13,000	*ERPG-3* 3,200		

Stofdocument deel A

CAS-nr: 86290-81-5/8006-61-9 **Benzine** **C_4-C_{12} koolwaterstoffen** **VN-nr: 1203** **GEVI: 33**

Synoniemen: autobenzine (Engels: Gasoline) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	510	510	510	510	510	510
Alarmeringsgrenswaarden	AGW (mg/m³)	11000	3600	3600	3600	3600	3600
Levensbedreigende waarden	LBW (mg/m³)	NA	NA	NA	NA	NA	NA

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,329 ppm; 1 ppm = 3,037 mg/m³ *

Explosiegrens: LEL = 1,4% ≈ 14.000 ppm ≈ 67.000 mg/m³ (Damp met lucht exposief)

Geur: typerende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot strogele, deels vluchtige vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,15

Molecuulmassa: ~115 g/mol

Zuurgraad: Niet afgeleid

LogKow: 2-7

Wateroplosbaarheid: 0,01-0,03 g/100 mL (Zeer slecht)

Verzadigde dampdruk: 50-400 mbar

Overige informatie

Publieke grenswaarde: 240 mg/m³

MAK: niet afgeleid

TLV-TWA: 1435 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: oogirritatie, tranen, keelpijn en hoest

VRW → AGW: euforie, hoofdpijn, duizeligheid

*Boven **AGW***: verwardheid, misselijkheid, slaperigheid, bewustzijnsdaling, convulsies, ademstilstand

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Blootstelling aan benzine kan leiden tot irritatie aan ogen en luchtwegen en stoornissen van het centrale zenuwstelsel (CZS).
- Benzine veroorzaakt depressie van het centrale zenuwstelsel.
- Narcotische effecten worden soms (niet altijd) voorafgegaan door een excitatiefase (opwinding, euforie/'high', delier).
- Benzine bestaat uit vluchtige componenten en de dampen kunnen door verdringing van zuurstof verstikkingsgevaar opleveren.

Effecten bij blootstelling aan vloeistof

Huidcontact: prikkeling, droge huid, roodheid.

Oogcontact: prikkeling, roodheid en pijn.

Carcinogeniteit

IARC classificatie: 2B

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, bij klachten arts raadplegen.

ogen: *uit*spoelen met water (evt. contactlenzen verwijderen).

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

* Deze conversiefactoren zijn berekend op basis van damp (uitgaande van een molecuulmassa van 73 g/mol).

Stofdocument deel B

CAS-nr: 86290-81-5/8006-61-9 **Gasoline** **C_4-C_{12} hydrocarbons** **UN-no: 1203**

Basis for the Dutch Intervention Values

VRW: Based on information as described in ERPG-document, different values are derived, other time-points added.

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added.

LBW: Not recommended.

Date: 31-10-2017 | ERPG, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	510	510	510	510	510	510	Eye and throat irritation in humans
AGW	11000	3600	3600	3600	3600	3600	Unsteadiness and dizziness in humans
LBW	NR	NR	NR	NR	NR	NR	Not recommended

Derivation of the Dutch Intervention Values

VRW: The VRW is based on a human study evaluating the acute irritation during controlled exposure to air containing gasoline vapour. Male and female volunteers were exposed in various groups to various concentrations gasoline vapour. At concentrations of 500 ppm (1518 mg/m³) for one hour, tested in 9 males, slight irritation of the eyes and throat were observed. Similar effects were also observed at 900 ppm (2733 mg/m³) for one hour. At 2600 ppm (7895 mg/m³) for one hour, slight dizziness and transient eye irritation was noticed, whereas 10,700 ppm (32491 mg/m³) applied for 4-7 minutes via facemask, resulted in unsteadiness (described as drunkenness). An exposure of 1518 mg/m³ for one hour was used as PoD for deriving the VRW values. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was not applied as eye and throat irritation is considered to be concentration-dependent rather than concentration x time-dependent.

AGW: The AGW is based on the same human volunteer study as used for VRW. An exposure of 10,700 ppm (32,491 mg/m³) applied for 4-7 minutes via facemask, resulted in unsteadiness (described as drunkenness). This was used as POD for deriving the AGW values. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Based on the composition of gasoline (consisting mostly of C5-C6 paraffins), in line with n-hexane and butane, a steady state blood concentration is assumed to be reached in approximately 30 minutes. Timescaling was therefore applied from 10 min to 30 min, for which the 4-7 min exposure duration from the human study was set equal to a 10 min exposure duration. The AGW-values from 30 min to 8 hour were flatlined.

LBW: LBW values are not recommended, because no appropriate animal data are available. It is not apparent that concentrations high enough to cause death can be attained. On the basis of the likelihood that lethal concentrations cannot be attained and sustained under ambient conditions, LBW values were not derived.

Additional toxicological information (including relevant results of a general literature search, if any)

Gasoline induces irritation of eyes, nose and throat; dizziness, mucous membrane irritation, anaesthesia, and central nervous system depression. Death is postulated to be due to either central nervous system depression due to asphyxia leading to respiratory failure or cardiac sensitization to circulating catecholamines leading to fatal arrhythmia.

Gasoline is not embryotoxic or reproductive toxic in animals.

H304: May be fatal if swallowed and enters airways; H340: May cause genetic defects; H350: May cause cancer.

Carcinogenicity and derivation of the CRP value
IARC classification: 2B (possibly carcinogenic to humans) No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value
Odour: characteristic odour OT_{50}: 2.3 mg/m^3 [API, 1994][5] LOA = 11.8 * OT_{50} * 1.33 = 36 mg/m^3 (The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT50) + 0.5. A correction factor of 1.33 is applied to this value) The LOA lies below the LBW, AGW, and VRW values.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)[6]

VRW level **510**	*AEGL-1* -	*ERPG-1* 654		*IDLH: -*
AGW level **3600**	*AEGL-2* -	*ERPG-2* 3270		
LBW level **NR**	*AEGL-3* -	*ERPG-3* 13,080		

[5] API (American Petroleum Institute). 1994. Odor threshold studies performed with gasoline and gasoline combined with MTBE, ETBE and TAME, with cover letter dated 02/22/95. API Publication 4592, prepared by TRC Environmental, Windsor, CT. OTS0557644, available from the National Technical Information Service, Springfield, VA.
[6] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 100-44-7 **Benzylchloride** **C_6H_5-CH_2Cl (cyclisch)** **VN-nr: 1738** **GEVI: 68**

Synoniemen: (chloormethyl)benzeen, alfa-chloortolueen (Engels: benzyl chloride) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	7,0	7,0	7,0	7,0	7,0	7,0
Alarmeringsgrenswaarden	AGW (mg/m³)	30	30	30	30	24	12
Levensbedreigende waarden	LBW (mg/m³)	200	140	110	89	71	35

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,190 ppm; 1 ppm = 5,27 mg/m³

Explosiegrens: LEL = 1,1 vol% ≈ 58.000 mg/m³

Geur: stekende geur

LOA: 3,4 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,0

Molecuulmassa:	126,6 g/mol
Zuurgraad:	geen data
LogKow:	2,3
Wateroplosbaarheid:	0,05 g/100 ml (30°C) (niet)
Verzadigde dampdruk:	1,2 mbar

Overige informatie

Publieke grenswaarde:
Niet afgeleid
MAK: 0,2 mg/m³

TLV-TWA: 5,3 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen

VRW → AGW: oogirritatie, tranenvloed

AGW → LBW: ernstige oogirritatie, brandende en pijnlijke ogen, irritatie neus, keel en luchtwegen, keelpijn, hoesten, niezen, speekselvloed, benauwdheid, longoedeem, bewustzijnsdaling

Boven LBW: ademnood, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Benzylchloride werkt irriterend op de ogen en luchtwegen en veroorzaakt ontsteking van de slijmvliezen in ogen, neus, mond en longen.
- Benzylchloride kan bij hoge concentraties longoedeem veroorzaken, waarbij de verschijnselen pas na enkele uren kunnen optreden en worden versterkt door lichamelijke inspanning.
- Benzylchloride kan depressie van het centrale zenuwstelsel veroorzaken.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, pijn, ernstige brandwonden.

Oogcontact: bijtend, roodheid, pijn, slecht zien.

Carcinogeniteit

IARC classificatie: 2A
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 100-44-7 **Benzyl chloride** **C_6H_5-CH_2Cl (cyclic)** **UN-nr: 1738**

Basis for the Dutch Intervention Values

VRW: Same point of departure as for ERPG but different values are derived, other time points added.

AGW: Same point of departure as for ERPG but different values are derived, other time points added

LBW: Based on other (additional) toxicological information than described in ERPG document.

Date: 16-12-2010 | ERPG document, 2006

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	7.0	7.0	7.0	7.0	7.0	7.0	Slight eye irritation in humans
AGW	30	30	30	30	24	12	Eye irritation in humans + 1/3LBW
LBW	200	140	110	89	71	35	Threshold for lethality in animals

Derivation of the Dutch Intervention Values

VRW: Human data were available to derive a VRW value. In a controlled exposure study benzyl chloride was tested for nasal irritation. Subjects lifted the cover of a small, strongly ventilated hood, placed their nose into the nose-piece and took one breath. To test eye irritation, subjects held one eye open to the airstream at the nosepiece for 10 seconds. Nasal irritation was rated as 'just perceptible' at 35 ppm (180 mg/m³). Ocular irritation was 'just perceptible' at 8 ppm (42 mg/m³), 'very unpleasant' at 17 ppm (90 mg/m³), 'painfully strong' yet voluntarily endurable at 37 ppm (190 mg/m³), and 'intolerable' at 80 ppm (420 mg/m³). These results are in line with the report of one investigator who noted severe burning sensation in the eyes and copious tearing when exposed to benzyl chloride at an estimated nominal concentration of 30 ppm (160 mg/m³).
As point of departure for the derivation of VRW values, the 'just perceptible' ocular irritation observed at 8 ppm (42 mg/m³) was chosen. Because this level concerns a LOAEL for slight irritation after exposure for a duration of only 10 seconds, a modifying factor of 2 was applied. To account for sensitive individuals an intraspecies factor of 3 was used. No time-scaling was performed because mild irritant effects generally do not vary greatly over time.

AGW: Besides the above mentioned study in humans, very few studies describing toxic effects of benzyl chloride consistent with the definition of AGW are available. For humans, ocular irritation was 'just perceptible' at a 10-second exposure to 8 ppm (42 mg/m³), 'very unpleasant' at 17 ppm (90 mg/m³), 'painfully strong' yet voluntarily endurable at 37 ppm (190 mg/m³), and 'intolerable' at 80 ppm (420 mg/m³). Eye irritation was observed in all cats exposed for 8 hours to concentrations of benzyl chloride ranging from 160 to 7000 mg/m³ (1-3 per concentration); cats closed their eyes within 30 min. Rabbits exposed to 10 ppm (53 mg/m³) benzyl chloride for 6 hr initially breathed rapidly, then rested quietly with no further observed signs of eye irritation.
The eye closure observed in a cat at 160 mg/m³ after 30 min of exposure is above the effects addressed by the AGW. Human data show that brief exposure to 90 mg/m³ is experienced as unpleasant and to 190 mg/m³ as painfully strong yet voluntarily endurable. The concentration of 90 mg/m³ is used as POD for AGW derivation. An intraspecies factor of 3 each was applied, because irritant effects are not expected to vary greatly between species or individuals. Since the effect of eye irritation is not expected to change over time the same AGW of 30 mg/m³ is derived for time points 10min – 2h. For time points 4h and 8h this value was considered too high. The AGW for 4h and 8h was calculated as 1/3 of LBW.

LBW: The LBW values were derived from an additional rat lethality study that was not described in the ERPG document (Bayer, 1979; due to confidentiality no access to complete study report). Groups of 10 rats/sex/group were exposed for 4 hours to 190, 504, 708, 1453 and 1980 mg/m³ benzyl chloride. Total lethality was 0, 0, 0, 6 and 9 out of 20 rats, respectively. In addition, a 60-min exposure to 2343 mg/m³ resulted in 2/20 deaths; this data point was not further considered for LBW derivation. The 4-hour LC_{01} value was calculated by Doseresp to be 709 mg/m³.To account for differences between species and for sensitive individuals, interspecies and intraspecies factors of 3 each were used (total factor of 10). Time scaling was performed using the equation $C^n \times t = k$, using the default values for n

of 1 and 3 to extrapolate to longer and shorter exposure durations respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

No information concerning reproduction toxicity after inhalation of benzyl chloride was found. In an oral reproduction toxicity study the only statistically significant observation in fetuses was reduced crown-rump length at 100 mg/kg, given daily on days 6 through 15 of gestation. Benzyl chloride did not statistically increase the number of skeletal and visceral variations.

H302: Harmful if swallowed; H315: Causes skin irritation; H318: May cause serious eye damage; H331: Toxic if inhaled; H335: May cause respiratory irritation; H350: May cause cancer; H373: may cause damage to organs through prolonged or repeated exposure

Carcinogenicity and derivation of the CRP value

IARC classification: 2A (probably carcinogenic to humans)

No carcinogenic risk potency (CRP) was derived.

No chronic inhalation toxicity/carcinogenicity studies were found. Chronic oral toxicity studies showed carcinogenic properties of benzyl choride in experimental animals.

Odour and derivation of the LOA value

Odour: pungent

OT_{50}: 0.216 mg/m^3 [AIHA]
LOA = 11.8 * OT_{50} * 1.33 = 3.4 mg/m^3

(The concentration Level leading to distinct Odour Awareness (l=3) is calculated using the formula: l = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is lower than the derived VRW values and hence odour perception may occur at exposure levels below the VRW.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **7.0**	*AEGL-1* not derived	*ERPG-1* 5.3		*IDLH:* 53 (30 minutes)
AGW level **30**	*AEGL-2* not derived	*ERPG-2* 53		
LBW level **110**	*AEGL-3* not derived	*ERPG-3* 260		

Stofdocument deel A

CAS-nr: 10294-33-4 **Boriumtribromide** **BBr3** **VN-nr: 2692**

GEVI: X88

Synoniemen: tribroomboraan, boortribromide, trona (Engels: boron tribromide) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m³)**	3,5	3,5	3,5	3,5	3,5	3,5
Alarmeringsgrenswaarden	**AGW (mg/m³)**	480	230	140	90	56	56
Levensbedreigende waarden	**LBW (mg/m³)**	1400	690	430	270	170	170

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,0959 ppm; 1 ppm =10,4 mg/m³

Explosiegrens: geen data

Boriumtribromide ontleedt zeer heftig tot explosief bij contact met water, alcoholen, aminen en carbonzuren onder vorming van giftige en bijtende dampen (o.a. broomwaterstof) met kans (indirect) op brand en explosie.

Geur: scherpe, irriterende geur

LOA: niet afgeleid; mogelijk kan de geur beneden AGW niveau waargenomen worden

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos rokende vloeistof
Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,5

Molecuulmassa:	250,6 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	72 mbar

Overige informatie

Publieke grenswaarde:
niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid
TLV-Ceiling: 10,4 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	geen klachten
VRW → AGW:	lichte tot matige neus-, keel-, oog en huidirritatie, hoesten, tranenvloed
AGW → LBW:	matige tot ernstige irritatie van neus, keel, ogen en huid. Irritatie onderste luchtwegen, druk op de borst, piepende ademhaling, benauwdheid, longoedeem
Boven LBW:	ademnood, bloed ophoesten, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Boriumtribromide ontleedt in aanwezigheid van water of vochtige lucht zeer heftig tot broomwaterstof en boorzuur.
- De toxiciteit van boriumtribromide wordt bepaald door de vorming van broomwaterstof.
- Broomwaterstof is corrosief/irriterende voor ogen, huid en slijmvliezen.
- Bij inhalatie kan broomwaterstof longontsteking en/of longoedeem veroorzaken waarbij de verschijnselen pas na enkele uren kunnen optreden en versterkt kunnen worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, brandwonden

Oogcontact: bijtend, verlies van gezichtsvermogen, ernstige brandwonden.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, spoelen met veel water / kleding verwijderen en direct spoedeisende medische hulp inzetten. (**N.B.** voorzichtigheid is geboden aangezien de stof explosief met water kan reageren)

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 10294-33-4 **Boron tribromide** **BBr_3** **UN-nr:2692**

Basis for the Dutch Intervention Values

VRW: Based on hydrogen bromide values, in accordance with AEGL, 2h value added

AGW: Same rationale than AEGL (analogy with hydrogen bromide values, one third of LBW values), 2h value added

LBW: Same rationale than AEGL (analogy with hydrogen bromide values), but using different value for n, 2h value added

Date: November 2015	AEGL document: Final, 2014

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	3.5	3.5	3.5	3.5	3.5	3.5	Analogy with hydrogen bromide; slight irritation (nose) in humans
AGW	480	230	140	90	56	56	Analogy with hydrogen bromide; One third of LBW values
LBW	1400	690	430	270	170	170	Analogy with hydrogen bromide; threshold for lethality animals

Derivation of the Dutch Intervention Values

VRW: No human or animal data were available to derive VRW values for boron tribromide as the reactive nature of boron tribromide precludes toxicity testing. VRW values for hydrogen bromide will be used (on ppm-basis) to derive VRW values for boron tribromide. The use of hydrogen bromide as a surrogate for boron tribromide was deemed appropriate since it is believed that the hydrolysis product, HBr, is responsible for the adverse effects. Based on the knowledge that one mole of boron tribromide hydrolyzes into three moles of HBr in moist air, the boron tribromide VRW was derived by dividing the HBr VRW of 1 ppm by 3.

Derivation of VRW values for HBr

The threshold for nose irritation in humans inhaling 3 ppm (10 mg/m³) HBr for several minutes was selected as the basis for the VRW. This concentration was considered a NOAEL for notable discomfort. The default uncertainty factor for intraspecies differences of 3 was considered sufficient.. Because adaptation to slight irritation occurs, the resulting 1 ppm concentration was used for all exposure durations. This value was also considered to be protective to asthmatics, because at low concentrations HBr is scrubbed well in the upper nasal passage. The 1 ppm concentration is supported by the VRW values of other hydrogen halides of 1.0 and 1.8 ppm for HF and HCl, respectively.

AGW: No human or animal data on boron tribromide were available to derive AGW values. Therefore, the AGW values for boron tribromide were based on the AGW values for HBr.

Derivation of AGW values for HBr

The AGW values for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data. The only study of HBr that addressed effects that meet the definition of an AGW, severe nasal lesions, was a study on hydrogen halides by Stavert et al. (1991). Nevertheless, this study was not considered a suitable basis for derivation of AGW values because 8% of the animals died after exposure to HBr at 1300 ppm (4375 mg/m³), only one concentration was tested and the number of animals tested was not specified.

LBW: No human or animal data on boron tribromide were available to derive LBW values. Therefore, the LBW values for boron tribromide were based on the LBW values for HBr. The use of hydrogen bromide as a surrogate for boron tribromide was deemed appropriate since it is believed that the hydrolysis product, HBr, is responsible for the adverse effects. Based on the knowledge that one mole of boron tribromide hydrolyzes into three moles of HBr in moist air, the boron tribromide LBW was derived by dividing the HBr LBW of 1 ppm by 3.

Derivation of LBW values for HBr

The basis for the LBW values was the 1-hour $BMCL_{05}$ of 1239 ppm (4170 mg/m^3) and the BMC_{01} of 1456 ppm (4900 mg/m^3) for HBr in rats. The 1-hour $BMCL_{05}$ of 1239 ppm (4170 mg/m^3) was chosen as the point of departure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. In contrast to the AEGL, the basis for time scaling, using the equation $C^n \times t = k$, was derived from data from the more robuste dataset of the toxicological comparable chemical, HCl, providing an n-value of 1.48 to scale to shorter and longer time points. To maintain consistency with other hydrogen halogenides, the 8 hour value was set equal to the 4 hour value, as performed for the most potent hydrogen halogenide HF.

Additional toxicological information (including relevant results of a general literature search, if any)

The mechanism of toxicity of boron tribromide appears to be related to the formation of hydrobromic acid (HBr). HBr is a severe irritant to the eyes, skin, and nasal passages; high concentration may penetrate to the lungs resulting in edema and hemorrhage. Boron tribromide undergoes rapid hydrolysis in the presence of water or moist air, producing heat, HBr, and boric acid. No information on the hydrolysis half-life was located, but reaction with water or moisture in the air is rapid and complete.

Based on the fact that one mole of BBr_3 breaks down into three moles of HBr, the toxicity of HBr and related hydrogen halides are relevant. Although the data base for HBr is sparse, additional data on the toxicity of HBr relative to those of hydrogen fluoride (HF) and hydrogen chloride (HCl) were available for comparison purposes. The data bases for HCl and HF are robust. For the endpoint of lethality, the relative toxicities to the rat and mouse are in the order of HF>HBr≥HCl. When considering sublethal concentrations the severity and extent of the lesions to the upper respiratory tract were in the order HF>HCl>HBr, although the severity and extent of the lesions were very similar among the three chemicals. The data also showed that all three chemicals are well scrubbed in the upper respiratory passages.

Individuals with asthma may respond to exposure to respiratory irritants such as HBr and HCl with increased bronchial responsiveness, but no information on the relative susceptibility to healthy individuals was located Stress and physical activity may cause greater deposition and pulmonary irritation than when a individual is at rest.

No information regarding reproductive and/or developmental toxicity was located for boron tribromide or HBr.

H300: Fatal if swallowed; H314: Causes severe skin burns and eye damage; H330: Fatal if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

No information on genotoxicity and chronic toxicity/carcinogenicity in animals was located for HBr.

Odour and derivation of the LOA value

Odour: a sharp or acrid, irritating odour

By analogy with hydrogen bromide, the acrid odour of boron tribromide should be detectable at 2 ppm (21 mg/m^3; between VRW and AGW level), but data were insufficient to derive a LOA.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **3.5**	*AEGL-1* 3.4	*ERPG-1* not derived		*IDLH:* not derived
AGW level **140**	*AEGL-2* 140	*ERPG-2* not derived		
LBW level **430**	*AEGL-3* 420	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 7637-07-2 **Boriumtrifluoride** BF_3 **VN-nr: 1008**

GEVI: 268

Synoniemen: trifluorboraan, boortrifluoride, boorfluoride (Engels: boron trifluoride)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	2,5	2,5	2,5	2,5	2,5	2,5
Alarmeringsgrenswaarden	AGW (mg/m³)	53	37	29	23	18	9,2
Levensbedreigende waarden	LBW (mg/m³)	160	110	88	70	55	28

Datum vaststelling: 28-11-2008

Conversiefactor: 1 mg/m³ = 0,355 ppm; 1 ppm = 2,82 mg/m³

Explosiegrens: geen data

Geur: Gerapporteerd als penetrante, verstikkende geur en als prettige, zure geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloos gas. Vormt nevels aan de lucht.
Brand: Niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,4

Molecuulmassa: 67,8 g/mol
Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: Reactie
Verzadigde dampdruk: geen data

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 3 mg/m³ (ceiling)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: lichte tot matige irritatie aan keel en bovenste luchtwegen

AGW → LBW: matige tot ernstige irritatie aan ogen en luchtwegen, benauwdheid, glottis- en larynxoedeem

Boven LBW: Chemische pneumonitis, longoedeem, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Boriumtrifluoride werkt irriterend op de ogen en luchtwegen. Ernstige irritatie aan de luchtwegen door boriumtrifluoride kan leiden tot ontstekingen, ademhalingsmoeilijkheden, longoedeem en sterfte.
- Inhalatie van hoge concentraties boriumtrifluoride kan aanleiding geven tot oedeemvorming van de larynx en glottis, met het risico van verstikking.
- Boriumtrifluoride kan waarschijnlijk type I inhalatoire intoxicatie veroorzaken.
- Blootstelling aan Boriumtrifluoride kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, branderig gevoel, pijn

Oogcontact: bijtend, roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: n.v.t.

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: n.v.t. (gas)

Specifieke behandeling en materialen*:* geen.
Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7637-07-2 **Boron trifluoride** **BF_3** **UN-nr: 1008**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value adopted (except 10 min value for which time scaling was applied), 2hr value added

LBW: AEGL value adopted (except 10 min value for which time scaling was applied), 2hr value added

Date:28-11-2008 | AEGL document: Final, 2009

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	2.5	2.5	2.5	2.5	2.5	2.5	Threshold of irritation
AGW	53	37	29	23	18	9.2	(one-third of LBW values)
LBW	160	110	88	70	55	28	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: The VRW is based on a NOAEL for irritation. Rats exposed for 4 hours to boron trifluoride hydrate vapour/aerosol at a concentration of 24.6 mg/m³ had no abnormal findings, while rats exposed to the next higher concentration of 74.4 mg/m³ had histopathological changes in the larynx and tracheal bifurcation indicative of irritation. The concentration of 24.6 mg/m³ therefore represents a threshold for notable irritation and is the point of departure for the VRW derivation. A total uncertainty factor of 10 was applied. The irritation is a direct contact effect; therefore, an interspecies uncertainty factor of 3 was applied because the mechanism of action is not expected to vary among species. An intraspecies uncertainty factor of 3 was applied because the mechanism of action is not expected to vary greatly in subpopulations. The derived value was set equal at all time points because the endpoint is a threshold level for mild irritation.

AGW: Acute toxicity data meeting the definition of an AGW defined endpoint was not available. Therefore, the LBW values were divided by 3 to obtain a reasonable estimate. Dividing the LBW values by 3 is reasonable based on the steep dose-response curve for lethality: 3/10 rats died at 1010 mg/m³, while 9/10 rats died at 1540 mg/m³. In contrast to the 10 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.
The resulting AGW values are supported by the histopathological findings in rats exposed for 4 hours to 74.4 mg/mg³ that were indicative of mild irritation only. Considering that this is an effect less severe than the AGW a total uncertainty factor of 3 would have sufficed, leading to a comparable 4 h AGW.

LBW: The LBW derivation is based on 4-hour lethality data in rats, with a calculated $BMCL_{05}$ value of 553 mg/m³ (exposures were to liquid aerosols of boron trifluoride dihydrate; concentrations reported are based on boron trifluoride). Because boron trifluoride is a corrosive irritant, an interspecies uncertainty factor of 3 and an intraspecies uncertainty factor of 3 were applied because the mechanism of action (irritation) is not expected to vary greatly among species or among subpopulations, respectively. An intraspecies uncertainty factor of 3 is also supported by the steep dose-response curve for lethality, which indicates there is not much variability in the response within a population. Because the irritation occurring at the LBW level is no longer mild, but rather severe irritation leading to death, the point of departure is not set equal across all time-points. Time scaling was performed using $C^n * t = k$, with the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

No definitive data were found addressing any aspects of boron trifluoride toxicity in humans.

Clinical signs observed in rats during a 4 hour exposure to 1000-1500 mg/m³ boron trifluoride included reduced activity, closed eyes, excessive lacrimation, and excessive oral and nasal discharge. The high concentration group also exhibited gasping. Four-hours post exposure, clinical signs of respiratory distress

(dry rales, moist rales, gasping) and/or irritation (excessive oral and nasal discharge and lacrimation) were noted in most of the exposed animals. Mortality was observed in all dosage groups.

No data were found regarding the potential for boron trifluoride exposure to cause developmental or reproductive effects in humans or experimental animals.

H314: Causes severe skin burns and eye damage; H330: Fatal if inhaled.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived. No data were found regarding the potential for boron trifluoride to cause cancer in humans or in experimental animals.	Odour: Reported as a pungent, suffocating odour and as a pleasant, acrid odour. No LOA was derived due to lack of reliable data.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **2.5**	*AEGL-1* 2.5	*ERPG-1* 2		*IDLH:* 71 mg/m^3 (30 minutes)
AGW level **29**	*AEGL-2* 29	*ERPG-2* 30		
LBW level **88**	*AEGL-3* 88	*ERPG-3* 100		

Stofdocument deel A

CAS-nr: 7726-95-6 **Broom** **Br-Br** **VN-nr: 1744**

GEVI: 886

Synoniemen: (Eng.: Bromine) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	3,3	3,3	3,3	3,3	3,3	3,3
Alarmeringsgrenswaarden	AGW (mg/m³)	33	19	13	9,4	6,6	4,7
Levensbedreigende waarden	LBW (mg/m³)	640	250	130	73	40	22

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,150 ppm; 1 ppm = 6,65 mg/m³

Explosiegrens: kans op explosie door reacties; geen explosiegrenzen beschikbaar

Geur: stekende geur

LOA: 1,1 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: roodbruine, rokende vloeistof met een stekende geur

Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,0

Molecuulmassa:	159,8 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	3,6 g/100 ml (matig)
Verzadigde dampdruk:	233 mbar

Overige informatie

Publieke grenswaarde:

0,2 mg/m³ (15 min)

MAK: niet afgeleid

TLV-TWA: 0,65 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: mogelijk lichte tranenvloed

VRW → AGW: oog- en luchtwegirritatie, tranenvloed, hoesten

AGW → LBW: ernstige oog- en luchtwegirritatie, benauwdheid, chemische pneumonitis, longoedeem

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Broom werkt irriterend op de slijmvliezen van o.a. ogen en luchtwegen.
- Blootstelling aan broom kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, ernstige brandwonden, moeilijk genezend.

Oogcontact: bijtend, roodheid, pijn, slecht zien, ernstige brandwonden.

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: Bij verbranding aan de huid (vastgeplakte) kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en direct spoedeisende medische hulp inzetten. LET OP: De stof is sterk oxiderend en kan daardoor de kleding doen ontbranden.

ogen: Minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen. Blijven spoelen tijdens vervoer.

inslikken: Mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Ontsmetting bij inademen/inslikken

Inademing/inslikken kan tevens leiden tot larynx- en glottisoedeem, met risico op verstikking (asfyxie) door zwellingen in de keel. Intubatie (borgen van vrije luchtwegen), eventueel gevolgd door beademing moeten in ernstige gevallen z.s.m. worden uitgevoerd (door specialisten). Vandaar de noodzaak om direct spoedeisende medische hulp in te roepen.

Specifieke behandeling en materialen: geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7726-95-6 **Bromine** **Br-Br** **UN-nr: 1744**

Basis for the Dutch Intervention Values

VRW: Different point of departure than AEGL values, 2 hr value added

AGW: Different point of departure than AEGL values, 2 hr value added

LBW: Different point of departure than AEGL values, 2 hr value added

Date: 24-09-2009 | AEGL document: Final, 2010

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	3.3	3.3	3.3	3.3	3.3	3.3	Analogy with chlorine; Mild, transient effects on pulmonary function (humans)
AGW	33	19	13	9.4	6.6	4.7	Analogy with chlorine; Shortness of breath in sensitive human subject
LBW	640	250	130	73	40	22	Analogy with chlorine; Calculated threshold for lethality in animals (rats).

Derivation of the Dutch Intervention Values

VRW: Much of the data on bromine is old, unreferenced, anecdotal or conflicting. The bromine VRW levels were based on the chlorine VRW on a ppm-basis. This is in contrast to the derivation of the AEGL-1 levels.
Chlorine is considered to have a higher reactivity as compared to bromine. By using the same point of departure as for the bromine AEGL-1 levels, the resulting VRW-levels of bromine would be lower as compared to the VRW level (and AEGL-1 level) of chlorine. The AEGL-1 for bromine was based on exposure of 20 healthy human subjects to concentrations of 0.1 to 0.9 ppm (0.67 to 6.0 mg/m^3), for up to 60 minutes. Eye irritation, but no nose or throat irritation, occurred during a 30-minute exposure to 0.1 ppm (0.67 mg/m^3). At concentrations higher than 0.5 ppm (3.3 mg/m^3), there was a stinging and burning sensation of the conjunctiva. The 0.1 ppm (0.67 mg/m^3) concentration was used as point of departure.
Derivation chlorine VRW levels: The chlorine VRW was based on a study with in the first part, 31 male and female human volunteers, including a susceptible individual, which were exposed to 0.0, 0.5, 1.0, 2.0 ppm (0.0, 1.5, 2.9, 5.9 mg/m^3) for 4h or 0.5 and 1.0 ppm (1.5 and 2.9 mg/m^3) for 8h. The volunteers did not know the test concentration. In the second part of the study eight non-smoking males were exposed to 0.0, 0.5, 1.0 ppm (0.0, 1.5, 2.9 mg/m^3) chlorine for 8h. A 15-minute exercise period during each hour of exposure was designed to increase the average heart rate to 100 beats per minute. During the exposures, the volunteers filled out subjective questionnaires on sensation (e.g. smell, shortness of breath). A concentration of chlorine at 0.5 ppm (1.5 mg/m^3) for 4 h produced no sensory irritation and resulted in only mild transient effects on pulmonary parameters in the healthy individuals. Pulmonary changes in the susceptible individual were greater than those in healthy subjects, but did not result in symptoms above the definition of the VRW. The point of departure is supported by other studies with human volunteers of both genders, including healthy, atopic, and asthmatic subjects and/or periods of exercise to simulate conditions of stress (1-h 0.4 ppm (1.2 mg/m^3) no-effect concentration for individuals with airway hyper-reactivity or asthma). Because of this variety of human subjects tested, including the most susceptible groups, no uncertainty factor for differences in human sensitivity was applied. The 0.5-ppm (1.5 mg/m^3) exposure was considered a threshold for more severe effects, regardless of exposure duration. No time-scaling was applied. The use of the same value across all exposure durations is supported by the fact that the response to the irritant effects of chlorine appears to be concentration-dependent rather than time-dependent.

AGW: Much of the data on bromine is old, unreferenced, anecdotal or conflicting. The bromine AGW levels were based on the chlorine AGW on a ppm-basis. This is in contrast to the derivation of the AEGL-2 levels. Chlorine is considered to have a higher reactivity as compared to bromine. By using the same point of departure as for the AEGL-2 levels, the AGW-levels of bromine would be lower as compared to the AGW level (and AEGL-2 level) of chlorine. The AEGL-2 bromine values were based on the same study as used for the derivation of the AEGL-1 bromine values, using the highest concentration of 0.9 ppm (rounded to 1 ppm (6.7 mg/m^3)) for 30 minutes as point of departure for the calculation. The volunteers exposed up to this concentration reported prickling or stinging of the eyes and nose and throat irritation.
Derivation chlorine AGW levels: The AGW values were based on the same studies used to derive the VRW value. In those studies healthy human volunteers experienced transient changes in pulmonary function measurements and a susceptible individual experienced an asthma-like attack (shortness of breath and wheezing) following a more than 4-h exposure to chlorine at 1.0 ppm (2.95 mg/m^3). The susceptible individual remained in the exposure chamber for the full 4 h before the symptoms occurred. Because both genders were tested, subjects were undergoing light exercise (making them more vulnerable to sensory irritation), and a susceptible individual was tested, no uncertainty factor was applied to account for differences in human sensitivity. If an uncertainty factor for intraspecies differences was applied, then the AGW-values would conflict

with the VRW values.
Similar effects and symptoms in individuals with airway hyper-reactivity or asthma exposed at 1.0 ppm (2.95 mg/m^3) for 1 h in another study supports the application of an intraspecies uncertainty factor of 1 for the 4-h concentration. Time-scaling was performed using the equation C^n x t = k, using n=2. This value was calculated by regression analysis of the percent of subjects reporting a nuisance irritation response to concentrations at 1 ppm (2.95 mg/m^3) and 2 ppm (5.90 mg/m^3) over exposure durations of 30 min and 120 min. In the AEGL document the 10 minute value was set equal to the 30 minute value so that the highest exposure of 4.0 ppm (11 mg/m^3) in the controlled human study was not exceeded. Considering that this highest human exposure level was established after 2 hours of exposure time scaling to 10 minutes seems reasonable.

LBW: Much of the data on bromine is old, unreferenced, anecdotal or conflicting. The bromine LBW levels were based on the chlorine LBW on a ppm-basis. This is in contrast to the derivation of the AEGL-3 levels. Chlorine is considered to have a higher reactivity as compared to bromine. By using the same point of departure as for the AEGL-3 levels, the LBW-levels of bromine would be lower as compared to the LBW level of chlorine. The AEGL-3 levels of bromine were based on two lethality studies with mice describing the inhalation toxicity of chlorine and bromine. Although both studies reported LC_{50} values for chlorine that were lower than those reported in more recent well-conducted studies, the study that reported the lower lethal concentrations for chlorine was used for the derivation of the LWB for bromine. The data in this study showed a clear concentration-response relationship. Using probit analysis, a 30-minute LC_{50} value of 204 ppm (1356 mg/m^3) and a 30-minutes LC_{01} of 116 ppm (771 mg/m^3) were calculated. The 116 ppm LC_{01} was divided by a combined uncertainty factor of 10. A factor 3 was applied for intraspecies difference because the mouse being the most sensitive species in halogen lethality tests. For intraspecies differences also a factor 3 was applied, because at high concentrations bromine is corrosive to the mucous membranes of the respiratory system and these effects are not expected to differ greatly among individuals. The LBW values were scaled across time using the relationship $C^{2.2}$ x t = k, with n (=2.2) based on the results of the second lethality study with mice.
Derivation chlorine LBW levels: The LBW values were based on a lethality study in rats, including three exposure durations of 10, 30 and 60 minutes and four to six concentrations. Probit analysis using DoseResp was performed and yielded and n of 1.1 and LC_{01} values for the 10 min, 30 min, 1-, 2-,4-, and 8hrs exposure durations of 2856, 1090, 594, 324, 176, and 96 mg/m^3, respectively, which were used as point of departure for LBW derivation. An uncertainty factor of 3 was used to account for interspecies differences because the data show that interspecies differences were within a factor of approximately 2 for lethality. In addition, chlorine is a contact site, direct-acting toxicant, and there is likely to be little difference between species in the response of biologic tissues to chlorine exposure. Also, for intraspecies differences, corrosive gases acting at the point of contact would predict low variability in a population; thus an uncertainty factor of 3 is applied to protect susceptible individuals.

Additional toxicological information (including relevant results of a general literature search, if any)

Bromine, a strong oxidizing agent, is a respiratory irritant and can cause pulmonary oedema in humans and animals. Bromine gas reacts at the site of contact and metabolic/kinetic considerations are not relevant regarding the determination of the VRW, AGW and LBW values. The irritating potential of mucus membrane irritants like bromine may be related to their water solubility. Individuals with asthma or other respiratory diseases may be more susceptible to the effects of respiratory irritants than healthy individuals. No data on bromine and the asthmatic population were located.

One study reported that a 4-hour exposure to 15 ppm affected spermatogenesis in male mice: further details were not reported. No further data concerning the reproductive and developmental effects of bromine in animals were identified in the available literature.

There are no additional relevant toxicological data apart from abdominal pain and diarrhoea and measles-like eruption of the trunk and extremities after prolonged exposure of several hours.

H314: Causes severe skin burns and eye damage; H330: Fatal if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

No data concerning the chronic toxicity or carcinogenicity of bromine in animals were located in the available literature.

Odour and derivation of the LOA value

The odour of bromine is characterized as pungent and strong. The odour threshold has been variously reported at approximately 0.01 to 3.8 ppm (0.07-25 mg/m^3).

ODT: 0.011 ppm (0.07 mg/m^3) [AIHA1989]
LOA = 11.8 * 0.07 * 1.33 = 1.1 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/ODT) + 0.5. A correction factor of 1.33 is applied to this value)

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **3.3**	*AEGL-1* 0.22	*ERPG-1* 0.67		*IDLH:* 19.9 (30 min)
AGW level **13**	*AEGL-2* 1.6	*ERPG-2* 3.3		
LBW level **130**	*AEGL-3* 57	*ERPG-3* 33		

Stofdocument deel A

CAS-nr: 10035-10-6 **Broomwaterstof** **H-Br** **VN-nr: 1048** **GEVI: 268**

Synoniemen: waterstofbromide, (Eng: hydrogen bromide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	3,4	3,4	3,4	3,4	3,4	3,4
Alarmeringsgrenswaarden	AGW (mg/m³)	470	220	140	87	55	55
Levensbedreigende waarden	LBW (mg/m³)	1400	670	420	260	160	160

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,297 ppm; 1 ppm = 3,37

Explosiegrens: geen data

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos, onder druk tot vloeistof verdicht, gas

Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,8

Molecuulmassa:	80,9 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	193 g/ 100 ml (zeer goed)
Verzadigde dampdruk:	21300 mbar

Overige informatie

Publieke grenswaarde: 6,7 mg/m³ (15 min, geen 8 uur waarde)

TLV-TWA: 10 mg/m³

MAK: 6,7 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: mogelijk lichte oog- en luchtwegirritatie

VRW → AGW: oog- en luchtwegirritatie, tranenvloed, hoesten, lichte benauwdheid

AGW → LBW: ernstige oog- en luchtwegirritatie, pijn op de borst, benauwdheid, longontsteking, longoedeem

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Broomwaterstof veroorzaakt irritatie van de slijmvliezen van ogen en luchtwegen.
- Broomwaterstof kan bij inhalatie longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, pijn, ernstige wonden.

Oogcontact: bijtend, roodheid, pijn en slecht zien.

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: n.v.t. (gas), maar in geval van *bevriezingswonden*: aan de huid vastgevroren kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en direct spoedeisende medische hulp inzetten.
In geval van huidcontact met een *HBr-oplossing*: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en direct spoedeisende medische hulp inzetten.

ogen: n.v.t. (gas), maar in geval van *bevriezingswonden* of oogcontact met een *HBr-oplossing*: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen. Blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas), maar in geval van inslikken van een *HBr-oplossing*: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Ontsmetting bij inademen/inslikken

Inademing/inslikken van sterke zuren kan tevens leiden tot larynx- en glottisoedeem, met risico op verstikking (asfyxie) door zwellingen in de keel. Intubatie (borgen van vrije luchtwegen), eventueel gevolgd door beademing moeten in ernstige gevallen z.s.m. worden uitgevoerd (door specialisten). Zet derhalve direct spoedeisende medische hulp in.

Specifieke behandeling en materialen: geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 10035-10-6 **Hydrogen bromide** **H-Br** **UN-nr: 1048**

Basis for the Dutch Intervention Values

VRW: AEGL-1 value is adopted, 2-hr value added

AGW: Same rationale as for AEGL (one third of LBW values)

LBW: Same point of departure as for AEGL, but using different value for *n*; 2-hr value added, and 8h value set equal to 4h value

Date: November 2015 | AEGL document: Final, 2014

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	3.4	3.4	3.4	3.4	3.4	3.4	Slight irritation (nose) in humans
AGW	470	220	140	87	55	55	One third of LBW values
LBW	1400	670	420	260	160	160	Threshold for lethality animals

Derivation of the Dutch Intervention Values

VRW: For the derivation of the VRW values the threshold for nose irritation in humans inhaling 3 ppm HBr (10 mg/m³) for several minutes was selected as point of departure. This concentration was considered a NOAEL for notable discomfort. An uncertainty factor for intraspecies differences of 3 was considered suitable, because the threshold for sensory irritation is not expected to vary greatly among individuals and the effect of slight (nose) irritation is below the definition of the VRW. Because adaptation to slight irritation occurs, the resulting 1 ppm (3.37 mg/m³) concentration was used for all exposure durations. This value was also considered to be protective to asthmatics, because at low concentrations HBr is scrubbed well in the upper nasal passage. The 1 ppm concentration is supported by the VRW values for other hydrogen halides of 1.0 ppm and 1.8 ppm for HF and HCl, respectively.

AGW: The AGW values for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data. The only study of HBr that addressed effects that meet the definition of an AGW, severe nasal lesions, was a study on hydrogen halides by Stavert et al. (1991). Nevertheless, this study was not considered a suitable basis for derivation of AGW values because 8% of the animals died after exposure to HBr at 1300 ppm (4375 mg/m³), only one concentration was tested and the number of animals tested was not specified.

LBW: The basis for the LBW values was the 1-hour $BMCL_{05}$ of 1239 ppm (4170 mg/m³) and the BMC_{01} of 1456 ppm (4900 mg/m³) for HBr in rats. The 1-hour $BMCL_{05}$ of 1239 ppm (4170 mg/m³) was chosen as the point of departure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. In contrast to the AEGL, the basis for time scaling, using the equation $C^n \times t = k$, was derived from data from the more robuste dataset of the toxicological comparable chemical, HCl, providing an n-value of 1.48 to scale to shorter and longer time points. To maintain consistency with other hydrogen halogenides, the 8 hour value was set equal to the 4 hour value, as performed for the most potent hydrogen halogenide HF.

Additional toxicological information (including relevant results of a general literature search, if any)

Although the data base for HBr is sparse, additional data on the toxicity of HBr relative to those of hydrogen fluoride (HF) and hydrogen chloride (HCl) were available for comparison purposes. The databases for HCl and HF are robust. For the endpoint of lethality, the relative toxicities to the rat and mouse are in the order of HF>HBr>HCl. When considering sublethal concentrations the severity and extent of the lesions to the upper respiratory tract were in the order HF>HCl>HBr, although the severity and extent of the lesions were very similar among the three chemicals. The data also showed that all three chemicals are well scrubbed in the upper respiratory passages. Individuals with asthma may respond to exposure to respiratory irritants such as HBr and HI with increased bronchial responsiveness, but no information on the relative susceptibility to healthy individuals was located. Stress and physical activity may cause greater deposition and pulmonary irritation than when an individual is at rest.

No information regarding reproductive and/or developmental toxicity located for HBr.

H314: Causes severe skin burns and eye damage; H335: May cause respiratory irritation.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified Derivation of the carcinogenic risk potency (CRP): not derived No information on genotoxicity and chronic toxicity/carcinogenicity in animals was located for HBr.	Odour: sharp. irritating An unreliable odour threshold of 2 ppm (6.7 mg/m^3) was reported in literature (Ruth, 1987) No LOA was derived due to lack of reliable data.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **3.4**	*AEGL-1* 3.4	*ERPG-1* Not derived		*IDLH:* 30 ppm (30 min) or 101 mg/m^3
AGW level **140**	*AEGL-2* 135	*ERPG-2* Not derived		
LBW level **420**	*AEGL-3* 400	*ERPG-3* Not derived		

Stofdocument deel A

CAS-nr: 106-97-8 **Butaan** CH_3-$(CH_2)_2$-CH_3 **VN-nr: 1011**

GEVI: 23

Synoniemen: n-butaan, butagas (Engels: n-butane) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	24.000 **	17.000 **	17.000 **	17.000 **	17.000 **	17.000 **
Alarmeringsgrenswaarden	AGW (mg/m³)	58.000 ***	40.000 ***	40.000 ***	40.000 ***	40.000 ***	40.000 ***
Levensbedreigende waarden	LBW (mg/m³)	190.000 ***	130.000 ***	130.000 ***	130.000 ***	130.000 ***	130.000 ***

Datum vaststelling: 13-05-2009

Conversiefactor: 1 mg/m³ = 0,414 ppm; 1 ppm = 2,42 mg/m³

Explosiegrens: LEL= 1,3 vol% ≈ 31.000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

** berekende interventiewaarde hoger dan 50% LEL

*** berekende interventiewaarde hoger dan LEL

Geur: zwakke, onaangename geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas

Brand: zeer brandgevaarlijk

Relatieve dichtheid gas: 2,0

Molecuulmassa: 58,1 g/mol
Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: niet
Verzadigde dampdruk: 2100 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: 2400 mg/m³
TLV-TWA: 1900 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: hoofdpijn, slaperigheid, lichte benauwdheid

AGW → LBW: ademnood, bewustzijnsdaling, hartritmestoornissen

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Butaan veroorzaakt asfyxie door verdringing van zuurstof in de lucht. Primaire doelorganen zijn de hersenen en het hart.
- Risico op letsel en sterfte door explosie bestaan al beneden de concentratie waarbij letsel en sterfte door toxiciteit optreden.
- Butaan heeft een steile concentratie-respons curve.

Effecten bij blootstelling aan vloeistof

Huidcontact: bij bevriezing: roodheid, pijn, blaren

Oogcontact: bij bevriezing: roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd.

CRP: niet afgeleid.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, en arts raadplegen.

Ontsmetting vloeistof

huid: *bij bevriezing*: aan de huid vastgevroren kleding NIET lostrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.

ogen: *bij bevriezing*: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (+31(0)30-274 88 88) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 106-97-8 **n-Butane** **CH_3-$(CH_2)_2$-CH_3** **UN-nr: 1011**

Basis for the Dutch Intervention Values

VRW: Same point of departure as AEGL, different time-scaling applied, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 13-05-2009 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	24,000 **	17,000 **	17,000 **	17,000 **	17,000 **	17,000 **	Threshold of CNS depression in humans
AGW	58,000 ***	40,000 ***	40,000 ***	40,000 ***	40,000 ***	40,000 ***	Disabling CNS depression in animals
LBW	190,000 ***	130,000 ***	130,000 ***	130,000 ***	130,000 ***	130,000 ***	LC_{01} for lethality in animals

* value higher than 10% of LEL; ** value higher than 50% of LEL; value higher than LEL

Derivation of the Dutch Intervention Values

VRW: Data from a study in human volunteers formed the basis for VRW derivation. From the study description it was concluded that 10 minute exposure to 10,000 ppm (24,000 mg/m³) can be regarded as a boundary for the drowsiness reported, some drowsiness may be noticed but it is concluded that this will not be experienced as discomfort. Although the study was performed with small groups of volunteers (n=3 or 6) of a relatively young age (20-30 years) an intraspecies uncertainty factor of 1 is considered adequate for the following reasons. Firstly, the concentration-response curve for CNS-effects appears to be very steep and thus the interindividual variability will be relatively small. Secondly, no noticeable irritation was reported up to a concentration of 100,000 ppm (240,000 mg/m³). Thirdly, the use of an intraspecies uncertainty factor of 3 will lead to VRW values that appear to be unrealistically low for butane (*e.g.* in comparison with the occupational standards). In contrast to the AEGL, time extrapolation was performed from 10 min to 30 minutes using the equation $C^n * t = k$, using a factor of n=3. The use of an n value of 3 was based on evaluation of data on anesthetic effects of butane that indicated that n will be relatively high. This is consistent with the fact that, in analogy to other anesthetics the effects of butane are assumed to be concentration dependent rather than time dependent. The effects of CNS depressing substances are assumed to be solely concentration dependent after reaching steady-state (which is within 30 min of exposure). Therefore the 30 min VRW value was adopted for the 1h, 2h, 4h and 8h time points. It is noted that all calculated VRW values are higher than 10% of the lower explosive limit.

AGW: The only available starting point adequate for AGW is provided by a study in which guinea pigs were exposed for 2 hours to a butane concentration varying between 50,000 and 56,000 ppm (120,000 and 140,000 mg/m³). Since the animals were able to walk the observed “dazed appearance” is considered not to be sufficiently serious to impair escape, and the lower value in the test range (i.e. 50,000 ppm, 120,000 mg/m³) is considered to be an appropriate starting point for the derivation of AGW. All the more, since the anesthetic effects are considered to be predominantly concentration dependent. A total uncertainty factor of 3 is considered sufficient for differences between individuals and interspecies differences. The concentration-response curve appears to be very steep indicating that a large factor is not necessary. Further, a higher uncertainty factor would lead to unrealistically low AGW values that would be rather similar to the proposed VRW values. The effects of CNS depressing substances are assumed to be solely concentration dependent after reaching steady-state (which is within 30 min of exposure). Therefore, the AGW values for 30 minutes, and 1, 4 and 8 hours of exposure will be set equal to the 2-hour concentration. Time extrapolation was performed from the 30 minute value to the 10 minutes using the equation $C^n * t = k$, using a factor of n=3 (see also derivation VRW). It is noted that the calculated AGW values are higher than the lower explosive limit.

LBW: A LC_{01} of 160,000 ppm (390,000 mg/m³) for mice and 172,000 ppm (420,000 mg/m³) for rats was calculated from a study in which mice and rats were exposed for 2 and 4 hours, respectively. The

reported data (LC_{16}, LC_{50}, LC_{84}) indicate that the concentration-response curve for a 2-hour exposure in mice and a 4-hour exposure in rats are very similar. The 2-hour LC_{01} for mice is chosen as point of departure for derivation of LBW values, as it is the lowest value in a possibly more susceptible species. A total uncertainty factor of 3 was considered sufficient for differences between individuals and interspecies differences for the following reasons. A species with a relatively high susceptibility is used as starting point. The concentration-response curve appears to be very steep indicating that a large factor is not necessary. Further, a higher uncertainty factor would lead to unrealistic low LBW values, which would be similar to the proposed AGW values. Mortality due to butane is preceded by CNS depression. Hence, after a steady-state has been reached no increase of effect-size by exposure duration is expected. Therefore, the LBW values for 30 minutes, and 1, 4 and 8 hours of exposure were set equal to that for the 2-hour exposure. The LBW values for the 10-min exposure was derived by time scaling the 30 minute value according to the dose-response regression equation $C^n * t = k$, using n=3 (see also derivation VRW). It is noted that the calculated LBW values are higher than the lower explosive limit.

Additional toxicological information (including relevant results of a general literature search, if any)

The toxicity of butane is low. Most cases of butane intoxication in humans originate from butane abuse or suicide attempts. The predominant effects observed in cases of high exposure are CNS-effects and cardiac effects. Cases of butane intoxication after repeated exposure are associated with brain damage and cardiac arrhythmias (tachycardia, fibrillation). Butane was reported to cause cardiac sensitization in dogs but the studies did not provide detailed information on exposure concentrations and duration or were performed under anesthesia. The gas can be suffocating due to displacement of oxygen in the air. Inhalation can cause shortness of breath, headache, drowsiness, and unconsciousness.

There is no information about more susceptible subpopulations.

Inhalation of butane during pregnancy (27th and 30th week of gestation) high enough to produce unconsciousness in the mother caused clearly underdeveloped brains in two fetuses. In both cases effects were considered to be due to intra-uterine anoxia. No information concerning reproduction or developmental toxicity of n-butane in experimental animals was found.

No harmonized H-sentences for human health

Carcinogenicity and derivation of the CRP value

IARC classification: not classified.

No carcinogenic risk potency (CRP) was derived.

No information on carcinogenicity of n-butane in humans or experimental animals was found.

Odour and derivation of the LOA value

Odour: faint disagreeable odor

No LOA was derived due to lack of reliable data.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **17,000**	*AEGL-1* 13,000	*ERPG-1* not derived		*IDLH:* not derived
AGW level **40,000**	*AEGL-2* 41,000	*ERPG-2* not derived		
LBW level **130,000**	*AEGL-3* 130,000	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 106-99-0 **1,3-Butadieen** $CH_2=CHCH=CH_2$ **VN-nr: 1010**
GEVI: 239

Synoniemen: bivinyl, erythreen, vinylethyleen (Engels: 1,3-butadiene) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m³)**	1500	1500	1500	1500	1500	1500
Alarmeringsgrenswaarden	**AGW (mg/m³)**	22.000*	15.000**	12.000*	9500*	7600*	6000*
Levensbedreigende waarden	**LBW (mg/m³)**	89.000*	62.000***	49.000***	39.000***	31.000***	15.000**

Datum vaststelling: 13-05-2009 Conversiefactor: 1 mg/m³ = 0,444 ppm; 1 ppm = 2,25 mg/m³

Explosiegrens: LEL = 1,1 vol% ≈ 25.000 mg/m³
* berekende interventiewaarde hoger dan 10% LEL
** berekende interventiewaarde hoger dan 50% LEL
*** berekende interventiewaarde hoger dan LEL

Geur: milde aromatische, rubberachtige geur
LOA: 8,5 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas
Brand: zeer brandgevaarlijk kan spontaan aan lucht ontbranden bij snel uitstromen

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa:	54,1 g/mol
Zuurgraad:	geen data
LogKow:	2,0
Wateroplosbaarheid:	Slecht
Verzadigde dampdruk:	2400 mbar

Overige informatie

Publieke grenswaarde: 2 mg/m³ (8 uur)
MAK: niet afgeleid
TLV-TWA: 4,5 mg/m³

Vormt explosief mengsel met lucht
Zeer vluchtig

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	geen effecten
VRW → AGW:	irritatie ogen, huid en luchtwegen, keelpijn, hoesten
AGW → LBW:	benauwdheid, hoofdpijn, duizeligheid, misselijkheid, tachycardie, opwinding, sufheid, bewustzijnsdaling
Boven LBW:	convulsies, hartritmestoornissen, ademstilstand, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- 1,3-butadieen werkt irriterend op de ogen, luchtwegen en de huid.
- De stof veroorzaakt effecten op het CZS, waarbij zowel stimulatie als depressie op kan treden.
- Overlijden treedt op door ademstilstand of ventrikel-tachycardie of –fibrillatie.
- 1,3-butadieen is mogelijk ook na kortdurende blootstelling kankerverwekkend. De **CRP** ligt onder de VRW.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, pijn, blaren
Oogcontact: irritatie, slecht zicht

Carcinogeniteit

IARC classificatie: 1
CRP: 615 mg/m³ (zie opmerking bij CRP in Deel B)

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust en arts raadplegen.

Ontsmetting vloeistof
huid: *bij bevriezingsletsel:* aan de huid vastgevroren kleding NIET lostrekken, spoelen met veel water / kleding verwijderen en arts raadplegen.
ogen: *bij damp:* uitspoelen met water (evt. contactlenzen verwijderen), *bij bevriezingsletsel:* minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: n.v.t. (gas).

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 106-99-0 **1,3-butadiene** **CH_2=CHCH=CH_2** **UN-nr: 1010**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 13-05-2009 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	1500	1500	1500	1500	1500	1500	Slight effects on eyesight in humans
AGW	22,000 **	15,000 **	12,000 **	9500 *	7600 *	6000 *	No AGW effects in humans
LBW	89,000 ***	62,000 ***	49,000 ***	39,000 ***	31,000 ***	15,000 **	LC_{01} for lethality rats

* value is higher than 10% of the LEL; ** value is higher than 50% of the LEL; *** value is higher than LEL

Derivation of the Dutch Intervention Values

VRW: Only one adequate human study is available that addresses VRW endpoints. Two males were exposed to nominal concentrations of 2000 ppm (4500 mg/m³) 1,3-butadiene for 7 hours, 4000 ppm (9000 mg/m³) for 6 hours, and 8000 ppm (18,000 mg/m³) for 8 hours. These exposure times are total times of actual exposure with all exposures interrupted for a one-hour lunch break in the middle of the exposure period. Subjective symptoms reported at 2000 (4500 mg/m³) and 4000 ppm (9000 mg/m³) included slight smarting of the eyes and difficulty in focusing. No subjective complaints were reported at 8000 ppm (18,000 mg/m³), according to the authors probably because of slight anxiety concerning the possibility of an explosion. Both subjects felt particularly alert. Results of a tapping test and a steadiness test revealed no differences in performance between the exposures. It is assumed that the absence of subjective symptoms at 8000 ppm (18,000 mg/m³) could indeed have been due to an increased awareness. If so, this would indicate that the complaints were of very minor severity, and possibly sub-VRW effects. The 7-hour exposure to 2000 ppm (4500 mg/m³) is therefore considered to be an appropriate point of departure without a further modifying factor. However, since only two humans were exposed an intraspecies factor of 3 is considered appropriate. Since the type of effect (local eye effects) is considered to be concentration- rather than time related VRW values will be set equal for all exposure periods.

AGW: Two studies are considered relevant for the derivation of AGW. The above mentioned study with two human volunteers showed no AGW effects during an 8-hour exposure to 8000 ppm (18,000 mg/m3). In a 1979 study, groups of 20 rats per sex were exposed for 6 h/d for 5 d/w for 3 months to 1000, 2000, 4000 or 8000 ppm (2250, 4500, 9000 and 18,000 mg/m³) 1,3-butadiene. The animals were thoroughly examined but no adverse effects due to 1,3-butadiene exposure were found. The 8000 ppm (18,000 mg/m³) exposure concentration, the highest concentration tested, is a NOAEL in semichronic exposure. This concentration is therefore a very conservative point of departure for AGW. The use of human data is preferable to the rat data as point of departure for AGW. The 8-hour exposure to 8000 ppm (18,000 mg/m³) is considered to be a conservative point of departure (no effects observed at the highest concentration tested) and an intraspecies factor of 3 is considered sufficient. No effects were observed in rats exposed to 8000 ppm (18,000 mg/m³) for 6 h/d, 5 d/w for 3 months. Because this study provides a very conservative point of departure (highest concentration tested, no effects observed, 3-month exposure) a total UF of 3 can be considered sufficient. This would lead to AGW values that are very similar to the proposed values. Time scaling was performed using the equation $C^n \times t = k$, and a default value of n=3 for extrapolation to shorter time periods. In contrast to the 10 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: There are no adequate human data for derivation of LBW values. Therefore, LBW will be based on animal data. The rat is concluded to be the most appropriate model for humans for non-neoplastic endpoints. The only study that provides adequate data is one where rats were exposed to butadiene for 4 hours. Since this study does not provide the individual experimental data but only the LC_{16}, LC_{50}, and

the LC_{84} as obtained by probit analyses, benchmark dose-response modelling is not possible. However, the LC_{01} can be calculated since the mean is known and the SD of the underlying lognormal distribution can be derived from these data. The calculated 4-hour LC_{01} for rats is then 41,000 ppm (92,000 mg/m^3). A total uncertainty factor of 3 is considered sufficient for toxicokinetic and toxicodynamic differences between individuals and interspecies differences for the following reasons. First, a higher uncertainty factor would lead to unrealistically low values for LBW values in comparison with the experiment showing that two humans showed no clear signs of toxicity during exposure to 8000 ppm (18,000 mg/m^3) for a total of 8 hours. Second, in vitro data obtained with human tissue samples show that overall the biotransformation rate in human liver is rather comparable to that in rats. Because of this and since humans have an approximately four times lower ventilation rate than rats, a higher factor is not warranted. Time scaling was performed using C^n x t = k with default values n=1 for extrapolation to longer time periods and n=3 for extrapolation to shorter time periods. In contrast to the 10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

The acute toxicity of 1,3-butadiene is rather low. It irritates the eyes and respiratory tract. The substance may cause effects on the central nervous system, resulting in lowering of consciousness. Rapid evaporation of 1,3-butadiene may cause frostbite.

No relevant human data were available on developmental or reproductive toxicity. Repeated exposure studies in rats and mice showed adverse effects on fetal development, but only at exposure concentration that also caused maternal toxicity. In two fertility studies in which male mice were exposed for 5 days effects were reported on sperm quality and on offspring. However, the relevance of these effects after single exposures is uncertain. No fetal abnormalities were observed in mice in a single exposure study.

H340: May cause cancer; H340: May cause genetic defects

Carcinogenicity and derivation of the CRP value

IARC classification: 1 (carcinogenic to humans)

Derivation of the carcinogenic risk potency (CRP):
10^{-4} risk level after inhalation: 2.81 * 10^{-3} mg/m^3 [AEGL]
CRP = (10^{-4} risk level * average life span in hours)/DRCF = (2.81 * 10^{-3} * 613,200) /2.8 = 615 mg/m^3

There is "sufficient evidence" from epidemiologic studies of exposed workers to consider 1,3-butadiene carcinogenic to humans. Excesses of lymphohemato-poietic cancers have been observed in 1,3-butadiene polymer production workers and monomer production workers in North America. A significant excess of leukemias was observed in polymer production workers, and significant excesses of non-Hodgkin's lymphomas. (EPA, IRIS, 2002b)
Note: Although repeated exposure to 14 mg/m^3 induces tumors in mice, no tumors were observed in mice during a 2-year follow-up after a single 2-hour exposure up to 22,000 mg/m^3.

Odour and derivation of the LOA value

Odour: mildly aromatic, rubbery

OT_{50}: 0.24 ppm (0,54 mg/m^3) [AEGL, 2008]
LOA = 11.8 * OT_{50} * 1.33 = 8,5 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is far lower than the VRW, AGW and LBW levels at all time points.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **1500**	*AEGL-1* 1500	*ERPG-1* 23		*IDLH:* 4500 (30 minutes)
AGW level **12,000**	*AEGL-2* 12,000	*ERPG-2* 450		
LBW level **49,000**	*AEGL-3* 50,000	*ERPG-3* 11,000		

Stofdocument deel A

CAS-nr: 123-86-4 **n-Butylacetaat** $CH_3\text{-}COO\text{-}(CH_2)_3\text{-}CH_3$ **VN-nr: 1123** **GEVI: 33**

Synoniemen: azijnzuur n-butylester, n-butylethanoaat (Engels: n-butylacetate) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	70	70	70	70	70	70
Alarmeringsgrenswaarden	AGW (mg/m³)	700	700	700	700	700	700
Levensbedreigende waarden	LBW (mg/m³)	14.000*	9.600*	7.600*	6.000*	4.800	2.400

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,207 ppm; 1 ppm = 4,833 mg/m³

Explosiegrens: 1,2 vol% ≈ 12.000 ppm ≈ 58.000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

Geur: zoete (banaan)geur

LOA: 24 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,04

Molecuulmassa:	116,2 g/mol
Zuurgraad:	pH 6,2 (0,5 g/100 ml)
LogKow:	2,3
Wateroplosbaarheid:	0,5 g/100 ml (slecht)
Verzadigde dampdruk:	12 mbar

Overige informatie

Publieke grenswaarde:
geen
MAK: 480 mg/m³
TLV-TWA: 725 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: keelpijn en hoesten

VRW → AGW: irritatie van ogen, neus en keel, duizeligheid, hoofdpijn

AGW → LBW: oogpijn, (brandende) neuspijn, (brandende) keelpijn, benauwdheid op de borst, duizeligheid, bewustzijnsdaling

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Acute blootstelling resulteert in irritatie van ogen, neus en keel.
- De vloeistof ontvet de huid.
- Erg hoge concentraties kunnen leiden tot effecten op het CZS, met als gevolg bewustzijnsdaling.
- Effecten op cardiovasculair systeem.
- Sterfte is waarschijnlijk het gevolg van CZS depressie en niet door direct effect (irritatie) van ademhalingsorganen.

Effecten bij blootstelling aan vloeistof

Huidcontact: prikkeling, droge huid, roodheid

Oogcontact: prikkeling, roodheid en pijn

Carcinogeniteit

IARC classificatie: geen
CRP: niet afgeleid.

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en bij aanhoudende klachten arts raadplegen.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen*.
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 123-86-4 **n-Butylacetate** CH_3-COO-$(CH_2)_3$-CH_3 **UN-nr: 1123**

Basis for the Dutch Intervention Values

VRW: Based on information as described in ERPG-document, different values are derived, other time-points added.

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added.

Date: 31-10-2017 **ERPG 2014**

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	70	70	70	70	70	70	Threshold for irritation to the throat in humans
AGW	700	700	700	700	700	700	Severe throat irritation and eye and nose irritation in humans
LBW	14,000*	9,600*	7,600*	6,000*	4,800	2,400	Threshold for lethality in rats.

* value higher than 10% of LEL

Derivation of the Dutch Intervention Values

VRW: The irritation produced by acute exposure to n-butyl acetate in healthy, non-smoking human subjects without any history of occupational solvent exposure was studied in three chamber experiments. Exposure levels tested in the different experiments were 350, 700, 1,050, and 1,400 mg/m³ in four 20-min sessions with 24 h rest periods between sessions (n=12f+ 12m), 70 and 1,400 mg/m³ in two 20 min sessions with 7 day rest periods between sessions (n=14f + 9 m), and 70 and 700 mg/m³ in two 4 h sessions with time interval of 7 days (n=5f + 7m). Rating scales, various measures of eye irritation, and pulmonary functions were used to evaluate the irritation produced by the exposures in different parts of the study. Irritation to the throat, breathing difficulties and sensation of a bad smell were reported in experiment 3 (4 hours to 70 or 700 mg/m³) as well as a borderline significance of irritation to the nose. These levels are supported by a study in healthy human volunteers who were exposed for 2-5 minutes to 200 ppm, equal to 967 mg/m³ (throat irritation) and 3-5 minutes at 300 ppm, equal to 1450 mg/m³ (eye and nose irritation and severe throat irritation). The effects reported after 20 min of exposure to 70 mg/m³ (very slight nose and throat irritation) were not considered significant and below the level of discomfort, and therefore used as point of departure for derivation of the VRW. Because effects were marginal, no uncertainty factor was applied to account for intraspecies differences. Time scaling was not applied, because exposure duration did not significantly influence the severity of the effects as is demonstrated by the comparable effects observed after 20 min exposure to 1400 mg/m³ and 4 hour exposure to 700 mg/m³.

AGW: For derivation of the AGW values, the same study was considered as for the VRW values. The highest 4-hour exposure concentration of 700 mg/m³ was chosen as point of departure. Because effects (irritation to eyes, nose and throat scored in the lower regions of the scale) were considered sub AGW, no uncertainty factor was applied to account for intraspecies differences. Time scaling was not applied, because exposure duration did not significantly influence the severity of the effects.

LBW: Eight acute inhalation toxicity studies have been performed in rats with very varying outcomes. The results have been compared and the reasons for the differences have been investigated thoroughly (Norris et al, 1997, WHO 2005). No explanation could be found, nor could results be reproduced even within laboratories. The study resulting in the lowest LC_{50} (head-only to aerosol) was not used as starting point, because none of the other nose- or head- only studies even came close to this level. In the study resulting in the next lowest LC_{50} (whole body aerosol) rats (5/sex/group) were exposed to 283 and 540 ppm (1368 and 2610 mg/m³). All rats died at the highest exposure concentration, whereas none of the rats died at the low exposure concentration. Using the lowest level as threshold for lethality, the default uncertainty factor of 10 (3x3) and the default values for time scaling to longer and shorter durations, respectively would result in unrealistic low LBW values (390, 270, 220, 170, 140, 68 mg/m³) in comparison with the human data used as basis for VRW and AGW. Therefore, these studies were not used as point of departure. The more so, since in repeated exposure studies at much higher concentrations no deaths were reported.
In two sub-chronic toxicity studies (14 wks and 13 wks) using exposure concentrations up to 3000 ppm n-butylacetate vapour, apart from transient signs of sedation and effects on body- and organ weights, no life threatening effects were observed. This provides sufficient support to use the acute toxicity studies yielding higher LC_{01} values for selecting a point of departure. Because no explanation could be found for the different findings between laboratories and within laboratories, the results found in three studies from one laboratory, all using whole body exposure to aerosols or vapours, were combined in DoseResp. A 4-hour LC_{01} of 4.798×10^4 mg/m³ was calculated and used as point of departure for the LBW. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$ with the default n = 1 and n= 3, to calculate to longer and shorter

durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

In the presence of water n-butylacetate slowly hydrolyses to acetic acid and n-butanol.

The substance does not elicit reproductive or developmental effects.

Carcinogenicity studies with n-butylacetate were not found.

H336: May cause drowsiness or dizziness

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

Derivation of the carcinogenic risk potency (CRP): No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: sweet, ester-like pleasant odour (banana-like).

$OT_{detection}$: 1.50 mg/m^3 [AIHA, 1989]
LOA = 11.8 * $OT_{detection}$ * 1.33 = 24 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies below all intervention values.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)[7]

VRW level **70**	*AEGL-1* -	*ERPG-1* 24		*IDLH:* 8200 mg/m^3 (30 min)
AGW level **700**	*AEGL-2* -	*ERPG-2* 950		
LBW level **7,600**	*AEGL-3* -	*ERPG-3* 14,250		

[7] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 141-32-2 **n-Butylacrylaat** $CH_2=CH-COOH(CH_2)_3-CH_3$ **VN-nr: 2348** **GEVI: 39**

Synoniemen: acrylzuur n-butylester, 2-propeenzuur n-butylester (Engels: n-butyl acrylate) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	44	44	44	44	44	44
Alarmeringsgrenswaarden	AGW (mg/m³)	5.900	2.500	1.500	870	510	300
Levensbedreigende waarden	LBW (mg/m³)	11000	4 700	2 700	1 600	940	550

Datum samenstelling: 28-11-2008

Conversiefactor: 1 mg/m³ = 0,188 ppm; 1 ppm = 5,33 mg/m³

Explosiegrens: LEL = 1,2 vol% ≈ 64 000 mg/m³

Geur: zoete, ranzige, plastic geur

LOA: 0,046 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,02

Molecuulmassa:	128,2 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	0,1 g/100 ml (slecht)
Verzadigde dampdruk:	5 mbar

Overige informatie

Publieke grenswaarde: 11 mg/m³

MAK: 10,66 mg/m³

TLV-TWA: 10,66 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen gegevens

VRW → AGW: irritatie ogen en bovenste luchtwegen, tranenvloed, hoesten, keelpijn, rhinitis

AGW → LBW: benauwdheid, longoedeem

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- n-Butylacrylaat veroorzaakt irritatie van de ogen en bovenste luchtwegen.
- Door de carboxylesterase activiteit in het neusmembraan worden zure metabolieten gevormd die laesies in de (bovenste) luchtwegen veroorzaken. Effecten op de diepere luchtwegen (o.a. longoedeem) zijn ook mogelijk.
- De stof is mogelijk sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact!
- Kruisgevoeligheid voor andere acrylaten kan optreden.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, pijn, branderig gevoel

Oogcontact: bijtend, roodheid, pijn, tranenvloed

Carcinogeniteit

IARC classificatie: 3

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen:

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**:* geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 141-32-2 **n-butyl acrylate** **CH_2=CH-COOH(CH_2)$_3$-CH_3** **UN-nr: 2348**

Basis for the Dutch Intervention Values

VRW: AEGL values are adopted, 2-hr value added

AGW: Same point of departure as for AEGL values but difference in time scaling, 2-hr value added

LBW: AEGL values are adopted (except 10-minute value for which time-scaling was applied), 2-hr value added

Date: 28-11-2008 | Interim AEGL 2007

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	44	44	44	44	44	44	Threshold for irritation
AGW	5 900	2 500	1 500	870	510	300	Irritation of respiratory tract
LBW	11 000	4 700	2 700	1 600	940	550	Mortality animals (cardiopulmonary collapse)

Derivation of the Dutch Intervention Values

VRW: No suitable human data were available as basis for the derivation of VRW values. Limited data were available upon which to base the VRW values. A concentration of 25 ppm (133 mg/m^3), which did not result in any effects in pregnant rats following repeated exposure (6 hrs/day, on gestation days 6-15), was chosen as a concentration below the threshold for VRW effects. At the next higher level (135 ppm or 720 mg/m^3), eye and nasal discharge and ruffled fur were observed. Time extrapolations were not performed, because adaptation over time is expected for slight irritation. A total uncertainty factor of 3 was used, including 1 for interspecies extrapolation and 3 for intraspecies variation, because slight irritation is not expected to differ greatly between individuals.

AGW: No relevant human data are available. As starting point for the derivation of the AGW, the concentration of 211 ppm (748 mg/m^3) for 6 hours/day resulting in clinical signs of toxicity including nasal irritation but no mortality rats study, was used. Slight lesions of the nasal mucosa were seen histologically. A total uncertainty factor of 3 was used including 1 for interspecies extrapolation and 3 for intraspecies extrapolation. Use of greater uncertainty factors was not necessary because the mechanism of irritation is not expected to differ greatly between species and between individuals. Values were scaled using the equation $C^n \times t = k$. In contrast to the AEGL values where default values for n were used, the substance specific n-value of 1.3 was used for time scaling (see derivation LBW values). In contrast to the 10 minute AEGL-2, also time-scaling was applied for the 10 minute AGW.

LBW: No relevant human data are available for the derivation of LBW-values for n-Butyl acrylate. An LC_{50} study was used to calculate a 4-hour $BMCL_{05}$ value by a log-probit analysis using Benchmark Dose Software Proast version 17.06. The resulting 4-hour $BMCL_{05}$ of 1780 ppm or 9490 mg/m^3 (1652 ppm or 8800 mg/m^3, in old EPA software) was used to derive the 30-minute, and 1-, 2- 4- and 8-hour LBW values. Values were scaled using the equation $C^n \times t = k$, with n = 1.3. A total uncertainty factor of 10 was used including 3 for interspecies variation and 3 for intraspecies variation. Use of a greater uncertainty was not necessary because the mechanism of toxicity (local damage in the lower airways/lungs) is not expected to differ between individuals. In contrast to the 10 minute AEGL-3, time scaling was also applied to derive the 10 minute LBW.

Additional toxicological information (including relevant results of a general literature search, if any)

There is little information available on the mechanism of toxicity of n-Butyl acrylate in humans, which make the prediction of the toxicological effects during acute exposure to high concentration difficult. The substance is a primary irritant with presumably also sensitizing properties. In animal experiments the substance induces eye and nasal discharge, followed by dyspnea and gasping at higher dose levels. In the LC_{50} studies mortality was caused by cardiopulmonary collapse.

H315: Causes skin irritation, H317: May cause an allergic skin reaction, H319: Causes serious eye irritation, H335: May cause respiratory irritation

Carcinogenicity and derivation of the CRP value
IARC classification: 3 (not classifiable as to carcinogenicity to humans). No carcinogenic risk potency (CRP) was derived. n-Butyl acrylate was found to be negative in various *in vitro* and *in vivo* genotoxicity tests. In a chronic toxicity/carcinogenicity study with rats no evidence of carcinogenicity was found.

Odour and derivation of the LOA value
Odour: typical odour. ODT: 0.00055 ppm (0.0029 mg/m^3) [Nagata, 2003]. LOA = 11.8 * ODT * 1.33 = 0.046 mg/m^3 (The concentration Level leading to distinct Odour Awareness (l=3) is calculated using the formula: l = 2.33 * log (C/ODT) + 0.5. A correction factor of 1.33 is applied to this value) The LOA is far below all VRW values

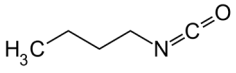
***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **44**	*AEGL-1* 44	*ERPG-1* 0.27		*IDLH: not established*
AGW level **1500**	*AEGL-2* 690	*ERPG-2* 130		
LBW level **2 700**	*AEGL-3* 2 600	*ERPG-3* 1 300		

Stofdocument deel A

CAS-nr: 111-36-4
C_5H_9NO

n-Butylisocyanaat



VN-nr: 2485
GEVI: 663

Synoniemen: butylisocyanaat (Engels:n-Butyl isocyanate)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	11	3,7	1,8	0,92	0,46	0,23
Levensbedreigende waarden	LBW (mg/m³)	33	11	5,5	2,8	1,4	0,69

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,243 ppm; 1 ppm = 4,12 mg/m³

Explosiegrens: 67.000 – 382.000 mg/m³

Geur: stekend

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot gele vloeistof
Brand: zeer brandgevaarlijk
Makkelijke vorming van explosieve mengsels; vluchtig.

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,05

Molecuulmassa: 99,1 g/mol

Zuurgraad: Geen data
LogKow: 2,3
Wateroplosbaarheid: reactie
Verzadigde dampdruk: 23 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW: irritatie ogen, neus en keel

AGW → LBW: matige tot ernstige irritatie van luchtwegen, tranenvloed, keelpijn, hoesten, benauwdheid, longoedeem, mogelijk effecten op de ongeboren vrucht

Boven LBW: ernstige longschade, sterfte

- *LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is*.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Primaire effecten zijn irritatie van de slijmvliezen van ogen, neus en keel.
- In analogie met methylisocyanaat kan niet worden uitgesloten dat n-butylisocyanaat embryotoxiciteit kan veroorzaken
- n-Butylisocyanaat kan een chemische longontsteking en/of longoedeem veroorzaken. De effecten hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- n-Butylisocyanaat is mogelijk sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact!

Effecten bij blootstelling aan vloeistof

Huidcontact: irritatie, roodheid, pijn

Oogcontact: irritatie, roodheid, pijn

Carcinogeniteit

IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen, zo nodig arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en onmiddellijk arts raadplegen.

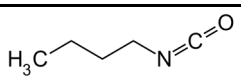
***Specifieke behandeling en materialen**: geen*.

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 111-36-4
C_5H_9NO

n-Butyl isocyanate



UN-nr: 2485

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: Same rationale as for AEGL values (one-third of LBW), 2h value added

LBW: Different point of departure as for AEGL values, different uncertainty factors and n-value are used, 2h value added

Date: November 2015	AEGL document: final 2013

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Insufficient warning properties; possible systemic effects at concentrations lower than those that produce irritation
AGW	11	3.7	1.8	0.92	0.46	0.23	One-third of LBW values
LBW	33	11	5.5	2.8	1.4	0.69	Threshold for lethality in rats

Derivation of the Dutch Intervention Values

VRW: VRW values were not derived for n-butyl isocyanate due to a lack of relevant human and animal data. The available data, however, shows that n-butyl isocyanate exerts toxic effects that are similar to methyl isocyanate (respiratory irritation and delayed lethality). VRW values are not derived for methyl isocyanate due to poor warning properties. On the basis of similarities between n-butyl isocyanate and methyl isocyanate, VRW values for n-butyl isocyanate were not derived. Absence of VRW values does not imply that concentrations below the AGW values are without any effect

AGW: The available human data and single-exposure animal toxicity data are regarded inadequate for derivation of AGW-values for n-butyl isocyanate. Data in workers lack sufficient information on exposure concentrations and health effects. Also the available animal data lack information on the incidence and severity of effects and histopathologic findings are absent. Without adequate data, the AGW values for n-butyl isocyanate were obtained by dividing the LBW-values by 3. This approach is justified by the steep concentration response curve as observed in mortality studies; no rats died after a 1-h exposure at 39 ppm (161 mg/m³), and 70% (7/10) died at 130 ppm (536 mg/m³).

LBW: The 4-hour LC_{50} of 15.6 ppm (64 mg/m³) for groups of 6 rats (Dupont, 1968) is the most appropriate basis for LBW derivation. The $BMCL_{05}$ and BMC_{01} for this study were 3.35 ppm (14 mg/m³) and 6.82 ppm (28 mg/m³) respectively, as determined by Benchmark Dose analysis. The 4-hour $BMCL_{05}$ of 3.35 ppm (14 mg/m³) was used as the PoD for LBW derivation. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The inconsistencies among the animal lethality data sets did not permit a valid assessment of the exposure concentration-exposure duration relationship and an empirical derivation of n was not possible. Time scaling was performed using $C^n \times t = k$, with the substance-specific value for n of 1 (based on analogy with methyl isocyanate) for extrapolation to longer and shorter exposure durations.

Additional toxicological information (including relevant results of a general literature search, if any)

No studies are available that address the mechanism(s) of toxicity of n-butyl isocyanate. It is thought that the mode of action might be equal to methyl isocyanate, which toxicity is clinically similar to that described for n-butylisocyanate (respiratory tract irritation with delayed lethality). The exact mechanism of action for the systemic effects is unknown. Cholinesterase inhibition by several diisocyanates has been hypothesized as a mechanism for the commonly observed respiratory toxicity associated with isocyanate exposure.

No reproductive or developmental data were located.

Some isocyanates are well known to cause skin and respiratory sensitization. However, there are no reports

of n-butyl isocyanate or other monoisocyanates causing respiratory sensitization. Cross-reactivity may occur between isocyanates.

H302: Harmful if swallowed; H330: Fatal if inhaled; H314: Causes severe skin burns and eye damage; H318: Causes serious eye damage; H317: May cause an allergic skin reaction; H335: May cause respiratory irritation.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
No information was found regarding the carcinogenic potential of n-butyl isocyanate in humans and animals. IARC classification: not evaluated No carcinogenic risk potency (CRP) was derived	Odour: pungent No LOA was derived due to the absence of consistent odour perception.

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)***

VRW level **NR**	*AEGL-1* NR	*ERPG-1* 0.041		*IDLH*: NR
AGW level **1.8**	*AEGL-2* 0.34	*ERPG-2* 0.21		
LBW level **5.5**	*AEGL-3* 1.0	*ERPG-3* 4.1		

Stofdocument deel A

CAS-nr: 1305-99-3 **Calciumfosfide** Ca_3P_2 **VN-nr: 1360**

GEVI: geen

Synoniemen: tricalciumdifosfide (Engels: calcium phosphide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	45	15	7,6	3,8	1,9	0,95
Levensbedreigende waarden	LBW (mg/m³)	82	27	14	6,8	3,4	1,7

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,132 ppm; 1 ppm = 7,579 mg/m³

Explosiegrens: geen data
Kans op explosie door reactie met water of zuren.

Geur: typerende geur (geur als bij fosfine)
LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: grijze brokken of bruinrood kristallijn poeder
Brand: Niet brandbaar. Echter, bij contact met vocht kans op brand en explosie.

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa: 182,2 g/mol

Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: reactie
Verzadigde dampdruk: geen data

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling
(gebaseerd op vrijkomen fosfine)

*Onder **AGW***: irritatie aan ogen, huid, neus en luchtwegen, hoofdpijn, misselijkheid, braken, zwakte, paresthesie, duizeligheid, tremor

AGW → LBW: benauwdheid, longoedeem, bewustzijnsdaling, hartritmestoornissen, nier- en leverfunctiestoornissen

Boven LBW: convulsies, cardiovasculaire collaps, myocardinfarct, ademnood, coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Calciumfosfide kan bij contact met vocht uit de lucht of luchtwegen omgezet worden in fosfine. De toxiciteit van calciumfosfide wordt bepaald door de vorming van fosfine.
- Fosfine verstoort door effecten op de celademhaling de zuurstofopname en energievoorziening van de cel.
- Fosfine werkt irriterend op de ogen, huid en luchtwegen.
- Blootstelling aan calciumfosfide kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Kinderen zijn mogelijk gevoeliger voor toxiciteit door fosfine.

Effecten bij blootstelling aan vloeistof
Huidcontact: roodheid
Oogcontact: roodheid, pijn, slecht zien

Carcinogeniteit
IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
ogen: spoelen met water (evt. contactlenzen verwijderen).
Ontsmetting vaste stof
huid: verontreinigde kleding uittrekken, afspoelen met water.
ogen: spoelen met water (evt. contactlenzen verwijderen).
inslikken: mond laten spoelen (uitspugen!), rust, GEEN mond-op-mondbeademing, actieve kool (carbomix) toedienen, en direct spoedeisende medische hulp inzetten.
***Specifieke behandeling en materialen**: geen.*
Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 1305-99-3 **Calcium phosphide** **Ca_3P_2** **UN-nr: 1360**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 16-10-2018 AEGL document: Final 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	(insufficient data)
AGW	45	15	7.6	3.8	1.9	0.95	Irritation nasal mucosa rats (phosphine)
LBW	82	27	14	6.8	3.4	1.7	Lethality rats (phosphine)

Derivation of the Dutch Intervention Values

VRW: No data are available for calcium phosphide. As toxicity of calcium phosphide is due to phosphine, which is formed due to reaction of calcium phosphide with moisture, data on phosphine could be used to derive intervention values. However, no appropriate data were available for derivation of VRW values for phosphine. Therefore VRW values are not recommended. This does not imply that exposure below AGW is without adverse effects.

AGW: Since no appropriate data exist for calcium phosphide, AGW values for phosphine will be used (on ppm-basis) to derive AGW values for calcium phosphide. The use of phosphine as a surrogate for calcium phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because two moles of phosphine are produced for every mole of calcium phosphide, a molar adjustment factor of 2 was applied to the calcium phosphide AGW values.

Derivation of AGW values for phosphine

The phosphine AGW values were based on red mucoid nasal discharge in rats exposed to 10 ppm (14 mg/m³) phosphine for 6 hours, corresponding to 37.90 mg/m³ calcium phosphide. Since this endpoint is less severe than effects defined by AGW, the resulting values should be protective. The default uncertainty factor of 3 was applied to account for interspecies variability. An uncertainty factor of 10 was applied to account for intraspecies variability since the human data suggest that children may be more sensitive than adults when exposed to presumably similar phosphine concentrations. For example, in two reports, exposed children died, but exposed adults survived. Time scaling was performed using the equation $C^n \times t = k$, and an n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine).

LBW: Since no appropriate data exist for calcium phosphide, LBW values for phosphine will be used (on ppm-basis) to derive LBW values for calcium phosphide. The use of phosphine as a surrogate for calcium phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because two moles of phosphine are produced for every mole of calcium phosphide, a molar adjustment factor of 2 was applied to the calcium phosphide LBW values.

Derivation of LBW values for phosphine

The highest concentration yielding no deaths in rats (18 ppm = 25 mg/m³) for 6 hours was used as point of departure for the calculation of the LBW values, corresponding to 68.21 mg/m³ calcium phosphide. The default uncertainty factor of 3 for interspecies and an intraspecies factor of 10 were applied for reasons provided above. Time scaling was performed using the equation $C^n \times t = k$ and a chemical specific n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine). These values are considered protective since workers were repeatedly exposed for “brief” periods of time to phosphine concentrations up to 35 ppm (49 mg/m³) with no life-threatening effects and workers exposed to >50 ppm (>70 mg/m³) for 2-5 minutes experienced only odour.

Additional toxicological information (including relevant results of a general literature search, if any)

When calcium phosphide reacts with moisture, phosphine gas will be formed. Phosphine is considered to induce acute toxic effects following oral and inhalation exposure. Children are thought to be more vulnerable to phosphine exposure. Common clinical signs after exposure to phosphine are headache, vomiting, coughing, shortness of breath, paresthesia, weakness, tremors and jaundice. Pulmonary congestion, pleural effusion, and congestive heart failure may be observed upon post-mortem examination.

In vitro, phosphine reacts with cytochrome c and cytochrome c oxidase, thereby inhibiting mitochondrial oxygen uptake. In vitro studies have also shown that phosphine can react with the heme moiety of hemoglobin in the presence of oxygen. Cell death and loss of cell membrane integrity accounted for the increased liver enzymes, bronchiolytic effects, cloudy swelling of renal tubular epithelia, and hemorrhagic myocardial lesions.

No reproductive or developmental data were found.

H300: Fatal if swallowed; H311:Toxic in contact with skin; H318: Causes serious eye damage; H330: Fatal if inhaled

Carcinogenicity and derivation of the CRP value

IARC classification: not evaluated.

No carcinogenic risk potency (CRP) was derived.

No data concerning carcinogenicity of calcium phosphide are available.

Fumigation workers exposed long-term to phosphine have a higher incidence of both stable and less stable chromosomal aberrations. Molecular analysis of these lesions suggests that the breakpoints are near proto-oncogenes involved in non-Hodgkin's lymphoma, possibly contributing to the increased incidence of lymphomas in pesticide workers.

Odour and derivation of the LOA value

Odour: no information.

Pure phosphine is odourless at concentrations up to 200 ppm. Technical-grade phosphine has a garlic-like odour (may be due to impurities).

For phosphine, no LOA was derived due to lack of reliable data. Ruth (1986) reported an odour range of 0.028-3.6 mg/m^3 for phosphine.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*[8]

VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH:* not derived
AGW level **7.6**	*AEGL-2* 7.5	*ERPG-2* -		
LBW level **14**	*AEGL-3* 13	*ERPG-3* -		

[8] Note that the AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL

Stofdocument deel A

CAS-nr: 353-50-4 **Carbonylfluoride** COF_2 **VN-nr: 2417**

GEVI: 268

Synoniemen: carbonyldifluoride (Engels: carbonyl fluoride) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	4,6	3,2	2,5	2,0	1,6	0,79
Levensbedreigende waarden	LBW (mg/m³)	14	9,5	7,6	6,0	4,8	2,4

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,364 ppm; 1 ppm = 2,75 mg/m³

Explosiegrens: geen data

Geur: stekend, irriterende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloos gas
Brand: Niet brandbaar

Molecuulmassa: 66,01 g/mol

Zuurgraad: geen data

LogKow: geen data

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,29

Wateroplosbaarheid: Reactie
Verzadigde dampdruk: 56.134 mbar

Overige informatie

Publieke grenswaarde: uitgedrukt als F, incl. PTFE-pyrolyseproducten1 mg/m³ (15 min TGG)
MAK: niet afgeleid
TLV-TWA: 5,5 mg/m³ (incl. PTFE-pyrolyseproducten)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW: lichte irritatie, hoesten, keelpijn

AGW → LBW: longschade, benauwdheid

Boven LBW: sterfte

LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De substantie is irriterend voor de ogen, huid en de luchtwegen.
- Een hoge concentratie kan longoedeem veroorzaken.
- Carbonylfluoride is een zeer hygroscopisch gas, en vormt in contact met water HF (waterstof fluoride).

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, pijn, bevriezingsletsel

Oogcontact: bijtend, brandwonden, bevriezingsletsel

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer (alternatief: druppelen met 1% calciumgluconaat).

huid: *bij bevriezing:* kleding uittrekken (NIET lostrekken), direct spoelen met veel water (minimaal 20 min.), dan pas eventueel aan de huid vastgeplakte kleding verwijderen en verder spoelen; en direct spoedeisende hulp inzetten.

inslikken: n.v.t. (gas).

Specifieke behandeling en materialen: Bij vergiftiging door deze stof is specifieke eerste hulp mogelijk; calciumgluconaatoplossingen en -gel moeten met gebruiksaanwijzing beschikbaar zijn.
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 353-50-4 **Carbonylfluoride** COF_2 **UN-nr: 2417**

Basis for the Dutch Intervention Values

VRW: Not recommended (in accordance with AEGL)

AGW: Same rationale as for AEGL (one-third of LBW), 2h value added

LBW: Same point of departure as for AEGL values, but using different uncertainty factors, 2h value added

Date: November 2015 | AEGL document: Final, 2014

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Insufficient data.
AGW	4.6	3.2	2.5	2.0	1.6	0.79	One third of LBW
LBW	14	9.5	7.6	6.0	4.8	2.4	Estimate $BMCL_{05}$ lethality threshold in rats

Derivation of the Dutch Intervention Values

VRW: The VRW values were not derived. No human data were available and animal data were insufficient. Therefore VRW values were not recommended.

AGW: In a study that was conducted in rats, the animals were exposed to concentrations of 2.5 or 5 ppm (6.9 or 14 mg/m³) for 2 or 2.5 hours. The no-effect level was 2.5 ppm (6.9 mg/m³) for both durations. The rats that were exposed to the 5 ppm (14 mg/m³) concentrations exhibited dyspnea and cyanosis. In another study rats were exposed to concentration of 5 or 10 ppm (14 or 28 mg/m³) for 4 hours and exhibited dyspnea and rapid shallow respiration. In this study a no-effect level was not identified. The animal studies that were found lack sufficient information on experimental conditions and observed effects to be used for derivation the AGW values. Furthermore, human data on the effects of carbonyl fluoride exposure is lacking. In the absence of relevant data, the AGW values are estimated by dividing the LBW values by a factor 3. This reduction is considered an estimate of the threshold for irreversible effects.

LBW: The LBW values were determined by using available mortality data in rats in a benchmark dose approach. The $BMCL_{05}$ value of 5.2 ppm (14.3 mg/m³) for 4 hours was considered to be the most conservative value to estimate the threshold for lethality in rats and was used as a point of departure for deriving the LBW values. For AEGL-3 derivation a total uncertainty factor of 10 was applied to account for interspecies and intraspecies differences. The resulting values are considered too low, given the TLV-TWA value of 5.5 mg/m³ and the Dutch public OEL value of 1 mg/m³ (TGG-15 min). As the variation in effects is not expected to vary much among species, an interspecies uncertainty factor of 1 was considered acceptable. This factor was also applied for derivation of the Intervention values of HF. An intraspecies uncertainty factor of 3 was maintained. A total uncertainty factor of 3 was applied. Time-scaling was performed using the equation $C^n \times t = k$, using the default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

The substance carbonyl fluoride is a contact irritant that hydrolyzes in the presence of water to hydrogen fluoride. The effects of carbonyl fluoride including skin, eyes and respiratory tract irritation are likely due to hydrogen fluoride. However, carbonyl fluoride is regarded more toxic than hydrogen fluoride due to a deeper lung penetration. Exposure via inhalation produces pulmonary hemorrhage, congestion and death in laboratory animals. Inhalation of high concentrations may cause lung edema. Steep concentration-response and time-response relationships appeared to be present for carbonyl fluoride.

Data on developmental and reproductive toxicity and carcinogenicity are too limited to draw conclusions.

No risk phrases were found.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: pungent and very irritating odour.

No LOA was derived due to lack of data.

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)***				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH: not derived*
AGW level **2.5**	*AEGL-2* 0.76	*ERPG-2* -		
LBW level **7.6**	*AEGL-3* 2.2	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 463-58-1 **Carbonylsulfide** **COS** **VN-nr: 2204**

GEVI: 263

Synoniemen: carbonoxysulfide (Engels: carbonyl sulfide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	250	170	140	110	86	56
Levensbedreigende waarden	LBW (mg/m³)	690	480	380	300	240	120

Datum vaststelling: november 2015

Conversiefactor: 1 mg/m³ = 0,400 ppm; 1 ppm =2,50 mg/m³

Explosiegrens: LEL = 6,5 Vol% ≈ 160.000 mg/m³

Geur: geurloos (pure stof), typerende geur (rotte eieren) in vochtige lucht

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,1

Molecuulmassa: 60,1 g/mol
Zuurgraad: Niet bekend
LogKow: -1,3
Wateroplosbaarheid: 0,14 g/100 ml
Verzadigde dampdruk: 11.000 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW: irritatie van ogen, neus en keel, keelpijn, hoesten, hoofdpijn, misselijkheid, versnelde ademhaling

AGW → LBW: hartkloppingen, ademnood, verwarring, bewusteloosheid, ademstilstand

Boven LBW: sterfte

LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Een hoge concentratie kan inwerken op het centrale zenuwstelsel, met als gevolg stuiptrekkingen en psychische stoornis met verwarring.
- De stof is irriterend voor de ogen, neus en keel.
- Vormt in contact met water H_2S (waterstofsulfide).

Effecten bij blootstelling aan vloeistof

Huidcontact: bevriezingsletsel

Oogcontact: bevriezingsletsel

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust, 100% zuurstof en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: *in geval van bevriezingswonden*: aan de huid vastgevroren kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en direct spoedeisende medische hulp inzetten.

ogen: *in geval van bevriezingswonden*: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer..

inslikken: n.v.t. (gas).

Specifieke behandeling en materialen: Bij vergiftiging door deze stof moet onmiddellijk zuurstof 100% worden toegediend.

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 463-58-1 **Carbonyl sulfide** **COS** **UN-nr: 2204**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value is adopted, 10 min value added, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: November 2015 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	250	170	140	110	86	56	No-effect level for clinical signs in rats
LBW	690	480	380	300	240	120	Estimate for lethality threshold in rats

Derivation of the Dutch Intervention Values

VRW: The VRW values are not derived. No human and animal data were available and therefore VRW values were not recommended.

AGW: To derive the AGW values for carbonyl sulfide the no-effect level for severe clinical signs and brain pathology at a concentration of 300 ppm (750 mg/m^3) for 6 hours in rats was used. The severe clinical signs observed at the next concentration of 600 ppm included hypothermia, lethargy, head tilt and ataxia. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was performed using the equation $C^n \times t=k$, using the default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively.

LBW: The LBW values were determined by using available mortality data in rats in a benchmark dose approach. The $BMCL_{05}$ value of 952 ppm (2,380 mg/m^3) for 4 hours in rats was used as a point of departure for deriving the LBW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was performed using the equation $C^n \times t=k$, using the default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Carbonyl sulfide is neurotoxic and causes respiratory paralysis. Hydrogen sulfide is produced from the metabolism of carbonyl sulfide via carbonic anhydrase and may be responsible for carbonyl sulfide toxicity. Steep concentration-response and time-response relationships appeared to be present for carbonyl sulfide.

Data on developmental and reproductive toxicity, genotoxicity and carcinogenicity are too limited to draw conclusions.

No harmonised hazard sentences were found.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: odourless (pure substance), typical odour (strong odour of rotten eggs) in moist air. Odour threshold: 0.25 mg/m^3 [US EPA, 1992]. No LOA was derived due to lack of data

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH: not derived*
AGW level **140**	*AEGL-2* 130	*ERPG-2* -		
LBW level **380**	*AEGL-3* 370	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 7782-50-5 **Chloor** Cl-Cl **VN-nr: 1017**

GEVI: 268

Synoniemen: - (Engels: Chlorine) ***Status***: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	1,5	1,5	1,5	1,5	1,5	1,5
Alarmeringsgrenswaarden	AGW (mg/m³)	14	8,3	5,9	4,2	3,0	2,1
Levensbedreigende waarden	LBW (mg/m³)	290	110	59	32	18	9,6

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,339 ppm; 1 ppm = 2,95 mg/m³

Explosiegrens: geen data

Geur: stekende geur

LOA: 3,6 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: geelgroen onder druk tot vloeistof verdicht gas

Brand: niet brandbaar, bij vele reacties kans op explosie.

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,5

Molecuulmassa: 70,9 g/mol

Zuurgraad: Geen data

LogKow: Geen data

Wateroplosbaarheid: 0,7 g/100 ml (slecht)

Verzadigde dampdruk: 6700 mbar

Overige informatie

Publieke grenswaarde: 1,5 mg/m³ (15 min)

MAK: 1,5 mg/m³

TLV-TWA: 1,5 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: oog- en luchtwegirritatie, tranenvloed, hoesten

AGW → LBW: ernstige oog- en luchtwegirritatie, benauwdheid, chemische pneumonitis, longoedeem

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Chloor werkt irriterend op de slijmvliezen van o.a. ogen en luchtwegen
- Blootstelling aan chloor kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Personen met verminderde longfunctie zijn gevoeliger voor de effecten van chloor.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, ernstige bevriezingsverschijnselen zoals pijn, blaren, (bevriezings)wonden.

Oogcontact: bij bevriezing: bijtend, roodheid, tranenvloed, hoornvliesbeschadiging, verlies van gezichtsvermogen, ernstige brandwonden.

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, *bij rode ogen, etc.*: halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen, arts raadplegen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas)

Specifieke behandeling en materialen:.

Neem contact op met het NVIC (tel: +31 (0)30 – 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 7782-50-5 **Chlorine** **Cl-Cl** **UN-nr: 1017**

Basis for the Dutch Intervention Values

VRW: AEGL value was adopted, 2h value added

AGW: AEGL value was adopted, 2h value added

LBW: Different point of departure and different n than AEGL values

Date: 24-09-2009 | AEGL document: Final, 2004

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	1.5	1.5	1.5	1.5	1.5	1.5	Mild, transient effects on pulmonary function parameters in humans
AGW	14	8.3	5.9	4.2	3.0	2.1	Shortness of breath in sensitive human subject
LBW	290	110	59	32	18	9.6	Calculated threshold for lethality in animals (rats).

Derivation of the Dutch Intervention Values

VRW: The VRW was based on a study with in the first part, 31 male and female human volunteers, including a susceptible individual, which were exposed to 0.0, 0.5, 1.0, 2.0 ppm (0.0, 1.5, 2.9, 5.9 mg/m^3) for 4h or 0.5 and 1.0 ppm (1.5 and 2.9 mg/m^3) for 8h. The volunteers did not know the test concentration. In the second part of the study eight non-smoking males were exposed to 0.0, 0.5, 1.0 ppm (0.0, 1.5, 2.9 mg/m^3) chlorine for 8h. A 15-min exercise period during each hour of exposure was designed to increase the average heart rate to 100 beats per minute. During the exposures, the volunteers filled out subjective questionnaires on sensation (e.g. smell, shortness of breath). A concentration of chlorine at 0.5 ppm (1.5 mg/m^3) for 4 h produced no sensory irritation and resulted in only mild transient effects on pulmonary parameters in the healthy individuals. Pulmonary changes in the susceptible individual were greater than those in healthy subjects, but did not result in symptoms above the definition of the VRW. The point of departure is supported by other studies with human volunteers of both genders, including healthy, atopic, and asthmatic subjects and/or periods of exercise to simulate conditions of stress (1-h 0.4 ppm (1.2 mg/m^3) no-effect concentration for individuals with airway hyper-reactivity or asthma). Because of this variety of human subjects tested, including the most susceptible groups, no uncertainty factor for differences in human sensitivity was applied. The 0.5-ppm (1.5 mg/m^3) exposure was considered a threshold for more severe effects, regardless of exposure duration. No time-scaling was applied. The use of the same value across all exposure durations is supported by the fact that the response to the irritant effects of chlorine appears to be concentration-dependent rather than time-dependent.

AGW: The AGW values were based on the same studies used to derive the VRW value. In those studies healthy human volunteers experienced transient changes in pulmonary function measurements and a susceptible individual experienced an asthma-like attack (shortness of breath and wheezing) following a more than 4-h exposure to chlorine at 1.0 ppm (2.95 mg/m^3). The susceptible individual remained in the exposure chamber for the full 4 h before the symptoms occurred. Because both genders were tested, subjects were undergoing light exercise (making them more vulnerable to sensory irritation), and a susceptible individual was tested, no uncertainty factor was applied to account for differences in human sensitivity. If an uncertainty factor for intraspecies differences was applied, then the AGW-values would conflict with the VRW values.
Similar effects and symptoms in individuals with airway hyper-reactivity or asthma exposed at 1.0 ppm (2.95 mg/m^3) for 1 h in another study supports the application of an intraspecies uncertainty factor of 1 for the 4-h concentration. Time-scaling was performed using the equation $C^n \times t = k$, using n=2. This value was calculated by regression analysis of the percent of subjects reporting a nuisance irritation response to concentrations at 1 ppm (2.95 mg/m^3) and 2 ppm (5.90 mg/m^3) over exposure durations of 30 min and 120 min. In the AEGL document the 10 minute value was set equal to the 30 minute value so that the highest exposure of 4.0 ppm (11 mg/m^3) in the controlled human study was not exceeded. Considering that this highest human exposure level was established after 2 hours of exposure time scaling to 10 minutes seems reasonable.

LBW: The LBW values were based on a lethality study in rats, including three exposure durations of 10, 30 and 60 minutes and four to six concentrations. Probit analysis using DoseResp was performed and yielded and n of 1.1 and LC_{01} values for the 10 min, 30 min, 1-, 2-,4-, and 8hrs exposure durations of 967, 370, 201, 110, 59.7. and 32.5 ppm (2856, 1090, 594, 324, 176, and 96 mg/m^3), respectively, which were used as point of departure for LBW derivation. An uncertainty factor of 3 was used to account for interspecies differences because the data show that interspecies differences were within a factor of approximately 2 for lethality. In addition, chlorine is a contact site, direct-acting toxicant, and there is likely to be little difference between species in the response of biologic tissues to chlorine exposure. Also, for intraspecies differences, corrosive gases acting at the point of contact would predict low variability in a population; thus an uncertainty factor of 3 is applied to protect susceptible individuals.

In contrast to the derivation of LBW values, the AEGL-3 values were based on an approximate threshold of lethality in animals: Because the experimental data in mice appeared to provide an overly conservative estimate of lethality that was not consistent with the overall preponderance of the data, a value less than the concentration that resulted in no deaths in rats but greater than the value that resulted in no deaths in mice was chosen as the basis for the AEGL-3 values. The 200-ppm (590 mg/m^3) value is below the 1-h highest nonlethal concentrations (213 ppm and 322 ppm; 628 and 950 mg/m^3) and the LC01 (288 ppm; 849 mg/m^3) in two well-conducted studies with rats and above the 1-h highest nonlethal concentration in mice, 150 ppm (442 mg/m^3). The 200-ppm (590 mg/m^3) concentration is an LC_{20} for the mouse.

Additional toxicological information (including relevant results of a general literature search, if any)

Chlorine is an eye and respiratory tract irritant and, at high doses, has direct toxic effects on the lungs. Chlorine is extremely reactive and enters into substitution or addition reactions with both inorganic and organic substances. Moist chlorine unites directly with most elements. Reaction with water produces hydrochloric (HCl) and hypochlorous acid (HClO).

No studies on developmental and reproductive effects in humans were located.

H315: Causes skin irritation; H319: Causes serious eye irritation; H331: Toxic if inhaled; H335: May cause respiratory irritation.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: pungent

Odour threshold: 0.078 ppm (0.23 mg/m^3) [U.S. EPA]

LOA = 11.8 * OT_{50} * 1.33 = 3.6 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is below the 10 min-2h AGW values, and below the LBW values.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **1.5**	*AEGL-1* 1.5	*ERPG-1* 2.9		*IDLH*: 29 (30 minutes)
AGW level **5.9**	*AEGL-2* 5.9	*ERPG-2* 8.8		
LBW level **59**	*AEGL-3* 59	*ERPG-3* 59		

Stofdocument deel A

CAS-nr: 78-95-5 **Chlooraceton** **CH_3COCH_2Cl** **VN-nr: 1695** **GEVI: 663**

Synoniemen: acetonylchloride, chloormethylmethylketon, 1-chloor-2-propanon (Engels: chloroacetone) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	31	21	17	8,4	4,2	4,2
Levensbedreigende waarden	LBW (mg/m³)	92	64	50	25	13	13

Datum vaststelling: 13-05-2009 — Conversiefactor: 1 mg/m³ = 0,260 ppm; 1 ppm = 3,85 mg/m³

Explosiegrens: LEL = 3,4 vol% ≈ 130.000 mg/m³

Geur: penetrante, verstikkende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof, wordt geelbruin aan de lucht

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,03

Molecuulmassa:	92,5 g/mol
Zuurgraad:	geen data
LogKow:	0,3
Wateroplosbaarheid:	10 g/100 ml (goed)
Verzadigde dampdruk:	16 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

TLV-Ceiling: 3,85 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW**:* oogirritatie, tranenvloed, irritatie aan luchtwegen, hoesten

AGW → LBW: ernstige irritatie, oogschade, longontsteking, ernstige longoedeem, benauwdheid

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Chlooraceton veroorzaakt irritatie van de ogen en luchtwegen.
- Chlooraceton kan longoedeem veroorzaken. Verschijnselen hiervan kunnen vertraagd optreden.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, ernstige brandwonden, blaren

Stof kan door de huid opgenomen worden.

Oogcontact: bijtend, roodheid, slecht zien, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding, en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**:* geen.

Neem contact op met het NVIC (Tel: +31(03)0 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 78-95-5 **Chloroacetone** **CH_3COCH_2Cl** **UN-nr: 1695**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 13-05-2009 | AEGL document: Final, 2012

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	-
AGW	31	21	17	8.4	4.2	4.2	One third of LBW values
LBW	92	64	50	25	13	13	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: Data are insufficient for derivation of VRW values for chloroacetone. Therefore, VRW values are not recommended.

AGW: The only data consistent with the definition of AGW with both concentration and duration parameters are the clinical signs observed in rats exposed to 132 ppm (508 mg/m^3) for 1-hour. However, in this rat study, 132 ppm was also the only concentration causing no mortality and it is the same as the concentration used as the point-of-departure for LBW values. Therefore, the AGW values for chloroacetone will be based upon a 3-fold reduction in the LBW values; this is considered an estimate of a threshold for irreversible effects.

LBW: The estimated 1-hour male rat lethality threshold of 131 ppm (504 mg/m^3) ($BMCL_{05}$) was used as the basis of the LBW values. Interspecies and intraspecies uncertainty factors of 3 each were applied because chloroacetone is highly irritating and clinical signs are likely caused by a direct chemical effect on the tissues; this type of port-of-entry effect is not expected to vary greatly between species or among individuals. The interspecies uncertainty factor of 3 is also supported by the fact that data suggest little species variability with regard to lethality from oral and dermal exposure to chloroacetone. The intraspecies uncertainty factor of 3 is considered sufficient because data from the more sensitive males were used as the point-of departure. Time-scaling was performed using the equation $C^n \times t = k$, using default values of n=1 and n=3 for extrapolation to longer and shorter exposure durations, respectively. The 4-hour value was also adopted as the 8-hour value because time scaling would yield an 8-hour LBW value approaching occupational standards.

Additional toxicological information (including relevant results of a general literature search, if any)

Chloroacetone is toxic by inhalation, ingestion, and dermal contact. No information regarding the mechanism of toxicity of chloroacetone was located. However, symptoms of acute inhalation exposure suggest that it is an irritant, causing immediate lacrimation at low concentrations and contact burns of the skin and eyes, nausea, bronchospasm, delayed pulmonary edema, and death at higher concentrations.

Human toxicity data are limited. Chloroacetone is highly irritating and causes ocular, upper-respiratory tract, and dermal irritation. Immediate lacrimation has been reported at approximately 5 ppm (19 mg/m^3). A concentration of 26 ppm (100 mg/m^3) was reportedly intolerable after 1 minute, and a concentration of 605 ppm (2328 mg/m^3) chloroacetone was reported to be lethal after 10 minutes of exposure.

Animal toxicity data are limited to acute lethality studies in rats, mice, and rabbits, and repeated-exposure studies in rats. The limited data suggest that male rats are approximately 2.3 times more sensitive than female rats to the effects of chloroacetone administered by inhalation. Oral lethality data suggest that mice and rats have similar sensitivities. Oral and dermal LD_{50} values show little variability with regard to species and route of exposure. Clinical signs included restlessness, labored breathing, nasal irritation, salivation, lacrimation, dyspnea, and pulmonary edema at necropsy.

Developmental/reproductive studies regarding acute human exposure or animal exposure to chloroacetone

were not found.

No harmonized H-sentences for human health.

Carcinogenicity and derivation of the CRP value
IARC classification: not classified No carcinogenic risk potency (CRP) was derived. Carcinogenicity studies regarding human exposure to chloroacetone were not available. Two available animal studies where equivocal with respect to tumor promoter activity of chloroacetone. No experimental carcinogenicity studies are available.

Odour and derivation of the LOA value
Odour: Pungent, suffocating odour. No LOA was derived due to lack of reliable data Odour is not considered a good warning property because the first effect experienced is lacrimation (at approximately 5 ppm (19 mg/m^3)) followed by irritation of the upper respiratory tract and skin.

Other standards and guidelines *(1h values in mg/m^3, unless otherwise indicated)*				
VRW level **N.R.**	*AEGL-1* N.R.	*ERPG-1* not derived		*IDLH*: not derived
AGW level **17**	*AEGL-2* 17	*ERPG-2* not derived		
LBW level **50**	*AEGL-3* 50	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 79-04-9

Chlooracetylchloride $ClCH_2$-COCl

VN-nr: 1752

GEVI: 668

Synoniemen: chloorazijnzuurchloride, chloorethanoylchloride. (Engels: chloroacetyl chloride)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,20	0,20	0,20	0,20	0,20	0,20
Alarmeringsgrenswaarden	AGW (mg/m³)	14	9,5	7,5	3,8	1,8	0,94
Levensbedreigende waarden	LBW (mg/m³)	440	310	240	120	61	31

Datum vaststelling: 13-05-2009

Conversiefactor: 1 mg/m³ = 0,213 ppm; 1 ppm = 4,69 mg/m³

Explosiegrens: Geen data

Geur: stekend

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos tot lichtgele vloeistof

Brand: moeilijk brandbaar, bij vele reacties kans op brand en explosie

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa: 112,9 g/mol

Zuurgraad: Geen data

LogKow: Geen data

Wateroplosbaarheid: Reactie

Verzadigde dampdruk: 25 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 0,23 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: Geen informatie

VRW → AGW: oogirritatie, traanverwekkend

AGW → LBW: sterke oogirritatie, slecht zien, moeilijk ademen, schade aan luchtwegen, ademnood

Boven LBW: longoedeem, sterfte.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Sterk irriterend voor ogen, huid, en luchtwegen.
- Chlooracetylchloride veroorzaakt lichte tot matige respiratoire effecten (vooral hogere luchtwegen) met hoesten en dyspneu komen voor bij ongevallen.
- Chlooracetylchloride kan blijvende longschade en longoedeem veroorzaken (type I inhalatoire intoxicatie).

Klachten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, pijn, ernstige brandwonden

Oogcontact: bijtend, slecht zien, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof

huid: eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Ontsmetting bij inademen/inslikken

Inademing/inslikken van sterke zuren kan tevens leiden tot larynx- en glottisoedeem, met risico op verstikking (asfyxie) door zwellingen in de keel. Intubatie (borgen van vrije luchtwegen), eventueel gevolgd door beademing moeten in ernstige gevallen z.s.m. worden uitgevoerd (door specialisten). Zet derhalve direct spoedeisende medische hulp in.

Specifieke behandeling en materialen: geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 79-04-9 **Chloroacetyl chloride** **$ClCH_2$-COCl** **UN-nr: 1752**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date:13-05-2009 | AEGL document: Interim, 2007

Proposal for the Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.20	0.20	0.20	0.20	0.20	0.20	Eye irritation
AGW	14	9.5	7.5	3.8	1.8	0.94	Impaired ability to escape, eye irritation (squinting) in animals
LBW	440	310	240	120	61	31	Threshold for animal lethality

Derivation of the Dutch Intervention Values

VRW: The VRW values were derived from a multiple-exposure study in which conjunctival redness was reported in rats after the initial 6-hour exposure to approximately 0.5 ppm (2.35 mg/m³). VRW values were derived using a single 6-hour exposure to 0.84 ppm (3.9 mg/m³) because this is the highest concentration that caused conjunctival redness but no other more serious effects after one exposure. A modifying factor of 2 was applied to estimate a no-effect level concentration for conjunctivitis. The same VRW value is adopted for 10 minutes to 8 hours because mild irritant effects do not vary greatly over time. A total uncertainty factor of 10 was applied: 3 for interspecies variability and 3 for intraspecies variability. The resulting VRW of 0.04 ppm (0.20 mg/m³) is consistent with the limited human data in which exposure to 0.023 ppm (0.11 mg/m³) for an undefined period was barely detectable but 0.140 ppm (0.66 mg/m³) was strong, and exposure to 0.05 ppm (0.23 mg/m³) was associated with odor that was objectionable but no adverse health effects were reported.

AGW: A 1- hour inhalation rat study (32, 208, 522, or 747 ppm; 150, 976, 2,451 or 3,508 mg/m³) was chosen for AGW derivation because it was the only well-conducted study in which effects within the scope of AGW occurred from a single exposure. All test groups squinted, lacrimated, had urine stains, and initially lost weight. At 208 ppm (976 mg/m³), rats had shallow breathing, lethargy, and reddish stains near the eyes, at 522 ppm (2,451 mg/m³), rats also had labored breathing, gasping, and salivation, and at 747 ppm (3,508 mg/m³), 5/6 males and 1/6 females died and necropsy revealed lung pathology, nasal congestion, and enlarged adrenals. The AGW endpoint was the NOEL for impaired ability to escape due to lacrimation and eye squinting, which was estimated by applying a modifying factor of 2 to the lowest concentration tested of 32 ppm (150 mg/m³). A total uncertainty factor of 10 was applied, consisting of 3 for interspecies variability and 3 for intraspecies variability. Scaling across time was performed using $C^n * t = k$, with the defaults n=3 and n=1 for extrapolation to shorter and longer exposure durations, respectively.

LBW: A 1-hour inhalation rat study (32, 208, 522, or 747 ppm; 150, 976, 2,451 or 3,508 mg/m³) was chosen for LBW derivation. The LBW toxic endpoint was the lethality threshold, which was taken as the highest concentration tested that caused no deaths (522 ppm = 2,451 mg/m³). A total uncertainty factor of 10 was applied. An interspecies uncertainty factor of 3 was used because lethality resulting from respiratory lesions and having a steep dose-response was seen in several studies with rats and mice, at chloroacetyl chloride concentrations within a factor of 2-3. An intraspecies uncertainty factor of 3 was applied because the threshold for lethality from direct destruction of respiratory tissue is not expected to vary greatly among humans, based on the steep dose-response seen in the animal studies. To obtain protective LBW values, scaling across time was performed using $C^n * t = k$, with the defaults n=3 and n=1 for extrapolation to shorter and longer exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)
Chloroacetyl chloride hydrolyzes to chloroacetic acid and hydrogen chloride, which may contribute to chloroacetyl chloride toxicity. No developmental or reprotoxicity studies were located for chloroacetyl chloride. H301: Toxic if swallowed; H311: Toxic in contact with skin; H314: Causes severe skin burns and eye damage; H331: Toxic if inhaled; H372: Causes damage to organs.

Carcinogenicity and derivation of the CRP value	***Odor and derivation of the LOA value***
IARC classification: Not classified. No carcinogenic risk potency (CRP) was derived.	Odor: Chloroacetyl chloride has a pungent odor. LOA could not be derived due to lack of data. The odor awareness level might be around the VRW level.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **0.20**	*AEGL-1* 0.19	*ERPG-1* 0.23		*IDLH:* not established
AGW level **7.5**	*AEGL-2* 7.5	*ERPG-2* 2.3		
LBW level **240**	*AEGL-3* 240	*ERPG-3* 47		

Stofdocument deel A

CAS-nr: 506-77-4 **Chloorcyaan** **Cl–C≡N** **VN-nr: 1589**

GEVI: geen

Synoniemen: chloorcyanide, cyanogeenchloride (Engels: cyanogen chloride) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,68	0,68	0,68	0,68	0,68	0,68
Alarmeringsgrenswaarden	AGW (mg/m³)	6,1	6,1	5,0	3,3	2,3	1,7
Levensbedreigende waarden	LBW (mg/m³)	39	22	15	10	7,0	5,0

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,391 ppm; 1 ppm = 2,558 mg/m³

Explosiegrens: niet afgeleid

Geur: stekende

LOA: 32 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: tot vloeistof verdicht gas

Brand: niet brandbaar

Relatieve dichtheid gas (lucht = 1): 2,2

Molecuulmassa: 61,5 g/mol

Zuurgraad: Niet afgeleid

LogKow: 0,6 (berekend)

Wateroplosbaarheid: 6,5 g/100 (matig)

Verzadigde dampdruk: 1336 mbar

Overige informatie

Publieke grenswaarde:
Niet afgeleid
MAK: niet afgeleid
TLV-ceiling: 0,77 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: oogirritatie

VRW → AGW: tranenvloed, keelpijn, hoesten, kortademigheid, hoofdpijn,

AGW → LBW: ademnood, bloed ophoesten

Boven LBW: bewusteloosheid, ademstilstand, hartstilstand, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Chloorcyaan veroorzaakt bevriezingsletsel, longschade en blauwzuurvergifting.
- De stof heeft een zeer sterk irriterende tot bijtende werking op de slijmvliezen en de longen.
- De stof kan tot cyanide intoxicatie leiden omdat cyaanwaterstof (HCN) vrij snel in het lichaam gevormd wordt. Sterfte is veelal het gevolg van ademhalingsdepressie.

Effecten bij blootstelling aan vloeistof

Huidcontact en oogcontact: thermische én chemische brandwonden, zie verder: Effecten bij inhalatoire blootstelling

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: direct 100% zuurstof toedienen, GEEN mond-op-mondbeademing, direct spoedeisende medische hulp inzetten, specifieke behandeling vereist!

Ontsmetting vloeistof

huid: direct 100% zuurstof toedienen, GEEN mond-op-mondbeademing, aan de huid vastgevroren kleding NIET lostrekken, spoelen met veel water / kleding verwijderen, direct spoedeisende medische hulp inzetten.

ogen: spoelen met water (evt. contactlenzen verwijderen), GEEN mond-op-mondbeademing, direct spoedeisende medische hulp inzetten, specifieke behandeling vereist!

inslikken: direct 100% zuurstof toedienen, GEEN mond-op-mondbeademing, direct spoedeisende medische hulp inzetten, specifieke behandeling vereist!

Specifieke behandeling en materialen*: Hulpverleners: Persoonlijke Bescherming!* Bij vergiftiging door deze stof is specifieke eerste hulp noodzakelijk; specifieke antidota (zoals 100% zuurstof en o.a. hydroxocobalamine en natriumthiosulfaat) moeten met gebruiksaanwijzing ter plekke beschikbaar zijn.
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 506-77-7 **Cyanogen chloride** **Cl–C≡N** **UN-nr: 1589**

Basis for the Dutch Intervention Values

VRW: Partly based on information as described in ERPG-document, in contrast to ERPG values are derived

AGW: Different rationale than ERPG, different values are derived, other time-points added.

LBW: Partly based on information as described in ERPG-document, different values are derived, other time-points added.

Date: 31-10-2017	ERPG,2013

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.68	0.68	0.68	0.68	0.68	0.68	Eye irritation
AGW	6.1	6.1	5.0	3.3	2.3	1.7	One-third of LBW, maximized at 10- and 30-min because of lachrymation in humans
LBW	39	22	15	10	7.0	5.0	Acute lethality in dogs

Derivation of the Dutch Intervention Values

VRW: The VRW is based on a human volunteer study where 5-7 subjects were exposed to cyanogen chloride for up to 3 minutes at nominal concentrations of 0.0061, 0.0122, 0.0244, 0.0488 and 0.0976 mg/L or 6.1, 12.2, 24.4, 48.8 and 97.6, mg/m³, respectively). The subjects were asked to note the point of eye irritation, tear formation and tear overflow. The lowest concentrations at which 100% of the subjects reported a response was 12.2 mg/m³ (eye irritation), 24.4 mg/m³ (tear formation), and 48.8 mg/m³ (tear overflow). At 6.1 mg/m³ the majority of the subjects (6/7) still reported eye irritation. In the absence of any other suitable data, the lowest concentration of 6.1 mg/m³ tested in this study was selected as a PoD for VRW derivation. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was not applied as eye irritation is considered to be concentration-dependent rather than time-dependent. An additional factor of 3, leading to a total uncertainty factor of 9, was applied because an effect level was used as PoD and data that address VRW effects at longer exposure durations are lacking.

AGW: The same human volunteer study as for the VRW was considered for deriving AGW values, as tear flow is a clear AGW effect. The first tear (flow) was already reported for 2/7 subjects at 6.1 mg/m³ and progressed to all the subjects at 24.4 mg/m³. The 3 min exposure to a concentration of 6.1 mg/m³ was considered as threshold for tear flow and was considered as the PoD for derivation of AGW values. However, the effect was observed after 3 minutes and time scaling would lead to unreasonably low AGW values for the longer durations. No data are available that address AGW effects at longer exposure durations. Therefore 1/3 x LBW was used as point of departure for the AGWs with an upper limit of 6.1 mg/m³ (from the human volunteer study) at the 10 and 30 minute AGWs. These values are supported by another study reporting that 1 ppm (2.6 mg/m³) cyanogen chloride was identified for man as the lowest irritant concentration for a 10-minute exposure; 2 ppm (5.1 mg/m³) for 10 minutes was an intolerable concentration; and 48 ppm (123 mg/m³) was fatal in 30 minutes. The primary report of this study could not be traced.

LBW: The LBW is based on a large data base of acute inhalation toxicity studies in rat, mouse, guinea pig, rabbit, dog and goat exposed to analytically determined concentrations of cyanogen chloride for 1 to 240 minutes. An overview of lethality data at various time points and exposure concentrations is given in Sommerville (2016). The results do not vary greatly between study reports, e.g. LC_{50}s as reported by Sommerville at 30 min exposure are 370-458 mg/m³ (mouse), 272 mg/m³ (rat), 176-199 mg/m³ (dog), 793 mg/m³ mg/m³ (guinea pig), 470 mg/m³ (rabbit), 478 mg/m³ (cat) and 513 mg/m³ (monkey), At 7.5 min exposure the reported LC_{50} values were 605, 764, 583, 1153, 791 mg/m³ for mouse, rat, dog, guinea pig and rabbit, respectively. Based on the study with the most Cxt data points (Marshall and Miller, 1918), the LC_{01} values for 10 min, 30 min, and 1, 2, 4, and 8 hour were calculated for the rat (313, 157, 101, 66, 42, 27 mg/m³ and n= 1.6), mouse (184, 87, 55, 34, 21, 13 mg/m³ and n=1.5), rabbit (472, 370, 317, 272, 233, 200 mg/m³ and n=4.5), guinea pig (401, 267, 207, 160, 124, 96 mg/m³ and n=2.7) and dog (116, 65, 45, 31, 22, 15 mg/m³ and n=1.9) using Dose Resp. The dog appears to be slightly more sensitive to cyanogen chloride than mouse and rat.

Rabbit and guinea pig were the least sensitive. The calculated LC_{01} values for the dog were used as PoD for deriving LBWs. The use of default uncertainty factor of 3 for intrapecies differences was considered sufficient. An uncertainty factor of 1 for interspecies differences was considered sufficient because data show that there are no large differences between species, that the dog is the most sensitive species and because a larger factor would lead to values conflicting with the available, though limited, human data (reported fatality after 30 minutes of exposure to 125 mg/m^3).

Additional toxicological information (including relevant results of a general literature search, if any)

Cyanogen chloride has been investigated rather extensively as a chemical warfare agent by US and UK governments in the WW-I and II era. Processed data of this classified information has been referenced in several documents, not always in a consistent manner. Very recently the primary publications have become publically available. For the purpose of intervention values we have focused on the acute inhalation toxicity studies performed in rat, mouse and dog (Marshall and Miller, 1918). For an overview of all data the recent publication of Sommerville, 2016 (Allometric modeling of mammalian cyanogen chloride inhalation lethality, Issues in Toxicology 2016; volume 26, 264-306) is referred to. This publication was aimed at combining all the existent confidential and non-confidential information on cyanogen chloride from US and UK and was used next to the ERPG document as basis for deriving intervention values.

To calculate the LC_{01} values, the primary study of Marshall and Miller, 1918[9] was used. Dog, mouse, rat, rabbit and guinea pig (1-6/ concentration/time level) were exposed to air concentrations varying from 50-4800 mg/m^3 for 2.5-240 minutes.

Cyanogen chloride induces respiratory irritation and interferes with cellular metabolism due to the formation of the cyanide ion. The conversion from cyanogen chloride to free cyanide is a result of a reaction between cyanogen chloride and hemoglobin and subsequently with glutathione. Glutathione also reacts directly with cyanogen chloride to produce cyanide ions. Effects of cyanogen chloride include severe lacrimation, pulmonary irritation and pulmonary edema.

There is no information on the reproductive and developmental toxicity via the inhalation route in the available literature. Nevertheless, the teratogenic potential of inorganic cyanide was studied by infusing sodium cyanide to hamsters. Based on the results of this study and the results of studies with sodium cyanide, aliphatic nitriles and cyanogenic glycosides, it can be concluded that the teratogenic activities can be attributed to the cyanide released through metabolism of the parent compounds.

No harmonised H-sentences for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

Derivation of the carcinogenic risk potency (CRP):

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: Sharp, irritating odour

OT: 2.05 mg/m^3 [Ruth, 1986]

LOA = 11.8 * 2.05 * 1.33 =32 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies above the VRW, AGW, and LBW values, except for the 10-min LBW.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)[10]

VRW level **0.68**	*AEGL-1* -	*ERPG-1* NR		*IDLH:* ND[11]
AGW level **5.0**	*AEGL-2* -	*ERPG-2* 0.125		
LBW level **15**	*AEGL-3* -	*ERPG-3* 10		

[9] Marshall E.K. and Miller E.J. Toxicity of cyanogen chloride in the dog, rabbiot, guinea pig, rat and mouse on inhalation. Report NO. 222 in Marshal, E.K. ed. Pharmacological and Research Section Monongraphs. War Department Chemical Warfare Service, Research Division, American University Experiment Station, Washington DC, c. 1918.

[10] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

[11] ND=Not determined (25 mg/m^3 for CN)

Stofdocument deel A

CAS-nr: 75-68-3 **1-Chloor-1,1-difluorethaan** $C_2H_3ClF_2$ **VN-nr: 2517**

GEVI: 23

Synoniemen: HCFC-142b, monochloordifluorethaan, R142b (Engels:1-chloro-1,1difluoroethane) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	14.000	9.600	7.600	6.000	4.800	3.100
Alarmeringsgrenswaarden	AGW (mg/m³)	35.000*	35.000*	35.000*	26.000*	13.000	6.500
Levensbedreigende waarden	LBW (mg/m³)	240.000**	170.000**	84.000*	42.000*	21.000*	10.000

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,239 ppm; 1 ppm = 4,18 mg/m³

Explosiegrens: LEL = 4,4 vol% ≈ 184.000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

** berekende interventiewaarde hoger dan 50% LEL

Geur: (nagenoeg) reukloos

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos onder druk tot vloeistof verdicht gas

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 3,5

Molecuulmassa:	100,5 g/mol
Zuurgraad:	geen data
LogKow:	1,6
Wateroplosbaarheid:	0,19 g/100 ml (matig)
Verzadigde dampdruk:	2895 mbar

Overige informatie

Publieke grenswaarde: Niet afgeleid

MAK: 4170 mg/m³

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: irritatie luchtwegen, sufheid

AGW → LBW: ernstige irritatie luchtwegen, bewustzijnsdaling, hartritmestoornissen

Boven LBW: hartstilstand, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- 1-Chloor-1,1-difluorethaan veroorzaakt luchtwegirritatie en bewustzijnsdaling.
- Blootstelling aan 1-chloor-1,1-difluorethaan kan het hart overgevoelig maken voor adrenaline.
- Door verdringing van zuurstof uit de lucht kan het gas verstikkend werken.

Effecten bij blootstelling aan vloeistof

Huidcontact: bevriezingsverschijnselen zoals roodheid, pijn, blaren

Oogcontact: bij bevriezing: roodheid en pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust en arts raadplegen..

Ontsmetting vloeistof

huid: N.v.t. (gas). *Bij contact met de vloeistof*: aan de huid vastgevroren kleding NIET lostrekken, spoelen met veel water / kleding verwijderen en arts raadplegen.[1)].

ogen: *bij gasblootstelling en bevriezing*: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, *bij bevriezing*: blijven spoelen tijdens vervoer.

inslikken: N.v.t. (gas).

Specifieke behandeling en materialen*: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 75-68-3 **1-chloro-1,1-difluoroethane** **$C_2H_3ClF_2$** **UN-nr: 2517**

Basis for the Dutch Intervention Values

VRW: Based on toxicological information in ERPG document

AGW: Based on toxicological information in ERPG document

LBW: Based on toxicological information in ERPG document

Date: 16-12-2010	ERPG document 1999

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	14,000	9,600	7,600	6,000	4,800	3,100	No effect level in animals
AGW	35,000 *	35,000 *	35,000 *	26,000 *	13,000	6,500	Threshold of cardiac sensitization in dogs Threshold of unconsciousness in rats
LBW	240,000**	170,000 **	84,000 *	42,000 *	21,000 *	10,000	Threshold of lethality in rats

* value higher than 10% of LEL; ** value higher than 50% of LEL

Derivation of the Dutch Intervention Values

VRW: As point of departure for the derivation of VRW values, a 6 hour exposure to 10,000 ppm (42,000 mg/m³) was chosen. This concentration had no adverse effects (clinical, hematological, histopathological) in a 90-day inhalation toxicity study in dogs and rats exposed for 6 hours/day 5 days/week. In a 2-week inhalation toxicity study in rats during exposure to 20,000 ppm (84,000 mg/m³) for 6 hour/day 5 days/week, salivation was observed. Inter- and intraspecies uncertainty factors of 3 each were applied to account for differences between species and between individuals. Time scaling was performed using the equation $C^n \times t = k$, using the default values of n =1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively.

AGW: For the derivation of the AGW values two points of departure were used. For the 10-minutes, 30-minutes and 1-hour AGW values the NOAEL for cardiac sensitization was used. In beagle dogs cardiac sensitization was observed in 0 out of 6 dogs exposed for approximately 5 minutes to 25,000 ppm (105,000 mg/m³) and in 5 out of 12 dogs exposed to 50,000 ppm (210,000 mg/m³). As beagle dogs are considered to be especially sensitive to cardiac sensitization no interspecies factor was applied. An intraspecies factor of 3 was applied to account for sensitive individuals. No time scaling was performed. As point of departure for derivation of the 2, 4, and 8-hour AGW values, 30 minute exposure to 250,000 ppm (1,000,000 mg/m³) was chosen (see additional toxicological information). This was the highest concentration that did not result in unconsciousness and severe pulmonary irritation in rats. Inter- and intraspecies factors of 3 each were applied to account for differences between species and between individuals. Time scaling was performed using the equation $C^n \times t = k$, using the default value of n =1 for extrapolation to longer exposure durations.

LBW: As point of departure for the derivation of LBW values 400,000 ppm (1,700,000 mg/m³) was chosen. This concentration caused severe pulmonary irritation and unconsciousness but no mortality in rats exposed for 30 minutes. The next highest concentration of 500,000 ppm (2,100,000 mg/m³) resulted in mortality. Inter- and intraspecies factors of 3 each were applied to account for differences between species and between individuals. Time scaling was performed using the equation $C^n \times t = k$, using the default values of n =1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively.

The choice of the point of departure is supported by 1) a reported 2 hour LC_{50} for mice of 447,000 ppm (1,870,000 mg/m³) from which a threshold for lethality of 447,000 / 3 = 149,000 ppm (623,000 mg/m³) can be calculated; and 2) a reported approximate lethal concentration in rats after 4 hours exposure of 128,000 ppm (535,000 mg/m³).

Additional toxicological information (including relevant results of a general literature search, if any)

The AGW values for time points 2h, 4h and 8h were based on a study of Lester and Greenberg (1950). In this

study, rats were exposed to 150000-800000 ppm (627062-3344336 mg/m^3) 1-chloro-1,1-difluoroethane. Disappearance of the postural reflex was seen at 200000 ppm 836084 mg/m^3). Unconsciousness occurred at 300000 ppm (1254125 mg/m^3) and death at 500000 ppm (2090210 mg/m^3).

1-chloro-1,1-difluoroethane has a low order of acute inhalation toxicity. It can cause irritation of the respiratory tract and has anesthetic effects at high inhalation levels. The compound can sensitize the heart to adrenalin and cause cardiac arrest.

There was no evidence of embryotoxicity/teratogenicity or effect on male fertility of 1-chloro-1,1-difluoroethane in rats exposed to concentrations up to 10,000 ppm (42,000 mg/m^3) or 20,000 ppm (84,000 mg/m^3), respectively.

No harmonized H-sentences for human health.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived. In a 2-year combined chronic toxicity/carcinogenicity study in rats exposed to 1000, 10,000, or 20,000 ppm (4200, 42,000, or 84,000 mg/m^3) for 6 hours/day 5 days/week, 1-chloro, 1,1-difluoroethane was not carcinogenic.	Odour: nearly odourless No LOA was derived.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **7,600**	*AEGL-1* not derived	*ERPG-1* 42,000		*IDLH:* not derived
AGW level **35,000**	*AEGL-2* not derived	*ERPG-2* 63,000		
LBW level **84,000**	*AEGL-3* not derived	*ERPG-3* 100,000		

Stofdocument deel A

CAS-nr: 10049-04-4 **Chloordioxide** **O=Cl=O** **VN-nr:** nvt

GEVI: geen

Synoniemen: chlooroxide, chloorperoxide (Engels: chlorine dioxide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m³)**	0,84	0,84	0,84	0,84	0,84	0,84
Alarmeringsgrenswaarden	**AGW (mg/m³)**	3,9	3,9	3,1	2,4	1,9	1,3
Levensbedreigende waarden	**LBW (mg/m³)**	44	15	7,3	7,3	7,3	7,3

Datum vaststelling: 28-11-2008

Conversiefactor: 1 mg/m³ = 0,356 ppm; 1 ppm = 2,81 mg/m³

Explosiegrens: LEL = 10 vol% ≈ 281.000 mg/m³

Geur: stekende chloorachtige geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: roodgeel tot geelgroen gas bij kamertemperatuur

Brand: niet brandbaar, bij vele reacties kans op brand en explosie

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,3

Molecuulmassa: 67,5 g/mol
Zuurgraad: Geen data
LogKow: Geen data
Wateroplosbaarheid: 0,8 g/100 ml (slecht)
Verzadigde dampdruk: 1400 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: 0,28 mg/m³
TLV-TWA: 0,28 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW geen effecten

VRW → AGW: irritatie van luchtwegen en ogen: hoesten, rode ogen, keelpijn, tranenvloed,

AGW → LBW: benauwdheid, bloed ophoesten, chemische pneumonie.

Boven LBW: pulmonaire congestie, longoedeem, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Inhalatie van chloordioxide resulteert primair in irritatie van luchtwegen en ogen.
- Chloordioxide veroorzaakt een type I inhalatoire intoxicatie.
- Blootstelling aan chloordioxide kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn, branderig gevoel, brandwonden

Oogcontact: *bijtend*, roodheid en pijn.

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof

huid: n.v.t. (gas), maar na huidblootstelling aan gas of oplossingen:
eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen, en direct arts raadplegen.

ogen: n.v.t. (gas), maar na oogcontact met gas of oplossingen:
minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: n.v.t. (gas) maar na inslikken van oplossingen met meer dan 3%:
mond laten spoelen (uitspugen!), GEEN braken opwekken, en direct spoedeisende medische hulp inzetten;
na inslikken van oplossingen met minder dan 3%:
mond laten spoelen (uitspugen!), rust, arts raadplegen.

Specifieke behandeling en materialen: geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 10049-04-4 **Chlorine dioxide** **O=Cl=O** **UN-nr: -**

Basis for the Dutch Intervention Values

VRW: Same point of departure as for AEGL values but using different uncertainty factors, 2h value added

AGW: AEGL value is adopted, 2 h value added

LBW: Same point of departure as for AEGL values but using different uncertainty factors and difference in time scaling, 2h value added, 2 h value added

Date: 28-11-2008 | AEGL document: Final, 2007

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.84	0.84	0.84	0.84	0.84	0.84	Slight irritation (animals)
AGW	3.9	3.9	3.1	2.4	1.9	1.3	Irritation (animals)
LBW	44	15	7.3	7.3	7.3	7.3	Congestion and pulmonary oedema

Derivation of the Dutch Intervention Values

VRW: No human data are available. The VRW was based on slight salivation, slight lacrimation and slight chromodacryorrhoea in rats exposed to 3 ppm (8.4 mg/m^3) chlorine dioxide for 6 hours. A modifying factor was considered to be not necessary, viewing the severity of the effects. Inter- and intraspecies uncertainty factors of 3 each are applied because chlorine dioxide is highly reactive and clinical signs are likely caused by a direct chemical effect on the tissues and this type of effect is not expected to vary greatly between species or among individuals. Thus the total uncertainty factor is 10. The VRW values were held constant across all time points because minor irritation is not likely to be time dependent.

AGW: The lacrimation, salivation, dyspnoea, weakness, and pallor noted in rats exposed to 12 ppm (33.7 mg/m^3) chlorine dioxide for 6 hours were used to derive the AGW. A modifying factor of 2 was applied to account for the sparse dataset for AGW-effects. Inter- and intraspecies uncertainty factors of 3 each will be applied because chlorine dioxide is highly reactive and clinical signs are likely caused by a direct chemical effect on the tissues and this type of effect is not expected to vary greatly between species or among individuals. Thus the total uncertainty factor is 20. The concentration-exposure time relationship $C^n \times t = k$ was used using n=3 and n=1. The 30-min AGW was adopted as the 10-minute AGW because time scaling from 6 hours to 10 min introduces a too large uncertainty.

LBW: Several animal lethality studies are available; the LBW is based on the most robust study in rats but supported by the other studies. No deaths were observed after a 6-hour exposure of 4 rats to 26 ppm (73 mg/m^3). Both two animals exposed to 38 ppm (107 mg/m^3) for 6 hours died, with one death after 4.5 hours of exposure. Also two animals exposed to 54 ppm (152 mg/m^3) for 1 hour died during exposure. These data show that the threshold for lethality is approximately similar for a single exposure from 1 to 6 hour, i.e., approximately 26 ppm (73 mg/m^3). This is supported by the additional available data. Therefore, LBW values for the time durations of 1 to 8 hours will be set equal. Chlorine is highly reactive and causes serious adverse effects in the lung, including congestion and pulmonary oedema. These effects are presumed to be the cause of death and are likely caused by a direct chemical effect on the tissue in the lung. As this effect is not considered to vary greatly among individuals or between species, intraspecies and interspecies uncertainty factors of 3 each were applied. Starting from 73 mg/m^3 and application of a total uncertainty factor of 10 provides an LBW value of 7.3 mg/m^3 for 1-, 2-, 4- and 8-hour exposures. In addition, no mortality was found in rats exposed to 70 ppm (197 mg/m^3) for 30 min supporting time scaling with n=1 from the 1-hour value of 7.3 mg/m^3 to 30 and 10 min.

Additional toxicological information (including relevant results of a general literature search, if any)

Inhaled chlorine dioxide primarily acts as a respiratory tract and ocular irritant. Lacrimation, salivation, dyspnoea, weakness, pallor and pulmonary congestion and oedema were noted in rats after acute exposure.

Alveolar congestion and haemorrhage, bronchial inflammation, and peribronchiolar oedema have also been noted in rats and rabbits after inhalation of chlorine dioxide. Limited data from human exposure also indicate respiratory irritation.

No reproductive or developmental effects expected after single inhalation exposure.

H301: Toxic of swallowed; H314: Causes severe skin burns and eye damage.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived.	Pungent chloride odour No LOA was derived, due to lack of data. It is unclear whether the substance can be smelled at intervention value levels.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **0.84**	*AEGL-1* 0.42	*ERPG-1* N.R.		*IDLH:* 14 (30 min)
AGW level **3.1**	*AEGL-2* 3.1	*ERPG-2* 1.4		
LBW level **7.3**	*AEGL-3* 6.7	*ERPG-3* 8.4		

Stofdocument deel A

CAS-nr: 107-20-0 **2-Chloorethanal** **$ClCH_2$-CHO** **VN-nr: 2232** **GEVI: 66**

Synoniemen: chlooraceetaldehyde, monochloroacetaldehyde (Engels: chloroacetaldehyde)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	37	15	8,3	4,6	2,6	1,5
Alarmeringsgrenswaarden	AGW (mg/m³)	64	26	14	8,1	4,5	2,5
Levensbedreigende waarden	LBW (mg/m³)	140	58	32	18	10	5,7

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,306 ppm; 1 ppm = 3,27 mg/m³

Explosiegrens:
Geen data

Geur: penetrant, stekend

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: niet brandbaar maar kan boven 88°C een brandbaar/explosief mengsel vormen.

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,7

Molecuulmassa: 78,50 g/mol
Zuurgraad: Geen data
LogKow: 0,37
Wateroplosbaarheid: Goed
Verzadigde dampdruk: 133 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 3,3 mg/m³ ceiling

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte irritatie van ogen, neus en luchtwegen

VRW → AGW: sterke irritatie van ogen, neus en luchtwegen, tranenvloed

AGW → LBW: tranenvloed, verlies van gezichtsvermogen, longoedeem, benauwdheid

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof is bijtend voor de ogen, huid en de luchtwegen. De damp van de stof is sterk irriterend tot bijtend.
- Blootstelling aan de stof kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: Roodheid en pijn. Blaarvorming. Gele verkleuring van de huid. Brandwonden.

Oogcontact: Oogirritatie, pijn.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

Ontsmetting vloeistof

huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, spoelen met veel water / kleding verwijderen, en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer..

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 107-20-0 **Chloroacetaldehyde** **$ClCH_2$-CHO** **UN-nr:2232**

Basis for the Dutch Intervention Values

VRW: Same point of departure as for AEGL values, but modifying factor was deleted, 2h value added

AGW: Same point of departure as for AEGL values, but modifying factor was deleted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: November 2015 | AEGL document: Final, 2014

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	37	15	8.3	4.6	2.6	1.5	Threshold for ocular and nasal irritation in rats
AGW	64	26	14	8.1	4.5	2.5	Threshold for pulmonary effects in rats
LBW	140	58	32	18	10	5.7	Estimate $BMCL_{05}$ lethality threshold in rats

Derivation of the Dutch Intervention Values

VRW: The VRW values are based on animal data. A study showed that ocular and nasal irritation were slight to very slight in rats, mice and one rabbit when exposed to a concentration of 5 ppm (16 mg/m^3) for 7 hours. In guinea pigs no effects were reported at this concentration. The concentration of 5 ppm (16 mg/m^3) for 7 hours was used as point of departure for VRW derivation. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Data in rat indicate that the level of irritation was related to concentration as well as duration of exposure. At higher concentration other effects occurred including laboured breathing and slight drowsiness. Therefore it was considered to be inappropriate to use the same value for all exposure durations. Time scaling was performed using the equation $C^n \times t = k$ with the chemical specific value for n = 1.2 based on lethality data in rats to extrapolate from 420-min of exposure to 10, 30, 60, 120, 240 and 480-min exposures.

AGW: The AGW values are based on animal data. In a study in rats a concentration of 44 ppm (144 mg/m^3) at a duration of 1 hour was considered to be the LOAEL for decreased pulmonary function. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$ with the chemical specific value n = 1.2 based on lethality data in rats.

LBW: The LBW values were determined by using available mortality data in rats in a benchmark dose approach. The $BMCL_{05}$ value of 99 ppm (323 mg/m^3) for 1 hour was used as a point of departure for deriving the LBW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$ with the chemical specific value for n = 1.2 based on lethality data from a second rat study.

Additional toxicological information (including relevant results of a general literature search, if any)

Chloroacetaldehyde is a corrosive substance. The substance is irritating to the skin, eyes and respiratory tract. Exposure via inhalation resulted in impairment of the pulmonary function, pulmonary edema, and death in laboratory animals. Steep concentration-response and time-response relationships appeared to be present for chloroacetaldehyde

Data on developmental and reproductive toxicity and carcinogenicity are too limited to draw conclusions.

H330: Fatal if inhaled, H311: Toxic in contact with skin, H301: Toxic if swallowed, H314: Causes severe skin burns and eye damage, H351: Suspected of causing cancer

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: acrid, pentrating odour.

No LOA was derived due to lack of data.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*				
VRW level **8.3**	*AEGL-1* 4.2	*ERPG-1* -		*IDLH: 147*
AGW level **14**	*AEGL-2* 7.1	*ERPG-2* -		
LBW level **32**	*AEGL-3* 32	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 107-07-3 **2-Chloorethanol** CH_2ClCH_2OH **VN-nr: 1135**
GEVI: 663

Synoniemen: 2-chloorethan-1-ol, glycolchlorohydrine, ethyleenchloorhydrine (Engels: 2-chloroethanol)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	72	50	39	31	16	7,8
Levensbedreigende waarden	LBW (mg/m³)	220	150	120	94	47	23

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,299 ppm; 1 ppm = 3,35 mg/m³

Explosiegrens: LEL = 4,9 Vol% ≈ 164.000 mg/m³

Geur: zwakke ether-achtige geur

LOA: 21,0 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,01

Molecuulmassa: 80,5 g/mol
Zuurgraad: geen data
LogKow: -0,06
Wateroplosbaarheid: volledig
Verzadigde dampdruk: 7,3 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: 3,3 mg/m³
TLV-ceiling: 3,3 mg/m³ (huid)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW: keelpijn, hoesten, hoofdpijn, buikpijn, misselijkheid

AGW → LBW: duizeligheid, ademnood, braken, ernstige bloeddrukdaling, bewusteloosheid

Boven LBW: sterfte

LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Blootstelling aan 2-chloorethanol-1 kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- De stof kan gelijktijdig inwerken op alle organen. met als gevolg een meervoudig orgaanfalen.
- Afhankelijk van de ernst van de vergiftiging kan de latentietijd variëren van 30 minuten tot enkele uren
- De effecten van een systemische vergiftiging zijn vooral neurotoxisch van aard.

Effecten bij blootstelling aan vloeistof

Huidcontact: hoofdpijn, buikpijn, misselijkheid, braken, duizeligheid, ademnood, ernstige bloeddrukdaling, bewusteloosheid. De stof kan gemakkelijk door de huid worden opgenomen.
Oogcontact: roodheid en pijn, hoornvliesbeschadiging (reversibel, ca. 48 u).

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en direct spoedeisende medische hulp inzetten.

ogen: zie hierboven

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 107-07-3 **2-chloroethanol** **CH_2ClCH_2OH** **UN-nr: 1135**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL approach (1/3 LBW) is adopted, 2h value added

LBW: Same point of departure, different uncertainty factors, 2h value added

Date: November 2015 | AEGL document: Final, 2014

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Insufficient data
AGW	72	50	39	31	16	7.8	One third of LBW
LBW	220	150	120	94	47	23	Threshold for nonlethal effects in mice

Derivation of the Dutch Intervention Values

VRW: The VRW values were not derived for 2-chloroethanol. There are no exposure-response data in humans or animals consistent with VRW-level effects. The lack of VRW-values does not necessarily mean that exposure below AGW-levels is without any effects.

AGW: There are no exposure-response data consistent with AGW-level effects. Furthermore, the available human case reports lack adequate exposure descriptions and the effects that were found in the studies only cover lethality. There is no information provided about nonlethal effects. In absence of relevant data, the AGW values are estimated by dividing the LBW values by a factor 3. This reduction is considered an estimate of the threshold for irreversible effects.

LBW: Available data in humans do not provide sufficient information on exposure conditions. Available animal studies are performed with a limited number of animals and show either near 100% lethality or no lethality. Such data do not allow for a valid estimation of a lethality threshold using the benchmark dose method. Therefore, data from a study in mice was used which shows both a 100% lethal estimate (1,090 ppm / 3,651 mg/m³) and a nonlethal estimate (280 ppm / 938 mg/m³) at the same exposure duration of 2 hr. The nonlethal estimate of 280 ppm (938 mg/m3) for 2 hr was used as a point of departure for deriving the LBW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was performed using the equation $C^n \times t = k$, using the default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

The precise mechanism of toxicity of 2-chloroethanol is unknown. In studies a delay between exposure and onset of symptoms (including gastrointestinal disorders, CNS effects and respiratory tract irritation) in humans is noted, which suggests an absence of warning properties of exposure to 2-chloroethanol. The studies suggest a multi-organ involvement, after exposure. The substance is severely irritating to the eyes and the respiratory tract and may cause effects on the CNS, cardiovascular system, kidney and liver. Exposure to the substance can result in cardiac disorders, low blood pressure, kidney impairment, liver impairment, respiratory failure and death. A steep exposure-response relationship appeared to be present for 2-chloroethanol. The case reports in one of the studies showed that women may be somewhat more sensitive to develop symptoms than men.

Data on developmental and reproductive toxicity and carcinogenicity of 2-chloroethanol upon inhalation are too limited to draw conclusions.

H330: Fatal if inhaled, H310: Fatal in contact with skin, H300: Fatal if swallowed

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: faint ether-like odour

	Odour threshold: 1.34 mg/m^3 [ACGIH, 2001] No LOA was derived (due to lack of data)

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH: 23 (30 minutes)*
AGW level **39**	*AEGL-2* 3.9	*ERPG-2* -		
LBW level **120**	*AEGL-3* 12	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 107-30-2 **Chloormethylether** CH_3OCH_2Cl **VN-nr: 1239**

GEVI: 663

Synoniemen: methylchloormethylether, chloormethoxymethaan, CMME (Engels: chloromethyl methyl ether)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	2,9	2,0	1,6	1,2	1,0	0,72
Levensbedreigende waarden	LBW (mg/m³)	12	8,5	6,8	5,4	4,3	3,1

Datum vaststelling: 13-05-2009

Conversiefactor: 1 mg/m³ = 0,299 ppm; 1 ppm = 3,35 mg/m³

Explosiegrens: geen data

Geur: typerende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,4

Molecuulmassa:	80,5 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	213 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: luchtwegirritatie, hoesten

AGW → LBW: benauwdheid, longoedeem, koorts

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Stof werkt irriterend tot bijtend op ogen, huid en luchtwegen.
- Chloormethylether kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden.
- Bis(chloormethyl)ether kan als verontreiniging aanwezig zijn en is toxischer dan chloormethylether.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, pijn, brandwonden

Oogcontact: bijtend, roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: 1.
CRP: 1,30 mg/m³
(afgeleid van CRP voor dichloordimethylether)

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen).

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**:* geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 107-30-2 **Chloromethyl methyl ether** **CH_3OCH_2Cl** **UN-nr: 1239**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL.

AGW: AEGL value adopted (except 10 min value for which time scaling was applied), 2hr value added.

LBW: AEGL value adopted (except 10 min value for which time scaling was applied), 2hr value added.

Date: 13-05-2009 | AEGL document: Final, 2012

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	2.9	2.0	1.6	1.2	1.0	0.72	Threshold of irriversible lung lesions in animals
LBW	12	8.5	6.8	5.4	4.3	3.1	Threshold of animal lethality

Derivation of the Dutch Intervention Values

VRW: Not recommended, because no studies were available showing VRW type effects.

AGW: AGW values were based on an acute toxicity study in which rats and hamsters were exposed to 12.5-225 ppm (42-753 mg/m³) CMME (content of BCME not given) for 7 hours. Toxic effects were not attributed to specific concentrations, but it was stated that animals that died, and to a lesser degree, animals that survived, had increased relative lung weights, pulmonary congestion, edema, hemorrhage, and acute necrotizing bronchitis. Therefore, 12.5 ppm (42 mg/m³) was considered the LOAEL for serious or irreversible lung lesions in both species. An estimated NAEL of 4.2 ppm (14 mg/m³) for serious or irreversible lung lesions in both species was obtained by dividing the LOAEL by an adjustment factor of 3. An uncertainty factor of 10 was used: 3 for interspecies extrapolation and 3 for intraspecies variability. A modifying factor of 1.7 was also applied because the BCME content in technical grade CMME in the key study was unknown; it was obtained by assuming 10% BCME (the maximum reported) and accounting for the greater BCME toxicity (rat 7h-LC_{50} was 55 ppm (184 mg/m³) for CMME and 7 ppm for BCME in the key study), as follows: modifying factor = [0.1 x (55/7)] + [0.9 x 1] = 1.7. Scaling across time was performed using n=3 and n=1 for exposure durations shorter and longer, respectively, than 7 hours. In contrast to the 10 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: LBW values were based on the LC_{50} study in which rats and hamsters exposed for 7 hours to 12.5-225 ppm (42-753 mg/m³) CMME (content of BCME not given) had increased relative lung weights, congestion, edema, hemorrhage, and acute necrotizing bronchitis. The effects occurred in animals that died, and to a lesser degree, in animals that survived. The threshold for lethality, expressed as the 7h-$BMCL_{05}$, was approximately 18 ppm (60 mg/m³) for hamsters and 19 ppm (64 mg/m³) for rats if it is assumed that n=20 for all test concentrations (n, the number of animals, was not specified and thus had to be assumed; a lower number of animals per group would lower the $BMCL_{05}$, because less confidence is 'given' to the observed mortality percentage); 18 ppm (60 mg/m³) was used for derivation of LBW values. An uncertainty factor of 10 was used: 3 for interspecies extrapolation and 3 for intraspecies variability. As for AGW, a modifying factor of 1.7 was applied because the content of BCME in technical grade CMME in the key study was unknown. Time scaling was performed using $C^n * t = k$, with the default values of n = 1 and n = 3. In contrast to the 10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

The mechanism of CMME toxicity has not been elucidated. CMME hydrolyzes completely and irreversibly in water to form HCl, methanol, and formaldehyde. The HCl and formaldehyde can form BCME, although the kinetics of the conversion of CMME to BCME has not been defined. The respiratory tract is the primary site of technical grade CMME toxicity.

No studies on the developmental or reproductive effects in humans and/or animals were located.

H302: Harmful if swallowed; H312: Harmful in contact with skin; H332: harmful if inhaled; H350: May cause cancer.

Carcinogenicity and derivation of the CRP value
IARC classification: 1 (carcinogenic to humans) Technical grade CMME may have carcinogenic potency, but this is expected to be based on the contaminant BCME (bis-chloromethyl ether). No carcinogenicity data are available foor CMME but the AEGL TSD provides a preliminary carcinogenicity assessment for CMME with a 10% BCME contamination. Assuming that BCME is ten-fold more potent than CMME provides a CRP for CMME of 0.39 ppm (1.30 mg/m^3).

Odour and derivation of the LOA value
Typical odour No LOA was derived due to lack of reliable data. Although a LOA was not established, data from workers show that workers detect the odour at or around the AGW level and therefore, odour is regarded not useable as warning for health effects.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* NA		*IDLH:* not established
AGW level **1.6**	*AEGL-2* 1.5	*ERPG-2* 3.4		
LBW level **6.8**	*AEGL-3* 6.7	*ERPG-3* 33		

Stofdocument deel A

CAS-nr: 76-06-02 **Chloorpicrine** CCl_3NO_2 **VN-nr: 1580**

GEVI: 66

Synoniemen: nitrochloroform, trichloornitromethaan (Engels: chloropicrin) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,34	0,34	0,34	0,34	0,34	0,34
Alarmeringsgrenswaarden	AGW (mg/m³)	1,0	1,0	1,0	1,0	1,0	1,0
Levensbedreigende waarden	LBW (mg/m³)	16	11	8,6	6,8	5,4	2,7

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,146 ppm; 1 ppm = 6,84 mg/m³

Explosiegrens: geen. Alleen kans op explosie door reacties en bij snelle verhitting.

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze olieachtige vloeistof

Brand: niet brandbaar, maar bij vele reacties kans op brand en explosie

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,1

Molecuulmassa:	164,4 g/mol
Zuurgraad:	Geen data
LogKow:	2,6
Wateroplosbaarheid:	0,2 g/100 ml (slecht)
Verzadigde dampdruk:	ca 25 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: 0,68 mg/m³
TLV-TWA: 0,68 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen

VRW → AGW: tranen, keelpijn, kortademigheid, hoest, branderig gevoel achter het borstbeen, hoofdpijn, duizeligheid, flauwvallen, misselijkheid, braken

AGW → LBW: bronchitis, ademnood

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De (damp van de) stof werkt sterk irriterend tot bijtend op de ogen, de huid en de luchtwegen.
- Inademing kan chemische longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Hoofdpijn en misselijkheid kunnen tot meer dan een maand na blootstelling aan hoge concentraties chloorpicrine ervaren worden.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, brandwonden.

Oogcontact: tranenvloed, roodheid en pijn, hoornvliesbeschadiging, ernstige brandwonden.

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding, direct spoedeisende medische hulp inzetten

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 76-06-2 **Chloropicrin** **CCl_3NO_2** **UN-nr: 1580**

Basis for the Dutch Intervention Values

VRW: AEGL values adopted, 2h value added

AGW: AEGL values adopted, 2h value added

LBW: Same point of departure, using different value for n, time scaling applied to 10 min value, 2h value added

Date: 06-10-2016 | AEGL Document: Interim, June 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.34	0.34	0.34	0.34	0.34	0.34	Threshold for ocular irritation in humans
AGW	1.0	1.0	1.0	1.0	1.0	1.0	Severe ocular irritation in humans
LBW	16	11	8.6	6.8	5.4	2.7	Estimated lethality threshold ($BMCL_{05}$) in rats

Derivation of the Dutch Intervention Values

VRW: The VRW values are based on human data. In a study performed in 3 phases, healthy human volunteers were exposed to chloropicrin in varying durations and exposure concentrations, examining chloropicrin-induced sensory irritation. In phase 1 identification of chloropicrin was assessed using odor, effects on eye (eye feel) or nose (nasal feel). Exposure consisted of a single sniff (odor), 25 (eye feel) or 7 (nasal feel) seconds of exposure to concentrations of 0, 0.36, 0.53, 0.80, or 1.2 ppm (0, 2.5, 3.6, 5.5, or 8.2 mg/m^3, respectively). In Phase 2, positive detection was assessed as irritation of the eyes, nose, or throat, in subjects exposed for 20-30 minutes to 0, 0.05, 0.075, 0.10, and 0.15 ppm (corresponding to 0.34, 0.51, 0.68, and 1.0 mg/m^3, respectively) in a walk-in chamber. Phase 3 was similar but also assessed clinical signs and changes in pulmonary function in subjects exposed for 60 min on each of the 4 consecutive days to 0, 0.10, and 0.15 ppm, corresponding to 0.68 and 1.0 mg/m^3, respectively). The point-of-departure for deriving the VRW is the 20-30 min exposure to 0.050 ppm (or 0.34 mg/^{3}) which represents a NOAEL for ocular irritation. This is supported by a 1-hour $BMCL_{10}$ of 73 ppb (0.073 ppm; 0.50 mg/m^3) based on the analysis of the abovementioned data on ocular irritation in human volunteers. Time scaling was not applied as data indicate that the observed effect does not increase with duration of exposure. An intraspecies uncertainty factor was not applied either, as sensitive individuals were included in the study and did no show large variability.

AGW: The AGW values are based on the same human volunteer study as the VRW values. In the third phase of this study human volunteers were exposed to 0.1 or 0.15 ppm corresponding to 0.68 and 1.0 mg/m^3, respectively) or 60 minutes on 4 consecutive days with some participants reporting severe eye irritation during the first exposure. Though the effects were reversible and only marginally suitable for AGW derivation, human data are preferred as basis for derivation of intervention values and according to the volunteers, the symptoms were “hard to tolerate” at both exposure concentrations (8/32 and 7/32 subjects), though symptom rating was highest at the 1.0 mg/m^3. The 60 min exposure to 0.15 ppm (1.0 mg/m^3) was used as point of departure for the AGW. In accordance with the VRW derivation, time scaling was not applied as data indicate that the observed effect does not increase with duration of exposure. An intraspecies uncertainty factor was not applied either, as sensitive individuals were included in the study and did no show large variability.

LBW: The LBW values were determined by using available mortality data in rats in a benchmark dose approach. F344 rats (6-8 male rats/group) were exposed to 8.8, 11.0, 11.4, 12.1, 13.6 or 16.0 ppm (corresponding to 60, 75, 78, 83, 93, 110 mg/m^3, respectively) for 240 min and to 21.7 or 45.5 ppm (150 or 311 mg/m^3) for 30 min. The $BMCL_{05}$ value of 7.9 ppm (54 mg/m^3) for 4 hour was used as a point of departure for deriving the LBW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$ with the default n = 1 and n= 3, to calculate to longer and shorter durations, respectively. The default values for n are applied instead of the chemical specific value of 2.3 based on the rat lethality data, because only two time points support this value.

Additional toxicological information (including relevant results of a general literature search, if any)

Chloropicrin is irritating to the skin, eyes and respiratory tract. Exposure via inhalation resulted in impairment of the pulmonary function, pulmonary edema, and death in laboratory animals. The mode of action is not fully understood. Chloropricrin reacts with sulfhydryl groups of hemoglobin resulting in compromised oxygen transport.

Data on developmental and reproductive toxicity and carcinogenicity upon inhalation exposure are too limited to draw conclusions.

H330: Fatal if inhaled, H302: Harmful if swallowed; H319: Causes serious eye irritation; H335: May cause respiratory irritation, H315: Causes skin irritation

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

Derivation of the carcinogenic risk potency (CRP):

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: pungent odour

Despite reported odour detections at very low concentration no suitable threshold level was established to derive a LOA.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **0.34**	*AEGL-1* 0.34	*ERPG-1* 0.51		*IDLH:* 14 (30 min)
AGW level **1.0**	*AEGL-2* 1.0	*ERPG-2* 1.0		
LBW level **8.6**	*AEGL-3* 9.4	*ERPG-3* 10		

Stofdocument deel A

CAS-nr: 7790-94-5 **Chloorsulfonzuur** **$ClHO_3S$** **VN-nr: 1754**

GEVI: X88

Synoniemen: chloorzwavelzuur, monochloorzwavelzuur (Engels: chlorosulfonic acid) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,12	0,12	0,12	0,12	0,12	0,12
Alarmeringsgrenswaarden	AGW (mg/m³)	14	10	9,0	7,0	5,8	4,8
Levensbedreigende waarden	LBW (mg/m³)	120	89	74	61	51	42

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,206 ppm; 1 ppm = 4,846 mg/m³

Explosiegrens: geen, maar stof reageert heftig tot explosief bij contact met water.

Geur: sterke stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot lichtgele vloeistof

Brand: bij vele reacties kans op brand en explosie

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,0

Molecuulmassa: 116,5 g/mol

Zuurgraad: pH <1

LogKow: geen data

Wateroplosbaarheid: reactie

Verzadigde dampdruk: 0,5 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte irritatie aan de ogen

VRW → AGW: keelpijn en hoesten, rode en pijnlijke ogen, tranenvloed, branderig gevoel achter het borstbeen, moeizaam ademen

AGW → LBW: brandwonden, troebel zicht, blindheid, kortademigheid, ademnood

Boven LBW: ernstige kortademigheid, ademnood, kans op sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Blootstelling aan de stof kan ernstige chemische brandwonden veroorzaken. De damp van de stof werkt bijtend op de ogen, de huid en de luchtwegen.
- Inademing van de damp kan bronchitis en longoedeem veroorzaken, echter uitsluitend na verschijnselen van bijtende effecten op de slijmvliezen van ogen en/of hogere luchtwegen. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- In ernstige gevallen kans op verstikking door zwellingen in de keel en/of dodelijke afloop.
- De stof ontleed bij verhitting en vorm dan o.a. chloorwaterstof en zwaveldioxide.
- In contact met vocht vorming van o.a. zoutzuur en zwavelzuur; bij contact met warm water en waterdamp zeer heftig tot explosief; de stof vormt aan de lucht giftige en bijtende nevels

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, ernstige brandwonden.

Oogcontact: bijtend, roodheid en pijn, ernstige brandwonden, verlies van gezichtsvermogen.

Carcinogeniteit

IARC classificatie: niet geclassificeerd*

CRP: niet afgeleid

* de stof zelf is niet geclassificeerd, maar H_2SO_4 bevattende mist wel (cat 1, IARC 2012).

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding, direct spoedeisende medische hulp inzetten

Ontsmetting vloeistof

huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, spoelen met veel water / kleding verwijderen, direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7790-94-5 **Chlorosulfonic acid** **$ClHO_3S$** **UN-nr: 1754**

Basis for the Dutch Intervention Values

VRW: Based on sulfuric acid, in accordance with AEGL, 2 hr value added.

AGW: Same rationale as for AEGL (analogy with sulfuric acid values), but in contrast to AEGL-2 time-scaling is performed to derive values for other time points, 2h value added

LBW: Same point of departure as AEGL, but using different UF and different value for n, time-scaling applied to the 8 hour value, 2 hr value added.

Date: 06-10-2016 | AEGL Document: Interim June 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.12	0.12	0.12	0.12	0.12	0.12	Based on sulfuric acid (nondisabling irritation in humans)
AGW	14	10	8.5	7.0	5.8	4.8	Based on sulfuric acid (absence of AGW effects in humans)
LBW	120	89	74	61	51	42	Threshold of rat lethality

Derivation of the Dutch Intervention Values

Chlorosulfonic acid is a strong corrosive acid and hydrolyzes exothermically *in situ* upon contact with moist mucous membranes to form equimolar amounts of the strong corrosive acids HCl and H_2SO_4. Animal studies indicated that chlorosulfonic acid is more acutely toxic than HCl or H_2SO_4, or a mixture of HCl + H_2SO_4, but do not allow determination of the relative toxicities of these chemicals. Because no human or animal studies were available for derivation of the VRW and AGW, the values are based on the structural analogy to H_2SO_4. This approach is considered valid because H_2SO_4 is a rapid hydrolysis product of, and is structurally related to, chlorosulfonic acid, and the two compounds have a similar mode of toxicity (eye and respiratory irritants).

VRW: Since no appropriate data exist for chlorosulfonic acid, VRW values for sulfuric acid will be used (on molar-basis) to derive VRW values for chlorosulfonic acid. The use of sulfuric acid as a surrogate for chlorosulfonic acid was deemed appropriate, because H_2SO_4 is a rapid hydrolysis product of, and is structurally related to, chlorosulfonic acid, and the two compounds have a similar mode of toxicity (eye and respiratory irritants).

Derivation of VRW values for sulfuric acid

The results of various studies clearly indicate that the first signs of respiratory irritation that can be characterized as notable discomfort occur at concentrations higher than 0.05 ppm in humans, including exercising asthmatics, justifying an intraspecies factor of 1. It was concluded that the concentration of 0.05 ppm can be used as the point of departure for VRW. In the absence of good time-concentration effect data and considering the type of effect, the value of 0.05 ppm was flat-lined across the 10- and 30-minute, and the 1-, 2-, 4-, and 8-hour exposure time points. This approach was considered appropriate because mild irritant effects generally do not vary greatly with time, and is in line with the derivation of VRW values for other respiratory irritants.

Based on molecular weight correction the PoD for chlorosulfonic acid is 0.238 mg/m³.
For chlorosulfonic acid a modifying factor (MF) of 2 was applied because chlorosulfonic acid is believed to be approximately 2-fold more toxic than sulfuric acid. This is because one molecule of chlorosulfonic acid yields a molecule of sulfuric acid as well as a molecule of HCl and heat, and removes a molecule of water upon hydrolysis in tissues.

AGW: Since no appropriate data exist for chlorosulfonic acid, AGW values for sulfuric acid will be used (on molar-basis) to derive AGW values for chlorosulfonic acid. The use of sulfuric acid as a surrogate for chlorosulfonic acid was deemed appropriate, because H_2SO_4 is a rapid hydrolysis product of, and is structurally related to, chlorosulfonic acid, and the two compounds have a similar mode of toxicity (eye and respiratory irritants).

Derivation of AGW values for sulfuric acid

Occupational studies indicate that no irreversible or other serious health effects or an impaired ability to escape are to be expected from single exposures to concentrations of up to 9 ppm. The concentration of 6 ppm (8-hour exposure) was used as the point of departure for AGW. Under these exposure conditions workers were perfectly able to complete their work shift. An intraspecies

uncertainty factor of 3 is needed to account for sensitive subpopulations. This results in an 8-hour AGW value of 2 ppm. This AGW level is considered to be rather conservative because no irreversible or disabling effects were observed following acute exposure to sulfuric acid in any of the relevant human volunteer studies. Time scaling was performed, with n=3.7 derived from LBW calculations for sulfuric acid.

Based on molecular weight correction the PoD for chlorosulfonic acid is 30.88 mg/m^3.
A modifying factor (MF) of 2 was applied because chlorosulfonic acid is believed to be approximately 2-fold more toxic than sulfuric acid. This is because one molecule of chlorosulfonic acid yields a molecule of sulfuric acid as well as a molecule of HCl and heat, and removes a molecule of water upon hydrolysis in tissues.

LBW: The highest non-lethal concentration of 735 mg/m^3 in an 1-hour acute inhalation toxicity study with rats was used as point of departure for the derivation of the LBWs. Clinical effects were observed at 1 hour of exposure to 379-735 mg/m^3 and at 1539-3096 mg/m^3 all but one animal died. In contrast to the AEGL, the default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n * t = k$, with the n-value of 3.7 for sulfuric acid. In absence of a substance-specific n-value for chlorosulfonic acid, taking into account that sulfuric acid is formed upon hydrolysis of chlorosulfonic acid, and the similar working mechanism of both substances, this was considered appropriate.

Additional toxicological information (including relevant results of a general literature search, if any)

Chlorosulfonic acid is a strong corrosive acid, and hydrolyzes exothermically *in situ* upon contact with moist mucous membranes to form equimolar amounts of the strong corrosive acids HCl and H_2SO_4. It is unknown to what degree chlorosulfonic acid and/or its hydrolysis products contribute to chlorosulfonic acid toxicity, although each is capable of lowering tissue pH at the contact site and causing cellular destruction. Consistent with contact-site toxicity, the respiratory system was the initial target organ for chlorosulfonic acid, HCl, and H_2SO_4 in animal inhalation studies. However, since chlorosulfonic acid hydrolysis also produces heat and uses a molecule of water for each molecule of hydrolyzed chlorosulfonic acid, it is likely that there are some differences in the toxicity of chlorosulfonic acid, HCl, and H_2SO_4. Animal studies indicated that chlorosulfonic acid is more acutely toxic than HCl or H_2SO_4, or a mixture of HCl + H_2SO_4.
No animal data were found on developmental and reproductive toxicity and genotoxicity upon inhalation exposure. The chlorosulfonic acid hydrolysis products HCl and H_2SO_4 do not appear to have significant developmental or reproductive toxicity, but both have some genotoxic potential. No carcinogenicity data for chlorosulfonic acid were available. But based on occupational data, IARC concluded that strong-inorganic acid mists containing sulfuric acid are carcinogenic to humans.
H314: Causes severe burns and eye damage, H335: May cause respiratory irritation

It is noted that the observed considerable variation among studies in the exposure concentration causing lethality is likely due to difficulty in achieving and maintaining the target chlorosulfonic aerosol concentrations.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

(Strong-inorganic-acid mists (containing H_2SO_4) are carcinogenic to humans (group 1))

No carcinogenic risk potency (CRP) was derived, because not suitable data are available.

Odour and derivation of the LOA value

Odour: strong and pungent odour

No LOA was derived, because no information was found regarding the threshold of awareness and recognition.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **0.12**	*AEGL-1* 0.10	*ERPG-1* 2		*IDLH: -*
AGW level **8.5**	*AEGL-2* 4.4	*ERPG-2* 10		
LBW level **74**	*AEGL-3* 25	*ERPG-3* 30		

Stofdocument deel A

CAS-nr: 79-38-9 **Chloortrifluorethyleen** $CF_2 = CFCl$ **VN-nr: 1082**

GEVI: geen

Synoniemen: 1,1,2-trifluor-2-chloorethyleen, CTFE (Engels: chlorotrilfuoroethylene) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	2900	1200	740	440	260	160
Levensbedreigende waarden	LBW (mg/m³)	8200	3600	2100	1300	750	440

Datum vaststelling: 06-10-2016 Conversiefactor: 1 mg/m³ = 0,206 ppm; 1 ppm = 4,846 mg/m³

Explosiegrens: 14,2 vol % ≈ 688.126 mg/m³

Geur: vage etherische geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas
Brand: "brandbaar"

Relatieve dichtheid van verzadigd damp-lucht mengsel: 4

Molecuulmassa: 116,5 g/mol

Zuurgraad: Geen data
LogKow: 1,65 (estimated)
Wateroplosbaarheid: 0,40 g/100 ml (slecht)
Verzadigde dampdruk: 6122 mbar

Overige informatie

Publieke grenswaarde:
Niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: prikkeling van de slijmvliezen, licht gevoel in hoofd, versnelde ademhaling en hoofdpijn
AGW → LBW: coördinatie stoornissen, hartkloppingen, sufheid
Boven LBW: spierzwakte, ademnood, bewusteloosheid, sterfte
LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Het primaire doelorgaan zijn de nieren.
- De stof veroorzaakt oog-, neus en keel irritatie
- De zuivere stof kan polymeriseren en daarom wordt in handelsvormen vaak een stabilisator toegevoegd. Meestal is dat tributylamine. Deze stof kan bijdragen aan de irritatie effecten.

Effecten bij blootstelling aan vloeistof

Huidcontact: irritatie (mogelijk ernstig)
Oogcontact: irritatie, beperkt zicht

Carcinogeniteit

IARC classificatie: geen
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust en bij aanhoudende klachten arts raadplegen.
ogen: uitspoelen met water (evt. contactlenzen verwijderen)
Ontsmetting vloeistof
huid: bij bevriezing: kleding uittrekken (NIET lostrekken), direct spoelen met veel water (minimaal 20 min.), dan pas eventueel aan de huid vastgeplakte kleding verwijderen en verder spoelen; (bij bevriezingsletsel) arts raadplegen.
ogen: bij bevriezing: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
***Specifieke behandeling en materialen**: geen.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 79-38-9 **Chlorotrifluoroethylene** **CF_2 = CFCl** **UN-nr: 1082**

Basis for the Dutch Intervention Values

VRW: Not recommended, in contrast to AEGL

AGW: AEGL values are adopted, slightly different n-value, 2 hr value added

LBW: AEGL values are adopted, slightly different n-value, 2 hr value added

Date: 06-10-2016 | AEGL document: Interim June 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	No recommended
AGW	2900	1200	740	440	260	160	Threshold for irreversible kidney effects in rats
LBW	8200	3600	2100	1300	750	440	Threshold of for lethality in mice

Derivation of the Dutch Intervention Values

VRW: VRW values are not recommended, because there are no exposure-response data in humans or animals consistent with VRW-level effects. The lack of VRW-values does not necessarily mean that exposure below AGW-levels is without any effects.

AGW: The threshold for irreversible kidney lesions following a single exposure was chosen as the basis for the AGW. The 4-hour exposure of rats to 540 ppm (2617 mg/m³), considered a NOAEL for irreversible kidney lesions, was chosen as the point of departure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences.
Acute kidney necrosis as well as pulmonary congestions are described as effects of CTFE. Despite the fact that is unclear which effect is the preliminary effect and what effect is the cause of death, time scaling was performed using the equation $C^n \times t = k$ using a value of 1.33 for n as was calculated for the LBW derivation.

LBW: An acute inhalation toxicity study in mice served as basis for the LBW derivation. The LBW values were derived using the ten Berge (2006) probit analysis dose-response program. The threshold for lethality at each exposure duration was determined based on data of a study using three concentration levels (1000, 3000, and 8000 ppm, equivalent with approximately 4.8, 14.5 and 38.8 g/m³) at various durations (60-720 minutes). The resultant LC_{01} values for the 10 min, 30 min, 1 hour, 2 hour, 4hour and 8 hour exposure duration were 82, 36, 21, 13, 7.5 and 4.4 g/m³. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$ using a factor of 1.33 for n as was calculated according to the program.

Additional toxicological information (including relevant results of a general literature search, if any)

The nephrotoxicity is partly based on the formation of glutathione conjugates and reactive halogenated cysteine conjugates that are generated.

The substance is not considered to be reprotoxic.

No harmonised hazard sentences for human health.

Persons with kidney diseases may be more susceptible to the effects of chlorotrifluoroethylene.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

Derivation of the carcinogenic risk potency (CRP): No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: vague ethereal odour

No LOA was derived, as no information on the odour threshold was located.

Other standards and guidelines (1h values in mg/m³, unless otherwise indicated)

VRW level **NR**	*AEGL-1* 78	*ERPG-1* 97		*IDLH: not derived*
AGW level ***740***	*AEGL-2* 420	*ERPG-2* 480		
LBW level **2100**	*AEGL-3* 2000	*ERPG-3* 1500		

Stofdocument deel A

CAS-nr: 7790-91-2 **Chloortrifluoride** ClF_3 **VN-nr: 1749**

GEVI: 265

Synoniemen: (Eng: Chlorine trifluoride) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,46	0,46	0,46	0,46	0,46	0,46
Alarmeringsgrenswaarden	AGW (mg/m³)	31	13	7,9	4,6	2,7	1,6
Levensbedreigende waarden	LBW (mg/m³)	320	140	80	48	28	28

Datum vaststelling: 28-11-2008

Conversiefactor: 1 mg/m³ = 0,26 ppm; 1 ppm = 3,85 mg/m³

Explosiegrens: geen data

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas

Brand: niet brandbaar, maar bevordert de verbranding van andere stoffen. Geeft giftige stoffen vrij in een brand en veel reacties kunnen brand of ontploffing veroorzaken.

Relatieve dichtheid van verzadigd damp-lucht mengsel: 3,18

Molecuulmassa:	92,5 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	1000 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

TLV-Ceiling: 0,39 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling:

Onder VRW	mogelijk lichte irritatie
VRW → AGW:	oog- bovenste luchtwegirritatie, tranenvloed, hoesten, lichte benauwdheid
AGW → LBW:	ernstige oog- en luchtwegirritatie, pijn op de borst, benauwdheid, longontsteking, longoedeem, hartkloppingen, spierkrampen
Boven LBW:	convulsies, hartstilstand, ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Chloortrifluoride is instabiel in lucht en hydrolyseert onder vorming van waterstoffluoride (HF) en chloorhoudende verbindingen zoals chloordioxide (ClO_2). De toxiciteit van chloortrifluoride wordt bepaald door HF en ClO_2.
- Chloortrifluoride is corrosief voor alle weefsels. Bij acute inhalatoire blootstelling kunnen luchtwegen (longonsteking en/of longoedeem), slijmvliezen en huid aangetast worden; bij hoge concentraties kan blijvende longschade ontstaan.
- HF kan aanleiding geven tot een daling van Ca en Mg in het bloedserum

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, pijn, blaren, ernstige brandwonden op de huid.

Oogcontact: roodheid, pijn, ernstige diepe brandwonden, blijvend verlies van gezichtsvermogen.

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Inademing/inslikken van chloortrifluoride kan leiden tot larynx- en glottisoedeem, met risico op verstikking (asfyxie) door zwellingen in de keel. Intubatie eventueel gevolgd door beademing moeten in ernstige gevallen z.s.m. worden uitgevoerd (door specialisten).

Ontsmetting gas

algemeen: frisse lucht, rust, halfzittende houding calciumgluconaatoplossing 4% als vernevelde oplossing laten inhaleren en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken (vastgevroren kleren niet lostrekken), afspoelen met water, daarna zo snel mogelijk calciumgluconaatgel 10% op de besmette huid aanbrengen[14] en blijven inwrijven en direct spoedeisende medische hulp inzetten.

ogen: *uit*spoelen met water (evt. contactlenzen verwijderen), daarna zo snel mogelijk calciumgluconaatoplossing 4% in de ogen druppelen[12], dan naar oogarts brengen. Blijven druppelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), 200 ml calciumgluconaat 4% laten drinken[13] , GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**:*

calciumgluconaatoplossing 4% (inademen, ogen[12] en inslikken[13]); calciumgluconaatgel 10% (huid[14])

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

[12] bij het ontbreken van de 4% calciumgluconaatoplossing ogen minimaal 15 min. spoelen met water.
[13] bij het ontbreken van de 4% calciumgluconaatoplossing maximaal 200 ml water of melk laten drinken.
[14] bij het ontbreken van de 10% calciumgluconaatgel de huid met veel water spoelen of douchen.

Stofdocument deel B

CAS-nr: 7790-91-2 **Chlorine trifluoride** ClF_3 **UN-nr: 1749**

Basis for the Dutch Intervention Values

VRW: AEGL values are adopted, 2 h value added

AGW: AEGL values are adopted, 2 h value added

LBW: AEGL values are adopted, 2 h value added

Date: 28-11-2008 | Final AEGL document 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.46	0.46	0.46	0.46	0.46	0.46	Mild irritation (nasal discharge)
AGW	31	13	7.9	4.6	2.7	1.6	Irritation, salivation, lacrimation, rhinorrhea, coughing and sneezing
LBW	320	140	80	48	28	28	Lethality in animals

Derivation of the Dutch Intervention Values

VRW: There are no suitable human data for the derivation of the VRW. The 1.17 ppm (4.5 mg/m³) exposure level, derived from a dog study (6 hr/d, 5 d/wk, 6 wks) was used as a starting point for the calculation of the VRWs. At this dose level, nasal discharge as observed, indicating nasal irritation within 45 minutes of exposure and obvious lacrimation was not observed until 3 hours of exposure. A total uncertainty factor of 10 (3 x 3) was applied; 3 for interspecies differences (the dog was more sensitive than the rat) and 3 for intraspecies differences (slight irritation should occur at similar level among the general population). Time-scaling was not applied, because adaptation to slight irritation occurs. Therefore, the calculated value of 0.12 ppm (0.46 mg/m³) was used for all time points. The resulting VRW values are in accordance with the VRW levels for ClO_2 of 0.15 ppm (0.41 mg/m³, slight sensory irritation) and HF of 0.8 mg/m³ (1.0 ppm), which are expected to be rapidly formed by hydrolysis (one mole of ClF_3 potentially forms three moles of HF and one mole of ClO_2).

AGW: For the derivation of the AGWs, the 5.15 ppm (20 mg/m³) level (6 hr/d, 5 d/wk, 6 wks) showing irritation, salivation, lacrimation, rhinorrhea, coughing, and sneezing in dogs, was used. Twenty rats exposed to this concentration for 6 hours appeared unaffected. However, repeated daily exposure of rats and dogs to this concentration resulted in increasingly severe signs of irritation. A combined uncertainty factor of 10 was applied; 3 for interspecies differences (the value is based on the dog, which was considerably more sensitive than the rat) and a factor 3 for intraspecies differences (irritation should occur at a similar concentration level among the general population). Scaling across time was done using the $C^n \times t = k$ relationship, with n= 1.3. Although the endpoint for time scaling was lethality in several species, the same time relationship can be used for the AGW and the LBW, because the difference between severe irritation (AGW) and lethality (LBW) is one of degree. The 10-minute value was time-scaled from the 6-hr point of departure, because time-scaling data were available for 13.5 to 222 minutes. The AGW values are considerably lower than the calculated AGW values for HF and similar to the longer term AGW values for ClO_2. The 10- and 30 minute values for ClF_3 are lower than the 10- and 30-min values for ClO_2, because in contrast to ClO_2, time-scaling data were available for ClF_3.

LBW: Of three species tested, the mouse is the most sensitive species as determined by the 1-hour LC_{50} of 178 ppm (685 mg/m³). However, based on the similar respiratory rates, gross respiratory tract anatomy, amount and distribution of types of respiratory epithelium, and nasal flow patterns, the monkey is the more appropriate model for chemical disposition in the human respiratory tract. The LBW values are based on the highest 1-hour concentration that resulted in no deaths in monkeys, 127 ppm (489 mg/m³). A total uncertainty factor of 6 was applied, 2 for interspecies differences (the monkey is an appropriate model for extrapolation to humans) and 3 for intraspecies differences (appropriate for differences among individuals in sensitivity to contact irritants should not differ greatly). Time scaling was performed using the equation $C^{1.3} \times t = k$. The value for n was calculated using lethality data of different species. The 8-hour LBW value was set equal to the 4-hour value because the time-scaled 8-hour value of 4.3 ppm (16.5 mg/m³) is inconsistent with the experimental data: dogs exposed to 21 ppm (81 mg/m³) for 2 days did not die during the following months of observation and dogs and rats tolerated repeated 6-hour exposures to 5.15 ppm (20 mg/m³) for several weeks before the first death was recorded.

Additional toxicological information (including relevant results of a general literature search, if any)

Chlorine trifluoride is corrosive to all tissues, especially the respiratory tract. In the moist respiratory tract, ClF_3 is predicted to hydrolyze to ClOF, which further degrades to ClO_2F and ClF. ClO_2F rapidly hydrolyzes to ClO_2, HF and ClO_x anions; the fist two products predominate and are thought to be responsible for ClF_3 toxicity as the ClO_x anions are relatively nontoxic.

No information on reproductive toxicity was found in the available literature.

No harmonized H-sentences for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified.

Derivation of the carcinogenic risk potency (CRP): No carcinogenic risk potency was derived.

No information on the chronic toxicity or carcinogenic potential of chlorine trifluoride either in humans or animals was located.

Odour and derivation of the LOA value

Pungent odour.

No LOA was derived due to lack of data. No ranges can be identified either.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level ***0.46***	*AEGL-1* *0.46*	*ERPG-1* *0.39*		*IDLH: 77 mg/m³ (30 min)*
AGW level ***7.9***	*AEGL-2* *7.7*	*ERPG-2* *3.9*		
LBW level ***80***	*AEGL-3* *81*	*ERPG-3* *39*		

Stofdocument deel A

CAS-nr: 7647-01-0 **Chloorwaterstof** **HCl**

VN-nr: 1050
GEVI: 268

Synoniemen: waterstofchloride, zoutzuurgas, hydrogeenchloride (Engels: hydrogen chloride)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	2,7	2,7	2,7	2,7	2,7	2,7
Alarmeringsgrenswaarden	AGW (mg/m³)	170	81	51	32	20	20
Levensbedreigende waarden	LBW (mg/m³)	510	240	150	95	60	60

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,659 ppm; 1 ppm = 1,52 mg/m³

Explosiegrens: geen data

Geur: scherpe, verstikkende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloos gas
Brand: Niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,3

Molecuulmassa: 36,5 g/mol
Zuurgraad: geen data
LogKow: 0,3
Wateroplosbaarheid: 72 g/100 ml
Verzadigde dampdruk: 42.000 mbar

Overige informatie

Publieke grenswaarde:
8,0 mg/m³ (8 uur)
MAK: 3,0 mg/m³
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW	geen informatie
VRW → AGW:	oog- en luchtwegirritatie, tranenvloed, hoesten, lichte benauwdheid
AGW → LBW:	oog- en luchtwegirritatie, pijn op de borst, benauwdheid, longontsteking, longoedeem
Boven LBW:	ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Inhalatie van chloorwaterstof veroorzaakt een type I inhalatie intoxicatie.
- Chloorwaterstof veroorzaakt irritatie van de slijmvliezen van ogen en luchtwegen.
- Chloorwaterstof kan bij inhalatie longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

(bij ongecontroleerd vrijkomen uit een drukhouder)

Huidcontact: blaren, roodheid, branderig gevoel, brandwonden

Oogcontact: branderig gevoel, roodheid en pijn, slecht zien, bindvliesontsteking

Carcinogeniteit

IARC classificatie: 3 (zoutzuur)

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Inademing kan tevens leiden tot larynx- en glottisoedeem, met risico op verstikking (asfyxie) door zwellingen in de keel. Intubatie (borgen van vrije luchtwegen), eventueel gevolgd door beademing moeten in ernstige gevallen z.s.m. worden uitgevoerd (door specialisten). Zet derhalve direct spoedeisende medische hulp in.

Ontsmetting vloeistof

huid: n.v.t. (gas), maar in geval van bevriezingswonden: aan de huid vastgevroren kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en arts raadplegen.

ogen: n.v.t. (gas), maar in geval van bevriezingswonden: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen. Blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas)

Specifieke behandeling en materialen: geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7647-01-0 **Hydrogen chloride** **HCl** **UN-nr: 1050**

Basis for the Dutch Intervention Values

VRW: AEGL-1 value is adopted, 2h value added

AGW: Different point of departure than AEGL

LBW: Based on more recent toxicological information than described in the AEGL TSD.

Date: November 2015 | AEGL document: Final, 2004

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	2.7	2.7	2.7	2.7	2.7	2.7	Threshold of irritation in humans
AGW	170	81	51	32	20	20	one-third of LBW
LBW	510	240	150	95	60	60	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: Because appropriate human data exist for exposure to HCl, they were used to identify VRW values. Exposure to HCl at 1.8 ppm (2.7 mg/m^3) for 45 min resulted in a no-observed-adverse-effect level (NOAEL) in 10 exercising young adult asthmatic subjects. Subjects rated lower respiratory tract symptoms (sore throat and nasal discharge) and upper respiratory tract symptoms (cough, chest pain or burning, dyspnea or wheezing), other symptoms (fatigue, headache, dizziness, unusual taste or smell) and pulmonary function. Because exercise will increase HCl uptake and exacerbate irritation, those asthmatic subjects are considered a sensitive subpopulation. Because the test subjects were a sensitive subpopulation and the endpoint was essentially a no-effect level, no uncertainty factory was applied to account for sensitive human subpopulations. The no-effect level was held constant across the exposure time points. That approach was considered appropriate because mild irritant effects generally do not vary greatly over time, and the end point of a no-effect level in a sensitive population is inherently conservative.

AGW: The AGW values for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data. The only study of HCl that addressed effects that meet the definition of an AGW, severe nasal lesions, was a study on hydrogen halides by Stavert et al. (1991). Nevertheless, this study was not considered a suitable basis for derivation of AGW values because 6% of the animals died after exposure to HCl at 1300 ppm (1974 mg/m^3), only one concentration was tested and the number of animals tested was inconsistent.

LBW: Two animal lethality studies of high quality were retrieved in addition to the AEGL document. Because of the robustness of these data (good quality data, multiple exposure times, multiple C*t datapoints) it was decided to use the data from these studies instead of adopting the AEGL-3 values. These data provided a slightly lower more conservative point of departure and a better-founded estimate of *n*. Since both studies are of equal quality, the Hartzell *et al.*(1987) study was selected over the study by Arts *et al.* (2000), because Arts and colleagues generally found 2 to 3 times higher levels compared to other animal lethality studies.
The LBW values were based on a lethality study in rats. The rat study included six exposure durations and various concentrations. Probit analyses using DoseResp was performed and yielded LC_{01} values for the 10 min, 30 min, 1-, 2-,4-, and 8hrs exposure durations of 3370, 1602, 1002, 627, 393 and 246 ppm (5116, 2433, 1522, 952, 596, and 373 mg/m^3), respectively, which were used as point of departure for LBW derivation. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The probit analyses yielded an n-value of 1.48, which was supported by the n-value of 1.59 calculated by Arts *et al.* (2000) from the C*t study. To maintain consistency with other hydrogen halogenides, the 8 hour value was set equal to the 4 hour value, as performed for the most potent hydrogen halogenide HF.

Additional toxicological information (including relevant results of a general literature search, if any)

HCl is a sensory and respiratory irritant and causes changes in the upper respiratory tract at relatively low concentrations and short exposure times. As concentrations and exposure times increase, effects progress to the lower respiratory tract and may involve pulmonary edema and histopathologic changes.

Two acute animal lethality studies in the rat were identified in a literature search. The study by Hartzell *et al.* (1985) exposed 6-8 animals per group (head-only) for six exposure durations and various concentrations. A probit analysis was performed on the data, providing a 30-min LC_{50} value of 4383 ppm (6654 mg/m^3) and an n-value of 1.48. The second study exposed rats according to the C*t protocol (Arts *et al.*, 2000). Following this protocol, two animals (one male, one female) were exposed (nose-only per C*t point) over a range of concentrations and exposure durations. A total of 29 C*t points were tested. Probit analyses yielded LC_{50} values that were 2- to 3-fold higher than found by Hartzell *et al.* (1985) and an n-value of 1.59.

No human developmental or reproductive toxicity data concerning HCl were identified in the available literature. Fetal mortality was higher in rats exposed to HCl during pregnancy and 12-16 d prior to mating than it was in unexposed rats; however, no validation of exposure concentrations was provided.

H314: Causes severe skin burns and eye damage; H331: Toxic if inhaled.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: 3 (Hydrochloric acid; not classifiable as to carcinogenicity to humans). No carcinogenic risk potency (CRP) was derived. Human data concerning carcinogenicity from exposure to HCl are equivocal and are confounded by occupational exposure to other chemicals. In two lifetime studies in rats, there was no increase in the incidence of cancerous lesions due to exposure to HCl.	Odor: pungent, suffocating odour An unreliable odour range of 0.38-15 mg/m^3 was reported in literature (AIHA, 1989). No LOA was derived due to lack of reliable data.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **2.7**	*AEGL-1* 2.7	*ERPG-1* 4.6		*IDLH:* 76 (10 minutes)
AGW level **51**	*AEGL-2* 33	*ERPG-2* 30		
LBW level **150**	*AEGL-3* 150	*ERPG-3* 230		

Arts, J.H.E., C. Mommers, and H. Muijser. Toxic Effects from Accidental Releases of Hazardous Substances (TEARHS) – Lethal and non-lethal effects in rats upon exposure during short periods of time. TNO Nutrition and Food Research, report V99.1136. Zeist (2000).

Hartzell, G.E., A.F. Grand, and W.G. Swiztzer. 1987. Modeling of toxicological effects of fire gases: VI. Further studies on the toxicity of smoke containing hydrogen chloride. J. Fire Sci. 5:368-391.

Stofdocument deel A

CAS-nr: 67-66-3 **Chloroform** **$CHCl_3$** **VN-nr: 1888** **GEVI: 60**

Synoniemen: trichloormethaan, methaantrichloride, R20 (Engels.: chloroform) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	580	400	320	250	200	150
Levensbedreigende waarden	LBW (mg/m³)	29.000	20.000	16.000	12.000	9.900	7.900
Datum vaststelling: 24-09-2009			Conversiefactor: 1 mg/m³ = 0,201 ppm; 1 ppm = 4,98 mg/m³				

Explosiegrens: Geen data

Geur: typerende aangename geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,7

Molecuulmassa: 119,4 g/mol
Zuurgraad: Geen data
LogKow: 2,0
Wateroplosbaarheid: 0,8 g/100mL (slecht oplosbaar)
Verzadigde dampdruk: 212 mbar

Overige informatie

Publieke grenswaarde: 5 mg/m³ (8 uur)
MAK: 2,5 mg/m³
TLV-TWA: 50 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling:

*Onder **AGW***: irritatie

AGW → LBW: effect op de ongeboren vrucht, irritatie, hoofdpijn, duizeligheid, misselijkheid, hartritmestoornissen, hypotensie, levernecrose, bewustzijnsdaling

Boven LBW: sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt irriterend op de ogen en bovenste luchtwegen.
- De stof werkt in op het centrale zenuwstelsel.
- Leververvetting en levernecrose kunnen optreden bij eenmalige blootstelling.
- De stof kan reprotoxische effecten veroorzaken.
- Sterfte is veelal het gevolg van acute effecten op het hart of vertraagde effecten op de lever.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, droge huid

Oogcontact: roodheid en pijn, slecht zien

Carcinogeniteit

IARC classificatie: 2B
CRP: 876 mg/m³ (blootstelling 1 uur)

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken en minimaal 20 min. spoelen met veel water of douchen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 67-66-3 **Chloroform** **$CHCl_3$** **UN-nr: 1888**

Basis for the Dutch Intervention Values

VRW: Not recommended

AGW: AEGL value adopted, 2hr value added

LBW: AEGL value adopted (except 10 min value for which time scaling was applied), 2hr value added

Date: 24-09-2009 | AEGL document: Final, 2012

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	580	400	320	250	200	150	Fetotoxic effects in animals
LBW	29,000	20,000	16,000	12,000	9,900	7,900	Threshold for animal mortality

Derivation of the Dutch Intervention Values

VRW: Available data on VRW like effects are insufficient to derive VRW values. Specifically, it would be difficult to identify exposures that would produce notable discomfort or mild sensory irritation without approaching levels that may be near a threshold for narcosis.

AGW: The increased fetotoxicity and embryolethality of rats exposed to 100 ppm (497 mg/m³) for 7 hrs/day on gestation days 6-15 was considered a sensitive critical effect and point-of-departure for developing AGW values. The assumption was made that the reported effects (increased fetotoxicity and embryolethality) occurring after the 10-day gestational exposure could result from a single 7-hour exposure. This contention is not without precedent as has been shown by analyses of developmental toxicity data for other chemicals. An intraspecies uncertainty factor of 3 was applied to account for individual variability in metabolism and disposition of chloroform. No adjustment was made for interspecies variability because available metabolism/kinetics data and PBPK models indicate that humans are less sensitive than laboratory species to the toxic effects of chloroform. Time scaling was performed using the equation $C^n * t = k$ with the defaults n=1 and n=3 for extrapolation to longer and shorter exposure durations, respectively.

LBW: Assuming the mouse to be the most sensitive species, the 560-minute LC_{50} of 4500 ppm (22,350 mg/m³) appears to be a valid basis for development of the LBW values. A 3-fold reduction in this value results in a point-of departure of 1500 ppm (7450 mg/m³) as an estimate of the lethality threshold for mice. No interspecies uncertainty factor was applied (see AGW derivation). Based on PBPK modeling, the internal exposure in humans is much lower. Therefore, no intraspecies factor is used. Time scaling was performed using the equation $C^n * t = k$ with the default n=3 for extrapolation to shorter exposure durations. In contrast to the 10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Chloroform is a well-known potent CNS depressor. Exposure will result in acute effects such as head ache, dizziness, vertigo, fatty liver and mild irritation of the respiratory tract, eyes and the skin. The substance also affects the heart which may result in cardiac arrhythmia, tachycardia and ultimately lead to death. Can induce narcosis. Substance is considered reprotoxic and this is the critical endpoint for AGW derivation.

Alternatively, for AGW derivation protection against severe hepato- or renal toxicity, or narcosis can be considered the critical effects. Human data suggest that exposures to 8500 ppm (42,220 mg/m³) will induce anesthesia; although the duration of this exposure is unknown, it is assumed that the exposure duration would be in the order of minutes. The human data reported by Lehmann and Hasegawa (1910) suggest that exposure to 7500 ppm (37,250 mg/m³) for 15 minutes or 4300-5100 ppm (21,360-25,330 mg/m³) for 20 minutes were approaching narcosis-inducing effects as determined by signs and symptoms of dizziness, and “intoxication”. These data and the anesthesia data reported by Whitaker and Jones (1965) are, however, compromised by the uncertainties regarding determination of exposure concentrations and specific concentration duration relationships.

H302: Harmful if swallowed; H315: Causes skin irritation; H319: Causes severe eye irritation; H331: Toxic if inhaled; H352: Suspected of causing cancer; H361d: Suspected of damaging the unborn child; H372: Causes

damage to organs.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: 2B (possibly carcinogenic to humans). Derivation of the carcinogenic risk potency (CRP): 10^{-4} risk level after inhalation: 0.004 mg/m^3 [US EPA 1992, 2005] CRP = (10^{-4} risk level * average life span in hours)/DRCF = (0.004 * 613.200) /2.8 = 876 mg/m^3 Based on a gavage study in mice, where a unit risk of 0.004 mg/m^3 was calculated for hepatocellular carcinomas.	Non-irritating and pleasant odour. No LOA was derived due to lack of reliable data.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **NR**	*AEGL-1* NR	*ERPG-1* NA		*IDLH: 2,480 (30 min)*
AGW level **320**	*AEGL-2* 320	*ERPG-2* 250		
LBW level **16,000**	*AEGL-3* 16,000	*ERPG-3* 25,000		

Stofdocument deel A

CAS-nr: 4170-30-3 (mengsel)
123-73-9 (trans)

Crotonaldehyde

$CH_3CH=CHCHO$

VN-nr: 1143
GEVI: 663

Synoniemen: trans-2-butenal, β-methylacroleine (Eng.: crotonaldehyde)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,56	0,56	0,56	0,56	0,56	0,56
Alarmeringsgrenswaarden	AGW (mg/m³)	80	26	13	6,6	3,2	1,7
Levensbedreigende	LBW (mg/m³)	120	49	27	15	8,7	4,9

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,339 ppm; 1 ppm = 2,95 mg/m³

Explosiegrens: LEL = 2,1 Vol% ≈ 62.000 mg/m³

Geur: stekende geur

LOA: 3,24 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk, bij vele reacties kans op brand en explosie

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,03

Molecuulmassa:	70,9 g/mol
Zuurgraad:	Geen data
LogKow:	0,6
Wateroplosbaarheid:	18 g/100ml (goed oplosbaar)
Verzadigde dampdruk:	40 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-ceiling: 0.86 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	(zeer) lichte irritatie aan ogen en luchtwegen
VRW → AGW:	lichte irritatie, traanvorming, hoesten, kortademigheid
AGW → LBW:	sterke irritatie aan luchtwegen, pijn in de borst, ademnood, longoedeem.
Boven LBW:	sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De damp is zeer sterk irriterend voor ogen, huid en luchtwegen.
- Kan cornea-beschadiging veroorzaken.
- Veroorzaakt irritatie aan longblaasjes en longoedeem (vergelijkbaar met de werking van fosgeen en acroleïne).
- Reikt diep in de longen en veroorzaakt longschade bij contact met weefsel.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, brandwonden

Oogcontact: bijtend, slecht zien, hoornvliesbeschadiging, ernstige brandwonden.

Carcinogeniteit

IARC classificatie: 3

CRP: 670 mg/m³ (blootstelling 1 uur)

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding, en direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen, arts raadplegen en direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen: (100% zuurstof).

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 4170-30-3 (mixture)
123-73-9 (trans)

Crotonaldehyde $CH_3CH=CHCHO$

UN-nr.: 1143

Basis for the Dutch Intervention Values

VRW: AEGL value adopted, 2hr value added

AGW: AEGL value adopted, 2hr value added

LBW: Same point of departure, but difference in time scaling, 2hr value added

Date: November 2015	AEGL document, final 2006

Proposal for the Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.56	0.56	0.56	0.56	0.56	0.56	Irritation (ocular) in humans
AGW	80	26	13	6.6	3.2	1.7	Threshold of (irreversible) lung damage in animals
LBW	120	49	27	15	8.7	4.9	Threshold of animal lethality

Derivation of the Dutch Intervention Values

VRW: VRW values were derived from an evaluation at a U.S. chemical plant where some workers exposed to approximately 0.56 ppm (1.7 mg/m³) crotonaldehyde reported occasional minor eye irritation. It is possible that some of the workers had become adapted (inured) to crotonaldehyde, but there was insufficient information to quantify the effect of this phenomenon (which is commonly experienced with other aldehydes, e.g. formaldehyde). Exponential scaling across time was not performed, rather, it was considered more appropriate to adopt the same exposure concentration for 10 minutes to 8 hours since the critical endpoint (ocular irritation) generally does not vary greatly over time. A total uncertainty factor of 3 was applied to account for intraspecies variability, because the eye irritation is a direct surface-contact effect not subject to pharmacokinetic differences between individuals

AGW: AGW values were derived from the pulmonary performance study where rats exposed to above 8000 ppm-min (23,600 mg/m³-min) (product of concentration and time) had reduced rates of gas absorption. This exposure was near the threshold for developing proliferative lesions of the respiratory bronchioles. Because the individual concentrations and exposure times were not given (exposure was 5 minutes to 4 hours to 10-580 ppm (29.5-1711 mg/m³), but only the concentration x time (Ct) values, and it appeared from the overall data that concentration and time were roughly equally important for toxicity (this is also supported by n=1.2 derived from an LC_{50} study, AGW values were calculated by dividing 8000 ppm-min (23600 mg/m³-min) by 10, 30, 60, 120, 240, or 480 minutes. A total uncertainty factor of 30 was used: a factor of 3 for interspecies uncertainty, a factor of 3 for intraspecies uncertainty and a modifying factor of 3, because the actual exposure concentration and time were not known for the key study and there was a lack of supporting animal studies.

LBW: The rat study, where LC_{50} values were obtained for exposures from 5 minutes to 4 hours, was considered the most relevant for derivation of LBW values. An extensive study where air crotonaldehyde concentrations were measured and 30-60 animals were used for each of the 6 exposure periods. Dose-Resp was used to calculate the LC_{01}. An n-value of 1.2 was derived. A total uncertainty factor of 10 was applied: 3 for interspecies uncertainty because interspecies variability was small (LC_{50} values for rats, mice, and guinea pigs were within a factor of 2.5), and 3 for intraspecies uncertainty because great human variability is unlikely given the homogeneity of the animal data, and a larger uncertainty factor yields 8-hour LBW concentrations that caused only mild irritation in workers exposed for up to 8 hours.

Additional toxicological information (including relevant results of a general literature search, if any)

The intervention values were derived for the trans and mixture (trans/cis) forms of crotonaldehyde. These are the most common forms and most data consider these forms. Crotonaldehyde is a strong local irritant to eyes and respiratory tract causing severe damage to respiratory tissues. May reach deep into the lungs generally causing damage to the bronchioles. Mostly, haemorrhage was observed after histopathology in laboratory species. Systemic effects may occur after high exposure, which already may cause death.

No data are available on reprotoxic or developmental toxic effects for crotonaldehyde.

H301: Toxic if swallowed; H311: Toxic in contact with skin; H315: Causes skin irritation; H318: Causes serious eye damage; H330: Fatal if inhaled; H335: May cause respiratory irritation; H341: Suspected of causing genetic defects; H373: May cause damage to organs.

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to carcinogenicity to humans)

Derivation of the carcinogenic risk potency (CRP):

10^{-4} risk level after inhalation: 3.06 * 10^{-3} mg/m^3 [AEGL]

CRP = (10^{-4} risk level * average life span in hours)/DRCF

= (3.06 * 10^{-3} * 613.200) /2.8 = 670 mg/m^3

The carcinogenicity assessment was based on a drinking water study in F344 rats. Assuming 100% absorption after inhalation the human equivalent concentration was determined. Using linearized multistage model the unit risk was calculated.

Odour and derivation of the LOA value

Pungent odour.

OT_{50}: 0.20 mg/m^3 [AEGL]

LOA = 11.8 * OT_{50} * 1.33 = 3.2 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies above the VRW and therefore the odor does not possess a warning function. Mild irritation might occur sooner. The LOA is below the 10, 30, 60, 120 and 240 min AGW values and all LBW values.

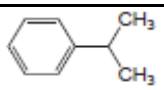
***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **0.56**	*AEGL-1* 0.55	*ERPG-1* 0.59		*IDLH:* 50 (30 min)
AGW level **13**	*AEGL-2* 13	*ERPG-2* 15		
LBW level **27**	*AEGL-3* 40	*ERPG-3* 44		

Stofdocument deel A

CAS-nr: 98-82-8
C_9H_{12}

Cumeen



VN-nr: 1918
GEVI: 30

Synoniemen: 2-fenylpropaan, isopropylbenzeen, (1-methylethyl)benzeen (Engels: cumene)

***Status*: geen**

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	250	250	250	250	250	250
Alarmeringsgrenswaarden	AGW (mg/m³)	2.700	1.900	1.500	1.200	950	630
Levensbedreigende waarden	LBW (mg/m³)	6.600*	4.600*	3.600	2.900	2.300	1.500

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,20 ppm; 1 ppm = 5,0 mg/m³

Explosiegrens:
LEL = 0,9% ≈ 45.000 mg/m³
* berekende interventiewaarde hoger dan 10% LEL

Geur: Typerende geur
LOA: 0,63 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,02

Molecuulmassa:	120,2 g/mol
Zuurgraad:	geen data
LogKow:	3,6
Wateroplosbaarheid:	0,005 g/100 ml (zeer slecht)
Verzadigde dampdruk:	5 mbar

Overige informatie

Publieke grenswaarde:
100 mg/m³ (8 uur)
MAK: niet afgeleid
TLV-TWA: 250 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	keelpijn en hoesten
VRW → AGW:	hoofdpijn, duizeligheid, misselijkheid
AGW → LBW:	ataxie, duizeligheid, verwardheid, sufheid
Boven LBW:	bewusteloosheid, toevallen, ademstilstand

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Blootstelling aan cumeen kan leiden tot depressie van het centrale zenuwstelsel.
- Bij lage concentraties beperkt zich dit in de meeste gevallen tot sufheid. Bij relatief hoge concentraties kan dit verergeren tot bewusteloosheid en ademstilstand.

Effecten bij blootstelling aan vloeistof

Huidcontact:	droge huid, roodheid.
Oogcontact:	roodheid en pijn.

Carcinogeniteit

IARC classificatie: 2B
CRP: Niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, en onmiddellijk arts raadplegen.

Ontsmetting vloeistof

huid:	verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen.
ogen:	minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), bij aanhoudende irritatieklachten (oog)arts raadplegen.
inslikken:	mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

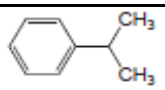
***Specifieke behandeling en materialen**:* geen.

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 98-82-8
C_9H_{12}

Cumeen



UN-nr: 1918

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added.

AGW: AEGL value is adopted, 2h value added.

LBW: AEGL value is adopted, 2h value added.

Date: 16-10-2018 | AEGL, interim (2007)

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	250	250	250	250	250	250	Eye and respiratory tract irritation
AGW	2,700	1,900	1,500	1,200	950	630	Mild reversible neurological changes
LBW	6,600*	4,600*	3,600	2,900	2,300	1,500	Threshold for lethality in rats

* value higher than 10% of LEL

Derivation of the Dutch Intervention Values

VRW: VRW values were based on a brief chemical company report that exposure to 300-400 ppm (1500-2000 mg/m³) was painful to the eyes and upper respiratory passages of most workers. A modifying factor of 2 was applied to obtain a concentration of 150 ppm (750 mg/m³) that is believed to cause effects within the scope of VRW, i.e., mild eye and respiratory irritation. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was not applied as mild irritation is considered to be concentration-dependent rather than concentration x time-dependent. The VRW is supported by human data. In a human metabolism study volunteers willingly tolerated exposure to 49-146 ppm (245-730 mg/m³) cumene for 7 hours over an 8-hour period. However, clinical observations were not recorded.

AGW: The AGW value is based on an acute neurotoxicity study (FOB) in which rats were exposed to 100 (500 mg/m³), 500 (2,500 mg/m³) or 1,200 ppm (6,000 mg/m³) cumene for 6 hours. No toxicity was seen at 500 mg/m³, 2,500 mg/m³ caused mild reversible neurobiological changes (increased activity and decreased toe-pinch withdrawal reflex), and 6,000 mg/m³ additionally caused gait abnormalities and decreased rectal temperature. The AGW was based on exposure to 2,500 mg/m³, which caused mild reversible neurological changes and was a NOEL for ataxia and an impaired ability to escape. An interspecies UF of 1 was considered sufficient because of the limited severity of the effects observed at 2500 mg/m³, the rat is the most sensitive species and because the use of an UF of 3 would yield AGW values close to or below VRW values, especially for the longer exposure durations. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter time points, respectively.

LBW: The LBW is based on an acute neurotoxicity study in rats. Rats were exposed for 6 hours to 1,200 ppm (6,000 mg/m³). This was considered an estimate of lethality threshold because (1) inhalation of 2,000 ppm (10,000 mg/m³) for 6 hours/day in a repeated exposure study caused 100% mortality in mice on day 2 and 50% mortality in rats on day 2-4 of exposure, and (2) up to 90 days of exposure to 6,000 mg/m³ for 6 hours/day, 5 days/week caused some toxicity but no lethality in several rat studies. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. An interspecies UF of 1 was used because the rat is the most sensitive species and the use of an UF of 3 would come into conflict with the data from human volunteers.

Additional toxicological information (including relevant results of a general literature search, if any)

The most commonly reported toxic effect and sensitive endpoint of cumene exposure is CNS depression. The exact mechanism by which this occurs is unknown, but it is believed to involve the affinity of cumene, which is lipid-soluble and not water-soluble, for nerve tissue due to its high lipid content. Cumene also causes sensory irritation

Cumene is found to be non-reprotoxic.

H304: may be fatal if swallowed and enters airways, H335: may cause respiratory irritation.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: 2B (possibly carcinogenic to humans) No carcinogenic risk potency (CRP) was derived.	Odour: Characteristic odour OT: 0.04 mg/m^3 [AEGL document] LOA = 11.8 * 0.04 * 1.33 = 0.63 mg/m^3 (The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value) The LOA is below the VRW values.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)*** [15]

VRW level **250**	*AEGL-1* 250	*ERPG-1* -		*IDLH:* 900 ppm (4500 mg/m^3) (30 minutes)
AGW level **1,500**	*AEGL-2* 1,300	*ERPG-2* -		
LBW level **3,600**	*AEGL-3* 3,600	*ERPG-3* -		

[15] Note that the AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL.

Stofdocument deel A

CAS-nr: 74-90-8 **Cyaanwaterstof** **C–H≡N** **VN-nr: 1613** **GEVI: 663**

Synoniemen: blauwzuur, hydrocyaanzuur, hydrogeencyanide, waterstofcyanide (Engels: hydrogen cyanide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m³)**	19	8,6	5,2	3,1	1,9	1,1
Alarmeringsgrenswaarden	**AGW (mg/m³)**	25	11	6,7	4,1	2,4	1,5
Levensbedreigende waarden	**LBW (mg/m³)**	110	51	31	18	11	6,7

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,890 ppm; 1 ppm = 1,12

Explosiegrens: LEL = 5,4 vol% ≈ 61.000 mg/m³

Geur: bittere amandelgeur

LOA: niet afgeleid.

Gerapporteerde geurdrempels: 0.58 - 5 ppm (0.66-5.65 mg/m³). Vanwege genetische redenen kan 20% van de populatie de geur niet onderscheiden.

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk
Relatieve dichtheid van verzadigd damp-lucht mengsel: 0,94

Molecuulmassa:	27,0 g/mol
Zuurgraad:	Geen data
LogKow:	0,7
Wateroplosbaarheid:	Zeer goed
Verzadigde dampdruk:	830 mbar

Overige informatie

Publieke grenswaarde:
1 mg/m³ (8 uur)
MAK: 2,1 mg/m³
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten te verwachten

VRW → AGW: hoofdpijn, misselijkheid

AGW → LBW: duizeligheid, verwardheid, braken, oogirritatie, amandel of bittere smaak, verlamming, snelle pols en rood worden van gezicht

Boven LBW: depressie van CZS en ademhaling, hartritmestoornissen, hypotensie, convulsies, coma en sterfte; mogelijk voorafgegaan door korte periode van CZS stimulatie, hypertensie en hyperventilatie

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Cyanide blokkeert de ademhalingsketen in de cel. Hierdoor wordt de energiehuishouding verstoord en kan lactaatacidose ontstaan.
- Primaire doelorganen zijn het centrale zenuwstelsel en het cardiovasculaire systeem.
- Sterfte is veelal het gevolg van ademhalingsdepressie.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid
Stof kan door de huid opgenomen worden
Oogcontact: roodheid en pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: 100% zuurstof, GEEN mond-op-mondbeademing, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: 100% zuurstof, GEEN mond-op-mondbeademing, verontreinigde kleding uittrekken, direct spoedeisende medische hulp inzetten, ondertussen overmaat stof met PEG 400 opdeppen en afspoelen met water.
ogen: uitspoelen met water (evt. contactlenzen verwijderen), 100% zuurstof, GEEN mond-op-mondbeademing en direct spoedeisende medische hulp inzetten.
inslikken: mond laten spoelen (uitspugen!), 100% zuurstof, GEEN mond-op-mondbeademing, GEEN braken opwekken, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen:. Bij vergiftiging door deze stof is specifieke eerste hulp noodzakelijk; specifieke antidota (zoals 100% zuurstof en o.a. hydroxocobalamine en natriumthiosulfaat) moeten met gebruiksaanwijzing ter plekke beschikbaar zijn. Voor aanwijzingen over verdere behandeling zo nodig het NVIC (+31(0)30-274 88 88) bellen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 74-90-8 **Hydrogen cyanide** **C−H≡N** **UN-nr: 1613**

Basis for the Dutch Intervention Values

VRW: Same point of departure as for AEGL values but using different value for n, 2 h value added

AGW: Same point of departure as for AEGL values but using different value for n, 2h value added

LBW: Different point of departure as for AEGL values, different uncertainty factors, 2h value added

Date: November 2015 | AEGL document: Final 2002

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	19	8.6	5.2	3.1	1.9	1.1	Mild headache in humans
AGW	25	11	6.7	4.1	2.4	1.5	Slight CNS depression in monkeys
LBW	110	51	31	18	11	6.7	Animal lethality

Derivation of the Dutch Intervention Values

VRW: The VRW levels were based on data from monitoring studies in workers. Although the exposures were of chronic duration, they represent the best available human data. Exposure in a cyanide-salt production facility (exposure duration 1-40 years) to a geometric mean concentration of 0.03-0.96 ppm (0.034- 1.08 mg/m^3) (+ possible excursions up to 6 ppm (6.7 mg/m^3)) in 63 male workers did not result in exposure-related health effects as compared to 100 referent workers. As point of departure, an 8 hour exposure to 1 ppm (1.123 mg/m^3) was used.

The choice for this point of departure is supported by 2 other studies, resulting in similar VRW levels:

- 8 hr and 5 ppm (5.6 mg/m^3), with an uncertainty factor of 3. This exposure in workers was identified as a no effect concentration.
- 1 hr at 8 ppm (9.0 mg/m^3), with an uncertainty factor of 3. This exposure in workers was evaluated to produce no more than mild headache.

Mild headache was considered a suitable critical endpoint. Therefore, mean exposure to 1 ppm (1.12 mg/m^3) with exposure duration of 8 hour was used as point of departure, since it was the best conducted study. In this study, the health of 63 cyanide-salt producing workers employed 1 to 40 years was compared with 100 referent workers from a diphenyl oxide plant. Results of clinical and physical examinations and evaluation of medical histories failed to reveal any exposure-related health problems. No specific susceptible populations were identified during the numerous occupational monitoring studies or during clinical use of nitroprusside solutions to control hypertension. Thus potential differences in susceptibility among humans are not expected to exceed 3-fold. All individuals, including infants, possess large amounts of cyanide detoxifying enzyme rhodanese (as well as other detoxifying enzymes) and normally have adequate amounts of sulfur-containing compounds. Therefore, using this point of departure no intraspecies uncertainty factor was used because it is the lowest NOAEL observed. The data were scaled across time using the relationship $C^n \times t = k$, with n=1.36 (see LBW).

AGW: The AGW values were derived from an animal study with 4 monkeys. Monkeys were exposed for 30 minutes to 60 ppm (67.4 mg/m^3) hydrogen cyanide. A slight depressive effect on the central nervous system was observed, as evidenced by changes in brain wave activity (EEG recordings) at the end of the exposure periods and reduced amplitude of the auditory cortical evoked potential during the late response. No physiological responses to the EEG changes were observed. Exposure to higher concentrations was reported to result in incapacitation, unconsciousness and possibly death. It was stated that concentrations below 60 ppm are unlikely to produce a significant impairment of escape capability. Exposure to 60 ppm (67.4 mg/m^3) for 30 minutes was used as point of departure. An interspecies uncertainty factor of 2 was applied because the respiratory tract of humans and monkeys are more similar than that of humans and rodents, and because both species have shown to be relatively insensitive to the incapacitative and lethal effect of hydrogen cyanide. The detoxifying enzyme is available in all humans, including newborns. The default intraspecies uncertainty factor of 3 was applied. Time scaling was applied using $C^n \times t = k$, with n=1.36 (see LBW).

Selection of this point of departure is supported by 2 animal studies. Exposure of rats for 30 minutes to 55 ppm (61.8 mg/m^3) resulted in changes in lung dynamics and lung phospholipids (not irreversible or long-lasting).

LBW: In contrast to AEGL, LBW values were based on a more recent rat lethality dataset (Sweeney et al., 2014/2015).

Groups of 10 male rats were exposed nose-only to hydrogen cyanide for 2.33, 5, 10, 15 and 30 min at concentrations ranging from 141.6 to 3175 ppm (159-3566 mg/m^3). LC_{01}values and the related time scaling factor were calculated using Doseresp, resulting in the following LC_{01} values for a 10 min, 30 min, 1h, 2h, 4h and 8h exposure period, respectively: 344.4 – 153.6 – 92.3 – 55.46 – 33.32 – 20.02 mg/m^3. Short exposure durations (i.e. ≤5 min) were excluded for analyses, as these were considered less reliable than longer exposure durations.
Lethal concentrations are very similar for various species, and study data show that man and the monkey are less sensitive to the effects of HCN than are the rat and dog. Relative to body weights, humans have a much lower respiratory rate and cardiac output than rodents. These are primary determinants of systemic uptake of volatile substances. Thus at similar exposure levels, rodents will absorb substantially more cyanide than primates. Lower detoxifying enzyme activity levels in primates will not be significant in high, acute HCN exposure levels. Based on this information, an interspecies uncertainty factor of 1 was applied. The available data do not demonstrate a susceptible population. The detoxifying enzyme is available in all humans, including newborns. The default intraspecies uncertainty factor of 3 was applied, leading to a total uncertainty factor of 3.

Additional toxicological information (including relevant results of a general literature search, if any)

A new dataset for rat lethality was available for hydrogen cyanide (Sweeney et al., 2014/2015). This was used for derivation of the LBW.

- Sweeney LM, Sommerville DR, Channel SR, Sharits BC, Gargas NM, Gut CP Jr. (2015). Evaluating the validity and applicable domain of the toxic load model: impact of concentration vs. time profile on inhalation lethality of hydrogen cyanide. Regul Toxicol Pharmacol. 2015 Apr;71(3):571-84.
- Sweeney LM, Sommerville DR, Channel SR. (2014). Impact of non-constant concentration exposure on lethality of inhaled hydrogen cyanide. Toxicol Sci. 2014 Mar;138(1):205-16.

There is no information on the reproductive and developmental toxicity via the inhalation route in the available literature. The teratogenic potential of inorganic cyanide was studied by infusing sodium cyanide to hamsters. Based on the results of this study and the results of studies with sodium cyanide, aliphatic nitriles and cyanogenic glycosides it can be concluded that the teratogenic activities can be attributed to the cyanide released through metabolism of the parent compounds: in each case, developmental toxicity was observed only at dose levels also inducing signs of maternal cyanide intoxication.

H330: Fatal if inhaled

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived due to lack of data.

Genotoxicity studies with cyanide salts were generally negative and no cancers were induced in rats in a 2-year feeding study with HCN.

Odour and derivation of the LOA value

The odour of HCN is bitter almonds. The detection level of the odour varies widely among individuals and 20% of the population is genetically unable to discern the characteristic odour. It is possible that individuals smell the almond odour at or under the LBW and that about 80% will smell hydrogen cyanide at and above the AGW. Odour thresholds of 0.58 - 5 ppm (0.66-5.6 mg/m^3) are reported, but no OT_{50} was derived.

No LOA was derived due to lack of reliable data.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **5.2**	*AEGL-1* 2.2	*ERPG-1* N.A.		*IDLH:* 56 (30 minutes)
AGW level **6.7**	*AEGL-2* 8.0	*ERPG-2* 11		
LBW level **31**	*AEGL-3* 17	*ERPG-3* 28		

Stofdocument deel A

CAS-nr: 108-91-8 **Cyclohexylamine** $C_6H_{11}NH_2$ **VN-nr: 2357**

GEVI: 83

Synoniemen: aminocyclohexaan, aminohexahydrobenzeen (Engels: cyclohexamine) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	7,5	7,5	7,5	7,5	7,5	7,5
Alarmeringsgrenswaarden	AGW (mg/m³)	65	45	36	28	22	11
Levensbedreigende waarden	LBW (mg/m³)	680	470	370	300	230	120

Datum vaststelling: 13-05-2009

Conversiefactor: 1 mg/m³ = 0,242 ppm; 1 ppm = 4,13 mg/m³

Explosiegrens: LEL = 1,5 vol% ≈ 62.000 mg/m³

Geur: sterke onaangename walgingwekkende geur

LOA: 8,4 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos tot gele vloeistof

Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,04

Molecuulmassa:	99,2 g/mol
Zuurgraad:	Geen data
LogKow:	1,5
Wateroplosbaarheid:	volledig
Verzadigde dampdruk:	15 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: 8,3 mg/m³

TLV-TWA: 41 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: milde oog- en luchtwegirritatie, hoofdpijn

AGW → LBW: ernstige oog- en luchtwegirritatie

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Cyclohexylamine is sterk irriterend voor ogen en de luchtwegen.
- Huidcontact veroorzaakt brandwonden en mogelijk huidsensibilisatie.
- De stof verstoort het centrale zenuwstelsel wat kan leiden tot duizeligheid, misselijkheid en hoofdpijn. Een verhoogde bloeddruk, tremor en hartkloppingen behoren tot de symptomen gerelateerd aan sympaticomimetische effecten.
- Kan bij inhalatie longontsteking en/of longoedeem veroorzaken. De stof is een veroorzaker van een type I inhalatoire intoxicatie. Inademing van hoge concentraties kan blijvende longschade veroorzaken.

Klachten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, ernstige brandwonden.

Oogcontact: bijtend, tranenvloed, roodheid en pijn, slecht zien, ernstige brandwonden, blijvend verlies gezichtsvermogen

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Ontsmetting bij inademing/inslikken

Inademing/inslikken van sterke zuren kan tevens leiden tot larynx- en glottisoedeem, met risico op verstikking (asfyxie) door zwellingen in de keel. Intubatie (borgen van vrije luchtwegen), eventueel gevolgd door beademing moeten in ernstige gevallen z.s.m. worden uitgevoerd (door specialisten).

Specifieke behandeling en materialen:.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 108-91-8 **Cyclohexamine** **$C_6H_{11}NH_2$** **UN-nr: 2357**

Basis for the Dutch Intervention Values

VRW: AEGL value adopted, 2hr value added.

AGW: AEGL value adopted (except 10 min value for which time scaling was applied), 2hr value added.

LBW: Same point of departure as for AEGL, different uncertainty factors used, 2hr value added.

Date: 13-05-2009 | AEGL document: Final, 2005

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	7.5	7.5	7.5	7.5	7.5	7.5	Respiratory tract and eye irritation in animals
AGW	65	45	36	28	22	11	Respiratory tract and eye irritation in animals
LBW	680	470	370	300	230	120	Estimated threshold for lethality in animals

Derivation of the Dutch Intervention Values

VRW: VRW values were derived from a rat study, in which exposure to 54.2 ppm (224 mg/m³) for 4 hours caused notable respiratory and ocular effects (laboured breathing, red nasal discharge, partially closed eyes). Because the effects are more severe than prescribed by the VRW definition, the point of departure was divided by a modifying factor of 3. Uncertainty factors of 3 each was applied for interspecies and intraspecies differences. The VRW is consistent with a study in which chemical workers exposed to 4-10 ppm (17-41 mg/m³) for an undefined duration (<8 hours) reported “no symptoms of any kind”. The same VRW values were set from 10 min to 8 hours because mild irritation is not expected to vary over time.

AGW: In the absence of human data AGW values were based on the same rat study as the VRW values. A 4-hour exposure to 54.2 ppm (224 mg/m³) at which concentration the rats showed moderate respiratory effects and ocular irritation. This concentration was considered to be a threshold for irreversible ocular lesions. An uncertainty factor of 10 was applied (3 for interspecies variability and 3 for intraspecies variability) because the effects seen at 54.2 ppm (224 mg/m³) were clearly reversible, and a larger uncertainty factor would yield values at or below the VRW. Time scaling was performed using the equation $C^n * t = k$, whit the defaults of n = 3 and n = 1 for extrapolation to shorter and longer exposure durations, respectively. In contrast to the 10 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: The study chosen for LBW derivation was a GLP study in which rats (5/sex/concentration) exposed to 567 ppm (2340 mg/m³) cyclohexylamine vapour for 4 hours had reversible dyspnoea, tremors, weight loss, and irreversible ocular lesions, although none died within the 3-week observation period. The LBW endpoints were irreversible ocular lesions and an estimated lethality threshold in rats. The same study reported that exposure to 542 ppm (2236 mg/m³) plus 612 mg/m³ aerosol for 4 hours resulted in deaths in 1/5 male rats and 1/5 female rats. An interspecies uncertainty factor of 3 and an intraspecies uncertainty factor of 3 were considered sufficient because tissue destruction caused by a severely corrosive agent is not expected to vary greatly between species or among humans, respectively. Time scaling was performed using the equation $C^n * t = k$, with the defaults of n = 3 and n = 1 for extrapolation to shorter and longer exposure durations, respectively. In contrast to the 10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Cyclohexylamine is further characterized by irritation to the eyes and respiratory tract and may be corrosive. Furthermore, human data from occupational settings show that the central nervous system (CNS) is affected as well. Headache, nausea, vomiting, dizziness amongst other are CNS symptoms observed in workers after exposure.

No animal studies were located that addressed the developmental or reproductive effects.

H302: Harmful if swallowed; H312: Harmful in contact with skin; H314: Causes severe skin burns and eye damage; H361f: Suspected of damaging fertility.

Carcinogenicity and derivation of the CRP value
IARC classification: not classified No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value
Odour: Strong unbearable foul odour OT_{50}: 0.13 ppm (0.536 mg/m^3) [AEGL, 2005] LOA = 11.8 * OT_{50} * 1.33 = 8.4 mg/m^3 (The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value) The LOA of cyclohexylamine is just above the VRW and below all other intervention values. Its odour is known to be a warning signal for serious health effects.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***				
VRW level **7.6**	*AEGL-1* 7.4	*ERPG-1* not derived		*IDLH:* not derived
AGW level **36**	*AEGL-2* 35	*ERPG-2* not derived		
LBW level **370**	*AEGL-3* 120	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 3173-53-3 **Cyclohexylisocyanaat** $C_6H_{11}N=C=O$ **VN-nr: 2488** **GEVI: 663**

Synoniemen: isocyaanzuur cyclohexylester, CHI (Engels: cyclohexylester isocyanic acid) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	6,3	2,1	1,0	0,52	0,26	0,13
Levensbedreigende waarden	LBW (mg/m³)	43	14	7,2	3,6	1,8	0,90

Datum vaststelling: November 2015 | Conversiefactor: 1 mg/m³ = 0,192 ppm; 1 ppm = 5,21 mg/m³

Explosiegrens: geen data

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos tot lichtgele vloeistof

Brand: brandgevaarlijk, bij veel reacties kans op brand en explosie

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,01

Molecuulmassa: 125,2 g/mol

Zuurgraad: Geen data

LogKow: Geen data

Wateroplosbaarheid: reactie

Verzadigde dampdruk: 2,2 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW: irritatie ogen, neus, keel

AGW → LBW: matige tot ernstige irritatie van luchtwegen, tranenvloed, keelpijn, hoesten, benauwdheid, longoedeem

Boven LBW: ernstige longschade, sterfte

- *LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.*

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Primaire effecten zijn irritatie van de slijmvliezen van ogen, neus en keel.
- Cyclohexylisocyanaat kan een chemische longontsteking en/of longoedeem veroorzaken. De effecten hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Cyclohexylisocyanaat is mogelijk sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact!

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn.

Oogcontact: tranenvloed, roodheid en pijn.

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen, zo nodig arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken en direct arts raadplegen.

Specifieke behandeling en materialen:.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 3173-53-3 **Cyclohexyl isocyanate** **$C_6H_{11}N=C=O$** **UN-nr: 2488**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: Same rationale as for AEGL (analogy with methyl isocyanate; note: AGW for MIC deviates from AEGL-2). No modifying factor applied.

LBW: Same rationale as for AEGL (analogy with methyl isocyanate; note: LBW for MIC deviates from AEGL-3). No modifying factor applied.

Date: November 2015 | AEGL document: Final, 2013

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	- (systemic effects cannot be excluded)
AGW	6.3	2.1	1.0	0.52	0.26	0.13	Based on AGW values for methyl isocyanate (decreased fetal body weight, cardiac arrhythmias, fetal death).
LBW	43	14	7.2	3.6	1.8	0.90	Based on LBW values for methyl isocyanate (threshold of animal lethality).

Derivation of the Dutch Intervention Values

VRW: VRW values were not derived for cyclohexyl isocyanate due to a lack of relevant human and animal data. The available data suggest that cyclohexyl isocyanate exerts toxic effects, including delayed lethality, that are similar to those induced by methyl isocyanate. VRW values were not derived for methyl isocyanate because it has poor warning properties, and because systemic toxicity is possible at concentrations lower than those associated with VRW values. On the basis of similarities between cyclohexyl isocyanate and methyl isocyanate, VRW values were not derived for cyclohexyl isocyanate. Absence of VRW values does not imply that concentrations below the AGW values are without any effect.

AGW: No appropriate data for derivation of AGW values are found for cyclohexylisocyanate. AGW values were based on the AGW values as established for the related compound methyl isocyanate.
The AGW-values for methyl isocyanate were based on 3 animal studies. Mice (n=12-24) were exposed to 0, 2, 6, 9, 15 ppm (0, 4.8, 14, 21, 36 mg/m³) methyl isocyanate for 3 hours on day 8 of gestation. The LOEL for lower fetal body weights in the absence of maternal toxicity was an exposure of mice at 2 ppm (4.8 mg/m³) for 3 hours on day 8 of gestation. In the second animal study rats were exposed to 3, 10, 30 ppm (7.1, 24, 71 mg/m³) methyl isocyanate for 2 hours. The exposure of rats at 3 ppm (7.1 mg/m³) for 2 h was a LOEL for cardiac arrhythmias evaluated 4 months post-exposure. In contrast to the AEGL, the AGW-level was also based on an additional point of departure. In the third animal study (neonatal survival study with mice) pregnant mice were exposed to 0, 1, 3 ppm (0, 2.4, 7.1 mg/m³) methyl isocyanate for 6h/d on day 14-17 of gestation. Although the exposures were repeated on 4 consecutive days, the exposure to the fetus is considered similar to a single exposure because the stage of development and potential susceptibility changes daily throughout gestation and is different on each of the exposure days. In addition, the lower pup survival seen experimentally following repeated maternal exposure is the same end point as fetal and infant death in humans observed following accidental exposure. A significant increase in the total number of dead fetuses at birth was observed in both exposure groups (controls: 0.4%; 1 ppm (2.4 mg/m³): 3.3%; 3 ppm (7.1 mg/m³): 6.4%). The 6-h exposure at 1 ppm was used as point of departure to derive AGW for methyl isocyanate. Analogously, a 6-h exposure to 1 ppm is also used as point of departure for cyclohexyl isocyanate (*i.e.,* 5.21 mg/m³ for cyclohexyl isocyanate).
These three exposure concentration and duration scenarios yield identical AGW values when used for derivation. As for methyl isocyanate, the experimental concentrations were reduced by a modifying factor of 3 to estimate a threshold for the observed effects. A total uncertainty factor of 10 was applied to account for inter- and intraspecies variation, a factor of 3 each. Time scaling was performed using the equation $C^n \times t = k$, using n=1 (derived from rat LC_{50} values).
In contrast to the AEGL-2 of cyclohexyl isocyanate, an additional modifying factor of 2 to account for

a possible higher toxicity for cyclohexyl isocyanate as compared to methyl isocyanate was not applied for the AGW.

LBW: No appropriate data for derivation of LBW values are found for cyclohexyl isocyanate. LBW values were determined by using the LBW values established for the related compound methyl isocyanate. The LBW-values for methyl isocyanate were based on mortality data from a rat study. Rats were exposed by inhalation to various concentrations methyl isocyanate (17.5-541 ppm; 41.7-1285 mg/m^3) for 7.5-240 minutes. Point of departure was the 1-hour LC_{50}-value of 41.3 ppm. Based on the rat LC_{50} data in this study a n-value of 1 was calculated. Analogously, for the derivation of LBW values for cyclohexyl isocyanate a 1-hour value of 41.3 ppm (215.08 mg/m^3) was used as point of departure. This concentration was divided by 3 to obtain an estimate of the threshold for lethality. An uncertainty factor of 3 was used for interspecies variation and an uncertainty factor of 3 was used for intraspecies variation. Time-scaling was performed using $C^n \times t = k$, with the chemical-specific n-value of 1.
In contrast to the AEGL-3 of cyclohexyl isocyanate, an additional modifying factor of 2 to account for a possible higher toxicity for cyclohexyl isocyanate as compared to methyl isocyanate was not applied for the LBW.

Additional toxicological information (including relevant results of a general literature search, if any)

No studies are available that address the mechanism(s) of toxicity of cyclohexyl isocyanate. It is thought that the mode of action might be equal to methyl isocyanate, which toxicity is clinically similar to that described for cyclohexyl isocyanate (respiratory tract irritation with delayed lethality). The exact mechanism of action for the systemic effects is unknown. High concentrations may cause lung edema.

No reproductive or developmental data were located for cyclohexyl isocyanate.

H302: Harmful if swallowed; H318: Causes serious eye damage; H311: Toxic in contact with skin; H330: Fatal if inhaled; H315: Causes skin irritation; H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled; H335: May cause respiratory irritation

Repeated or prolonged contact may cause skin sensitization. Repeated or prolonged inhalation exposure may cause asthma.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

No data are available concerning odour awareness.

No LOA was derived

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **NR**	*AEGL-1* NR	*ERPG-1* Not derived		*IDLH:* not established
AGW level **1.0**	*AEGL-2* 0.17	*ERPG-2* Not derived		
LBW level **7.2**	*AEGL-3* 0.52	*ERPG-3* Not derived		

Stofdocument deel A

CAS-nr: 329-99-7 **Cyclosarin** $C_7H_{14}FO_2P$ **VN-nr: n.v.t.**

GEVI: geen

Synoniemen: Agent GF; O-cyclohexylmethyl-fluorofosfonaat (Engels: Cyclosarin) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,0034	0,0020	0,0010	0,00071	0,00060	0,00042
Alarmeringsgrenswaarden	AGW (mg/m³)	0,043	0,025	0,018	0,013	0,0088	0,0063
Levensbedreigende waarden	LBW (mg/m³)	0,38	0,19	0,13	0,094	0,070	0,051

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,133 ppm; 1 ppm = 7,50 mg/m³

Explosiegrens: Geen data

Geur: zwakke fruitige of kruidige geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: visceuze, kleurloze, vluchtige vloeistof
Brand: Geen data

Relatieve dichtheid van verzadigd damp-lucht mengsel: 6,2

Molecuulmassa:	180,2 g/mol
Zuurgraad:	Geen data
LogKow:	1,67
Wateroplosbaarheid:	3.7 mg/l (bij 20 °C, slecht)
Verzadigde dampdruk:	0,044 (mmHg, 25°C)

Overige informatie

Publieke grenswaarde: Niet afgeleid
MAK: Niet afgeleid
TLV-TWA: Niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	hoofdpijn
VRW → AGW:	pupilvernauwing, misselijkheid, braken
AGW → LBW:	speekselvloed, zweten, tranenvloed, moeizaam ademen, zwaktegevoel, buikkrampen, spierkrampen, kleine spiertrekkingen, verlammingsverschijnselen, bewustzijnsdaling
Boven LBW:	convulsies, coma, verlamming, ademstilstand, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Cyclosarin is een zeer potente irreversibele cholinesterase remmer. Hierdoor wordt de afbraak van de neurotransmitter acetylcholine geremd en de zenuwimpuls bij de motorische eindplaat verstoord.
- Doelorganen zijn het centrale, het perifere en het autonome zenuwstelsel. De meeste effecten treden zeer snel op, echter neuropathologische effecten zoals verlamming kunnen vertraagd optreden en langdurig van aard zijn.
- Kinderen zijn gevoeliger voor de effecten van de stof dan volwassenen. Ook kan het klinische beeld bij kinderen anders zijn dan bij volwassenen.
- Mogelijk zijn vrouwen gevoeliger voor de effecten van de stof dan mannen.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, (lokale) spiertrekkingen, verder zie: 'Effecten bij inhalatoire blootstelling'

Oogcontact: roodheid en (hevige) pijn, nauwe pupillen, visusklachten, tranenvloed, verder zie: 'Effecten bij inhalatoire blootstelling'

Carcinogeniteit

IARC classificatie: Niet geclassificeerd
CRP: Niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, specifieke behandeling en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!) , specifieke behandeling en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: CAVE hulpverleners: draag persoonlijke bescherming!* Bij vergiftiging is specifieke eerste hulp noodzakelijk; 100% zuurstof en het specifieke antidotum atropine) moet met gebruiksaanwijzing ter plekke beschikbaar zijn. Toediening van andere middelen (zoals oximen) kan bij de spoedeisende hulpverlening (in het ziekenhuis) overwogen worden.

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 329-99-7 **Cyclosarin** **$C_7H_{14}FO_2P$** **UN-nr: -**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: November 2015 | AEGL document: Final, 2003

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.0034	0.0020	0.0010	0.00071	0.00060	0.00042	0.5 times the VRW values for Agent GB. End point for agent GB: EC_{50} for miosis in rats.
AGW	0.043	0.025	0.018	0.013	0.0088	0.0063	0.5 times the AGW values for Agent GB. End point for agent GB: miosis, dyspnea, RBC-ChE inhibition, single fibre electro-myography (SFEMG) changes in human volunteers.
LBW	0.38	0.19	0.13	0.094	0.070	0.051	LBW values for agent GB were adopted. End point for agent GB: lethality in rats (LC_{01}).

Derivation of the Dutch Intervention Values

VRW: Because of the sparse human and animal toxicity dataset for cyclosarin (agent GF) all Dutch Intervention Values for this nerve agent are based on the values for nerve agent GB (Sarin) by applying a relative potency method. This approach is justified given: 1) the reasonably complete dataset for the nerve agents as a group, and 2) the same mode of action for agent GB and agent GF.

The VRW values for agent GF were based on a well-conducted whole body inhalation study in adult female rats exposed to a range of GB vapor concentrations (0.01 to 0.48 mg/m³) over three time durations (10 min, 60 min, or 240 min). Female rats are reported to be more sensitive to GB vapor toxicity than males. Analysis of rat pupil diameters assessed pre- and postexposure allowed determination of EC_{50} values for miosis (which is defined as a postexposure pupil diameter of 50% or less of the preexposure diameter in 50% of the exposed population). Although the EC_{50} for miosis is not considered an adverse effect in humans, miosis is regarded the first measurable change in the continuum of effects caused by inhibition of acetylcholinesterase. As miosis is transient and reversible, this effect is thought to be the most relevant endpoint for VRW-levels. The selection of miosis induction as the basis for the VRW is supported by the observation that cholinesterase activity depression is too variable for application as critical effects. Human data are also available and showing rhinorrhea, headache, tightness in chest, cramps nausea, and miosis (mean maximal decrease in pupil diameter) in human volunteers exposed to GB at 0.05 mg/m³ for 20 min. These human data are considered secondary and supportive, leading to almost the same values.
The 10-min, 60-min and 240-min rat EC_{50} values for miosis of 0.068, 0.020 and 0.012 mg/m³ respectively were used as point of departure for determining VRW-levels. Time scaling was performed for the remaining 30-min, 2-h and 8-h values using the $C^n \times t = k$ equation, where n = 2 based on regression analysis of miosis and lethality data in rats. An interspecies uncertainty factor of 1 and an intraspecies uncertainty factor of 10 were used, resulting in a total uncertainty factor of 10. For miosis as a critical effect, comparison of the EC_{50} values for miosis in the eye of the rabbit indicated that agent GF is approximately twice as potent as agent GB. The VRW-values for agent GF are therefore set equal to 0.5 times the VRW-values derived for agent GB (correction applied to mg/m³ values).

AGW: The AGW values for agent GF were based on a study in which miosis, dyspnea, photophobia, inhibition of red blood cell cholinesterase (RBC-ChE), and changes in single fibre electromyography

(SFEMG) were observed in human volunteers following a 30-min exposure at 0.5 mg agent GB/m^3. The SFEMG changes noted in the study were not clinically significant and were not detectable after 15-30 months. Although the observed SFEMG changes were reversible and subclinical, these effects are considered an early indicator of exposures that potentially could result in more significant effects. Selection of this effect as a protective definition of an AGW level is considered appropriate given the steep dose-response toxicity curve of nerve agents. Time scaling was performed by using the C^n x t = k equation, where n = 2 based on regression analysis of miosis and lethality data in female rats. An interspecies uncertainty factor of 1 and an intraspecies uncertainty factor of 10 were used, resulting in a total uncertainty factor of 10. For miosis as a critical effect, comparison of the EC_{50} values for miosis in the eye of the rabbit indicated that agent GF is approximately twice as potent as agent GB. The AGW-values for agent GF are therefore set equal to 0.5 times the values derived for agent GB (correction applied to mg/m^3 values).

LBW: LBW values for agent GF were derived from recent whole-body inhalation studies in which the lethality of GB vapor in female rats was evaluated after various exposure periods. Female rats are reported to be more sensitive to GB vapor toxicity than males. Using probit analysis, the estimated LC_{01} values for female rats were as follows: 11.537 mg/m^3 for 10 min, 5.836 mg/m^3 for 30 min, 4.006 mg/m^3 for 60 min, 2.087 mg/m^3 for 4 h, and 1.761 mg/m^3 for 6 h. Time scaling was performed to derive the 2-h and 8-h value using the C^n x t = k equation, where n = 2 based on regression analysis of miosis and lethality data in female rats. An interspecies uncertainty factor of 3 and an intraspecies uncertainty factor of 10 were used, resulting in a total uncertainty factor of 30. For LBW effects agent GF and agent GB are considered equipotent based on lethality data in rats. The LBW-values for agent GF are therefore set equal to the values derived for agent GB.

Additional toxicological information (including relevant results of a general literature search, if any)

Nerve agents exert toxic effects on the central and peripheral nervous system indirectly through acetylcholinesterase inhibition, nerve agents may also affect nerve impulse transmission by additional mechanisms at neuromuscular junctions and at neurotransmitter receptor sites in the CNS. The first symptoms are related to the nerve conduction inhibition by the substance and consist of: pupil constriction (miosis), headache, shortness of breath, tightness of the chest. A runny nose and lacrimation can also be observed. At increasing exposure levels or prolonged exposures sweating, diarrhea, bradycardia, tremors, overall weakness, paralysis, unconsciousness, convulsions, suppression of respiration and death can occur. The dose-response relation is considered very steep and effects may occur rapidly. However, delayed neuropathological effects (such as paralysis) may occur.

The inhibited acetylcholinesterase can be reactivated by the process of dephosphorylation, but this is not possible once the nerve agent-cholinesterase complex undergoes “aging,” which is thought to happen because of a loss of an alkyl or alkoxy group. No information is found on the velocity of aging of agent GF.

No information found on human reproductive toxicity. Animal data from vapor and oral exposure studies for agent GB suggest that agent GB does not induce reproductive or developmental effects in mammals.

No harmonized hazard sentences were found.

Carcinogenicity and derivation of the CRP value

IARC classification: Not classified.

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: Sweet or musty odour of peaches

Odour thresholds of 10.4-14.8 mg/m^3 are reported, but no OT50 was derived.

No LOA was derived

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level 0.0010	*AEGL-1* 0.0010	*ERPG-1* NA		*IDLH: Not Derived*
AGW level 0.018	*AEGL-2* 0.018	*ERPG-2* NA		
LBW level 0.13	*AEGL-3* 0.13	*ERPG-3* NA		

Stofdocument deel A

CAS-nr: 19287-45-7 **Diboraan** B_2H_6 **VN-nr: 1911**

GEVI: geen

Synoniemen: boorethaan, boorhydride (Engels: Diborane) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	6,9	2,3	1,2	0,58	0,29	0,14
Levensbedreigende waarden	LBW (mg/m³)	25	8,5	4,2	2,1	1,1	0,53

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,866 ppm; 1 ppm = 1,15 mg/m³

Explosiegrens: LEL = 0,8 vol% ≈ 9200 mg/m³

Geur: typerende geur
LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos onder druk tot vloeistof verdicht gas.
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 0,96

Molecuulmassa: 27,7 g/mol
Zuurgraad: Geen data
LogKow: Geen data
Wateroplosbaarheid: Reactie
Verzadigde dampdruk: 42600 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 0.1 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: niet bekend, klachten worden niet uitgesloten

AGW → LBW: longschade, hoesten, misselijkheid, benauwdheid, pijn op de borst, longoedeem

Boven LBW: ademnood, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Diboraan ontleedt in contact met water (exotherme reactie) in boorzuur en waterstof.
- Diboraan veroorzaakt primair irritatie van de huid, ogen, slijmvliezen en luchtwegen. Longschade (bloedingen) en oedeem kan optreden.
- Polyboranen kunnen worden gevormd bij kamertemperatuur door polymerisatie. Polyboranen kunnen effecten op het centraal zenuwstelsel veroorzaken.
- Effecten op de lever- en nier bij proefdieren na inhalatie van diboraan zijn beschreven.
- Blootstelling aan diboraan kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bij bevriezing: ernstige bevriezingsverschijnselen zoals pijn, blaren en wonden

Oogcontact: bij bevriezing: bijtend, slecht zien.

Carcinogeniteit

IARC classificatie: niet geclassificeerd.
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: aan de huid vastgevroren kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas).

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 19287-45-7 **Diborane** **B_2H_6** **UN-nr: 1911**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value adopted (except 10 min value for which time scaling was applied), 2hr value added.

LBW: AEGL value adopted (except 10 min value for which time scaling was applied), 2hr value added.

Date: 24-09-2009 | AEGL document, final 2003

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	6.9	2.3	1.2	0.58	0.29	0.14	Reversible histological changes in the lungs in animals
LBW	25	8.5	4.2	2.1	1.1	0.53	Animal mortality

Derivation of the Dutch Intervention Values

VRW: Not recommended, because of a lack of suitable data.

AGW: The AGW values were based on reversible histological changes in the lungs in male ICR mice following a 2-h acute inhalation exposure to diborane at 5 ppm (5.8 mg/m³). No effects were observed in mice exposed at 5 ppm for 1 hour, while exposure at 5 ppm for 2 hours resulted in 4/10 mice developing multifocal and/or diffuse inflammatory epithelial degeneration in the bronchioles. A total uncertainty factor of 10 was applied. An interspecies factor of 3 and an intraspecies factor of 3 was applied. The use of higher uncertainty factors would result in AGW values that would be below concentrations causing effects in any species for an endpoint that is supposed to be disabling or cause irreversible effects in a human population. Time scaling was performed using $C^n * t = k$, with n=1 based on experimental data. In contrast to the 10 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: A 4-h LC_{50} study in mice was used to derive the estimated LC_{01} value of 9.2 ppm (10.6 mg/m³), which subsequently was used in the derivation of the LBW. A total uncertainty factor of 10 was applied. Because there was little observed variation between species in sensitivity to lethal concentrations of diborane, an interspecies factor of 3 was applied. An intraspecies factor of 3 was applied. Time scaling was performed using $C^n * t = k$, with n = 1, based on experimental data. In contrast to the 10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Diborane quickly hydrolyzes in water to produce boric acid, hydrogen, and heat and should undergo the same reaction in the lungs. However, the hydrolysis products alone do not explain the toxicity of diborane. It is likely that the mechanism of toxicity is due to direct interaction of diborane with cellular components, especially since diborane is such a potent reducer. Possibly, the heat formation caused by the exothermic reaction may cause damage to the lungs as well (still a hypothesis). There appears to be a similar mechanism of toxicity between species because the respiratory tract has consistently been the target organ, and the cause of death from diborane exposure has always been from pulmonary damage, including edema, hemorrhage, and congestion.
Signs and symptoms of exposure included chest tightness, shortness of breath and dyspnea, wheezing, nonproductive cough, and precordial pain. Workers exposed to diborane generally experienced a complete recovery within a short period following cessation of exposure.
No data are available on the reprotoxic and developmental toxic capacities of the substance in humans. Based on analogy with boric acid, diborane is classified A- reprotoxic (reduced fertility in males).

No harmonized H-sentences for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: Not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: Repulsive and sickly sweet odour.

No LOA was derived due to lack of reliable data.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level	*AEGL-1*	*ERPG-1*		*IDLH:* 17 (30 min)

NR	NA	NA		
AGW level **1.2**	*AEGL-2* 1.2	*ERPG-2* 1.2		
LBW level **4.2**	*AEGL-3* 4.3	*ERPG-3* 3.5		

Stofdocument deel A

CAS-nr: 79-36-7 **Dichlooracetylchloride** **$CHCl_2COCl$** **VN-nr: 1765**
GEVI: X80

Synoniemen: dichloroethanoylchloride, dichloorazijnzuurchloride (Engels: dichloroacetyl chloride) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,26	0,26	0,26	0,26	0,26	0,26
Alarmeringsgrenswaarden	AGW (mg/m³)	18	12	9,8	4,9	2,5	1,2
Levensbedreigende waarden	LBW (mg/m³)	580	400	320	160	80	40

Datum vaststelling: 13-05-2009 | Conversiefactor: 1 mg/m³ = 0,163 ppm; 1 ppm = 6,13 mg/m³

Explosiegrens: LEL=11,9 vol% ≈ 730.000 mg/m³

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze rokende vloeistof
Brand: brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,1

Molecuulmassa:	147,4 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	30,6 mbar

Overige informatie

Publiek grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 0,31

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: oogirritatie, tranenvloed

AGW → LBW: sterke oogirritatie, slecht zien, hoesten, benauwdheid, longoedeem

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Dichlooracetylchloride is sterk irriterend voor ogen en luchtwegen.
- Dichlooracetylchloride kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, ernstige brandwonden

Oogcontact: bijtend, roodheid en pijn, ernstige brandwonden.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof
huid: eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Ontsmetting bij inademen/inslikken
Inademing/inslikken van sterke zuren kan tevens leiden tot larynx- en glottisoedeem, met risico op verstikking (asfyxie) door zwellingen in de keel. Intubatie (borgen van vrije luchtwegen), eventueel gevolgd door beademing moeten in ernstige gevallen z.s.m. worden uitgevoerd (door specialisten). Zet derhalve direct spoedeisende medische hulp in.

Specifieke behandeling en materialen: geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 79-36-7 **Dichloroacetyl chloride** **$CHCl_2COCl$** **UN-nr: 1765**

Basis for the Dutch Intervention Values

VRW: Based on analogy with chloroacetyl chloride, in accordance with AEGL, 2h value added

AGW: Based on analogy with chloroacetyl chloride, in accordance with AEGL, 2h value added

LBW: Based on analogy with chloroacetyl chloride, in accordance with AEGL, 2h value added

Date: 13-05-2009 AEGL document: Interim, 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.26	0.26	0.26	0.26	0.26	0.26	Based on analogy with chloroacetyl chloride
AGW	18	12	9.8	4.9	2.5	1.2	Based on analogy with chloroacetyl chloride
LBW	580	400	320	160	80	40	Based on analogy with chloroacetyl chloride

Derivation of the Dutch Intervention Values

VRW: Analogy with chloroacetyl chloride. VRW values of chloroacetyl chloride (on a ppm-basis) were adopted. Below the VRW derivation of chloroacetylchloride is given.

The VRW values were derived from a multiple-exposure study in which conjunctival redness was reported in rats after the initial 6-hour exposure to approximately 0.5 ppm (2.35 mg/m³) chloroacetyl chloride. VRW values were derived using a single 6-hour exposure to 0.84 ppm (3.9 mg/m³) chloroacetyl chloride because this is the highest concentration that caused conjunctival redness but no other more serious effects after one exposure. A modifying factor of 2 was applied to estimate a no-effect level concentration for conjunctivitis. The same VRW value is adopted for 10 minutes to 8 hours because mild irritant effects do not vary greatly over time. A total uncertainty factor of 10 was applied: 3 for interspecies variability and 3 for intraspecies variability. The resulting VRW of 0.04 ppm (0.20 mg/m³) chloroacetyl chloride is consistent with the limited human data in which exposure to 0.023 ppm (0.11 mg/m³) chloroacetyl chloride for an undefined period was barely detectable but 0.140 ppm (0.66 mg/m³) chloroacetyl chloride was strong, and exposure to 0.05 ppm (0.23 mg/m³) chloroacetyl chloride was associated with odor that was objectionable but no adverse health effects were reported.

AGW: Analogy with chloroacetyl chloride. AGW values of chloroacetyl chloride (on a ppm-basis) were adopted. Below the AGW derivation of chloro acetylchloride is given.

A 1- hour inhalation rat study (32, 208, 522, or 747 ppm; 150, 976, 2,448 or 3,503 mg/m³) chloroacetyl chloride was chosen for AGW derivation because it was the only well-conducted study in which effects within the scope of AGW occurred from a single exposure. All test groups squinted, lacrimated, had urine stains, and initially lost weight. At 208 ppm (976 mg/m³) chloroacetyl chloride, rats had shallow breathing, lethargy, and reddish stains near the eyes, at 522 ppm (2,448 mg/m³), rats also had labored breathing, gasping, and salivation, and at 747 ppm (3,503 mg/m³), 5/6 males and 1/6 females died and necropsy revealed lung pathology, nasal congestion, and enlarged adrenals. The AGW endpoint was the NOEL for impaired ability to escape due to lacrimation and eye squinting, which was estimated by applying a modifying factor of 2 to the lowest concentration tested of 32 ppm (150 mg/m³). A total uncertainty factor of 10 was applied, consisting of 3 for interspecies variability and 3 for intraspecies variability. Scaling across time was performed using $C^n * t = k$, with the defaults n=3 and n=1 for extrapolation to shorter and longer exposure durations, respectively.

LBW: Analogy with chloroacetyl chloride. LBW values of chloroacetyl chloride (on a ppm-basis) were adopted. Below the LBW derivation of chloro acetylchloride is given.

A 1-hour inhalation rat study (32, 208, 522, or 747 ppm; 150, 976, 2,448 or 3,503 mg/m³)

chloroacetyl chloride) was chosen for LBW derivation. The LBW toxic endpoint was the lethality threshold, which was taken as the highest concentration tested that caused no deaths (522 ppm = 2,448 mg/m^3). A total uncertainty factor of 10 was applied. An interspecies uncertainty factor of 3 was used because lethality resulting from respiratory lesions and having a steep dose-response was seen in several studies with rats and mice, at chloroacetyl chloride concentrations within a factor of 2-3. An intraspecies uncertainty factor of 3 was applied because the threshold for lethality from direct destruction of respiratory tissue is not expected to vary greatly among humans, based on the steep dose-response seen in the animal studies. To obtain protective LBW values, scaling across time was performed using $C^n * t = k$, with the defaults n=3 and n=1 for extrapolation to shorter and longer exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

The AEGL values derived for chloroacetyl chloride were adopted for dichloroacetyl chloride due to limited data for the latter substance and lower toxicity of dichloroacetyl chloride. A comparison of rat 4-hour LC_{50} values indicated that chloroacetyl chloride is more toxic than dichloroacetyl chloride (LC_{50}-values of 660 ppm and >2000 ppm for chloroacetyl chloride and dichloroacetyl chloride respectively).

The substance is a contact irritant and may induce strong eye, skin and respiratory tract irritations. May cause lung edema.

H314: Causes severe skin burns and eye damage.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: Pungent odour.

No LOA was derived due to lack of data.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **0.26**	*AEGL-1* 0.24	*ERPG-1* Not derived		*IDLH:* not established
AGW level **9.8**	*AEGL-2* 9.8	*ERPG-2* Not derived		
LBW level **320**	*AEGL-3* 320	*ERPG-3* Not derived		

Stofdocument deel A

CAS-nr: 542-88-1 **Dichloordimethylether** $(CH_2Cl)_2O$ **VN-nr: 2249**

GEVI: geen

Synoniemen: BCME, bis(chloormethyl)ether, sym-dichloordimethylether (Eng.: bis chloromethyl ether)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	0,38	0,27	0,21	0,17	0,13	0,096
Levensbedreigende waarden	LBW (mg/m³)	1,6	1,1	0,87	0,69	0,55	0,36

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,21 ppm; 1 ppm = 4,78 mg/m³

Explosiegrens: LEL = 6,5 Vol% ≈ 311.000 mg/m³ (geschat)

Geur: stekende, "verstikkende" geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,0

Molecuulmassa: 115 g/mol

Zuurgraad: Geen data

LogKow: Geen data
Wateroplosbaarheid: Reactie
Verzadigde dampdruk: 0,14 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 0,0048 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW**:* irritatie van ogen, huid, luchtwegen

AGW → LBW: ernstige irritatie van ogen, huid, luchtwegen, benauwdheid

Boven LBW: longoedeem, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder AGW zonder effecten is

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Dichloordimethylether werkt zeer irriterend tot bijtend op de ogen, huid en de luchtwegen.
- Blootstelling aan dichloordimethylether kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Dichloordimethylether is mutageen en carcinogeen.

Klachten bij blootstelling aan vloeistof

Huidcontact: roodheid, pijn

Oogcontact: roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: 1
CRP: 0,35 mg/m³ (blootstelling 1 uur)

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen).

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**:* geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 542-88-1 **Bis-chloromethyl ether** $(CH_2Cl)_2O$ **UN-nr: 2249**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value adopted (except 10 min value for which time scaling was applied), 2hr value added.

LBW: AEGL value adopted (except 10 min value for which time scaling was applied), 2hr value added.

Date: November 2015 | AEGL document, final, 2012.

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	0.38	0.27	0.21	0.17	0.13	0.096	Irreversible respiratory lesions in animals
LBW	1.6	1.1	0.87	0.69	0.55	0.36	Threshold of animal lethality

Derivation of the Dutch Intervention Values

VRW: Not recommended, because effects exceeding the severity of the VRW occurred at concentrations that did not produce sensory irritation in humans or animals.

AGW: The AGW was based on the lowest LOAEL for irreversible respiratory lesions, i.e., 0.7 ppm (3.3 mg/m³) for rats and hamsters at 7 hr exposure followed by a lifetime observation. This LOAEL was divided by 3 to estimate a NAEL of 0.23 ppm (1.1 mg/m³). The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n * t = k$, with the default values of n=1 and n=3 for extrapolation to longer and shorter exposure durations, respectively. In contrast to the AEGL, time scaling was also applied to derive the 10-minute AGW.

LBW: LBWs were derived from the single-exposure scenario of the repeated dose study in which rats and hamsters were subjected to 1, 3, 10, or 30 times six-hour exposures of 1 ppm (4.8 mg/m³) BCME followed by lifetime observation. This study was chosen because it tested the highest BCME concentration that was shown to not cause lethality after lifetime observation. Another study by the same authors found a lethality NOEL of 0.7 ppm (7 h) for rats and hamster after lifetime observation. A 7-h LC_{50} study using rats and hamsters (Drew at al. 1975) was not used because it yielded a $BMCL_{01}$ of 2.3 ppm for rats, which exceeds 2.1 ppm (10 mg/m³), the concentration that caused mortality in rats and hamsters after single 7-h exposure to BCME in a life time study (also by Drew at al. 1975). The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n * t = k$, with n=3 and n=1 to for durations shorter and longer, respectively, than 6 hours. In contrast to the AEGL, time scaling was also applied to derive a 10-minute LBW.

Additional toxicological information (including relevant results of a general literature search, if any)

BCME is analogous to chloromethyl methylether (CMME), but considered more toxic. Both compounds are known irritants to the eyes and lungs. Their mechanism of action is not completely understood.
No studies were located assessing developmental or reproductive effects of BCME exposure on animals.

H302: Harmful if swallowed; H311: Toxic in contact with skin; H330: Fatal if inhaled; H350: May cause cancer.

Carcinogenicity and derivation of the CRP value

IARC classification: 1

Derivation of the carcinogenic risk potency (CRP):
10^{-4} risk level after inhalation: $1.6 * 10^{-6}$ mg/m³ [AEGL]

CRP = (10^{-4} risk level * average life span in hours)/DRCF

= $(1.6 * 10^{-6} * 613.200) / 2.8 = 0.35$ mg/m³

The CRP was based on a lifetime inhalation study in male

Odour and derivation of the LOA value

Odour: “Suffocating” odour.

No LOA was derived due to lack of reliable data.

Sprague-Dawley rats that were exposed to 0.48 mg/m^3 (0.1 ppm) BCME 6 hours/day, 5 days/week. Animals given 10-100 exposures had 40 nasal and/or lung cancers. The shortest number of exposures that resulted in cancer was 10 times.	

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*				
VRW level **NR**	*AEGL-1* NA	*ERPG-1* NA		*IDLH:* not established.
AGW level **0.21**	*AEGL-2* 0.21	*ERPG-2* 0.48		
LBW level **0.87**	*AEGL-3* 0.86	*ERPG-3* 2.4		

Stofdocument deel A

CAS-nr: 107-06-2 **1,2-Dichloorethaan** **$ClCH_2$-CH_2-Cl** **VN-nr: 1184** **GEVI: 336**

Synoniemen: ethyleendichloride, ethyleenchloride, glycoldichloride (Engels: 1,2-dichloroethane) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	160	110	87	69	55	44
Alarmeringsgrenswaarde	AGW (mg/m³)	2500	890	470	250	250	130
Levensbedreigende	LBW (mg/m³)	7200	2700	1400	760	410	220

Datum vaststelling: 31-10-2017 | Conversiefactor: 1 mg/m³ = 0,243 ppm; 1 ppm = 4,118 mg/m³

Explosiegrens: 4,2 vol% ≈42000 ppm=170000 mg/m³
Damp met lucht is explosief.

Geur: typerende zoete chloroformachtige geur
LOA: 1679 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof, die donker wordt bij blootstelling aan licht en (vochtige) lucht.
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,2

Molecuulmassa:	99,0 g/mol
Zuurgraad:	geen data
LogKow:	1,5
Wateroplosbaarheid:	0,8 g/100 ml
Verzadigde dampdruk:	87 mbar

Overige informatie

Publieke grenswaarde: 7 mg/m³
MAK: - (H)
TLV-TWA: 41 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling
Onder VRW: niet bekend
VRW → AGW: lichte irritatie ogen, neus en keel, euforie, duizeligheid, misselijkheid
AGW → LBW: keelpijn en hoesten, sufheid, zwakte, irritatie ogen, neus en keel
Boven LBW: bewusteloosheid, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling
- 1,2-dichloorethaan veroorzaakt irritatie van ogen, neus en keel
- Ethyleendichloride veroorzaakt depressie van het gastro-intestinale systeem en het centrale zenuwstelsel met als gevolg verlaagd bewustzijn.
- Bij blootstelling aan hoge concentraties, hersenoedeem bewusteloosheid en effecten op lever en nieren.
- Sterfte bij acute hoge blootstelling door respiratoire en circulatoire collaps met congestie, necrose en bloedingen in de meeste inwendige organen.

Effecten bij blootstelling aan vloeistof
Huidcontact: roodheid, prikkeling
Oogcontact: roodheid en pijn, slecht zien, hoornvliesbeschadiging

Carcinogeniteit
IARC classificatie: 2B
CRP: 15390 mg/m³

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, en direct spoedeisende medische hulp inzetten.
Ontsmetting vloeistof
huid: spoelen met veel water/kleding verwijderen, spoelen en wassen met water en zeep.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.
Specifieke behandeling en materialen*: geen*.
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: **1,2-dichloroethane** **$ClCH_2$-CH_2-C** **UN-nr: 1184**

Basis for the Dutch Intervention Values

VRW: Based on additional information to that described in ERPG-document, other time points added.
AGW: Based on additional information to that described in ERPG-document, other time points added.
LBW: Based on information as described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017	ERPG 2014

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	160	110	87	69	55	44	Very slight degeneration of nasal tissue in rats
AGW	2500	890	470	250	250	130	Neurobehavioral effects in rats
LBW	7200	2600	1400	720	380	200	Rat lethality data

Derivation of the Dutch Intervention Values

VRW: In an acute toxicity study in rats only very slight degeneration of the nasal tissue was observed following an 8-hour exposure to 435 mg/m³ (see additional information for study details). In the absence of human data, 435 mg/m³ was used as point of departure for derivation of VRW values. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$ with the default n= 3 to calculate to shorter durations. The chemical specific factor of 1.08 was not used, because the slight generation of nasal tissue is expected to be the result of a different mode of action than the effects observed at AGW and LBW level. The derived values are in line with the anecdotal human data as described in the rationale for the AGW.

AGW: Studies in animals, including developmental toxicity studies, show no or little toxicity up until levels causing death. Human studies are anecdotal and show signs of irritation of the mucous membranes of mouth, throat and bronchi in workers after long term exposure at 62-247 mg/m³ and in another study eye irritation, anorexia, nausea, weakness, tiredness and tremor at 250-825 mg/m³ after 2-8 months of exposure.
An acute (neuro)toxicity study in rats (see additional information for study details) was used for derivation of the AGW values. The local effects observed at concentrations above 435 mg/m³ (the PoD for the VRW) increased somewhat in intensity and frequency, but remained sub AGW effects. Therefore, the threshold for neurobehavioural effects of 2460 mg/m³ (4-hour exposure), derived from the same study was used as point of departure for derivation of the AGW values. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. In general, neurobehavioural effects are concentration dependent rather than concentration x time dependent. However, data show that a steady state is reached after approximately 2-3 hours. Therefore, time scaling was applied for exposure durations shorter than 2 hours, using the equation $C^n \times t = k$ and the chemical specific value of 1.08 for n, based on the rat lethality data (see LBW). Because the 8 hour value would come into conflict with the 8 hour LBW the 8-hour value was extrapolated from the 4-hour value, using n = 1.08.

LBW: In an acute inhalation toxicity study rats (10-54 rats/group) were exposed to several concentrations of 1,2-dichlororethane (actual concentrations tested were 1235, 2471, 3294, 4118, 6177, 12354, 49416, and 82360 mg/m³) at various time exposure durations of 6 to 480 minutes (1 to 9 exposure durations per concentration level). The lethality data are numerous and reported in the primary publication[16]. The LBW values were determined by calculating the LC_{01} values for each time point using DoseResp. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences.

Additional toxicological information (including relevant results of a general literature search, if any)

1,2-Dichloroethane is irritating to the skin, eye and respiratory tract at high concentrations.

[16] Spencer et al, (1951) Vapor toxicity of ethylene dichloride determined by experiments on laboratory animals AMA Archives of Industrial Hygiene and Occupational Medicine, Volume 4 (5): pp 482-493,

No reprotoxic or teratogenic effects were seen in rats, rabbits or mice.
An additional acute (neuro)toxicity study in rats (Hotchkiss et al, 2010)[17] was retrieved and used for selection of point of departure for both the VRW and AGW values. Rats (5/sex/concentration) were exposed, whole body, to actual concentrations of 0, 52.8 (local effects only), 196.4, 607.8, or 2029 ppm (corresponding to 0, 214, 795, 2460, and 8211 mg/m^3, respectively) for 4 hours or 0, 52.8, 107.5 or 155.8 ppm (corresponding to 0, 214, 435, or 631 mg/m^3, respectively) for 8 hours. Conversions from ppm to mg/m^3 are based on the laboratory specific conversion factor of 4.047. Acute toxic effects were assessed by broncho-alveolar lavage and histopathology of the respiratory tract and selected target organs. Based on olfactory epithelial degeneration/necrosis at 795 mg/m^3 ppm after 4 hours and at 435 mg/m^3 after 8 hours, the most sensitive indicator of toxicity in this study, the overall NOEC was assessed to be 52.8 ppm (214 mg/m^3) 1,2-dichloroethane for up to 8 h in rats. For derivation of intervention values the effects observed at 435 mg/m^3 after 8 hours of exposure were considered to be marginal effects (very slight degeneration unilateral in one male and 3 females). At 631 mg/m^3 (8 hour) and 795 mg/m^3 for 4 hours the effects were still very slight to slight, but observed in more animals (4 males and 5 females and 3 males and 4 females, respectively). All effects were reversible. This was considered the effect level for local effects, leading to a point of departure for VRW of 435 mg/m^3 for 8 hours.
Neurobehavioural effects consistent with central nervous system (CNS) depression were present at concentrations of 2460 mg/m^3 and higher and were restricted to day 1. The effects observed at 2460 mg/m^3 consisted only of urination in males and females. At the next concentration (8211 mg/m^3) the effects developed to significant effects on resistance to removal, palpebral closure, lacrimation (females only), extensor thrust, response to sharp noise, response to tail pinch (males only), urination, defecation (males only) and slight incoordination of gait. The exposure concentration of 2460 mg/m^3 was considered a NOAEL for neurobehavioural effects and was chosen as point of departure for AGW values.
H302 (Harmful if swallowed), H315 (Causes skin irritation), H319 (Causes serious eye irritation), H335 (May cause respiratory irritation) and H350 (May cause cancer).

Carcinogenicity and derivation of the CRP value

IARC classification: 2B (possibly carcinogenic to humans)
Derivation of the carcinogenic risk potency (CRP):
The BMD_{10} of 37.8 ppm (corresponding with 394 mg/m^3) based on a 6-h/day; 5-day/week exposure and as established by SCOEL, (SCOEL, 2016) was used to determine the CRP. This value was corrected to continuous human lifetime exposure (BMD_{10} × 6/24 × 5/7) and excess lifetime cancer risk of 10^{-4} (/1000)= 0.070 mg/m^3

CRP = (10^{-4} risk level * 613.000)/DRCF
= (0.070 * 613.000)/2.8 = 15390 mg/m^3

The URF of the SCOEL was based on the BMD_{10} calculation on the data of Nagano, 2006 (6 hr/day, 5 d/wk, 104 wks mice inhalation study), which was not yet available during the EPA and WHO evaluation in 1999 and 1998, resp. These evaluations were based on an NCI study (1978) in rats and mice, 78 wks gavage study). The data by Nagano have been evaluated by other authors leading to comparable BMD_{10} values.

Odour and derivation of the LOA value

Odour: chloroform-like, pleasant odour
OT_{50}: 107 mg/m^3 [AIHA, 1989]
LOA = 11.8 * OT_{50} * 1.33 = 1679 mg/m^3
(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)
The LOA is below the 30 and 10 minute LBW value.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)[18]

***VRW level* 87**	*AEGL-1* -	*ERPG-1* 202	*IDLH:* 200 mg/m^3 (30 minutes)
***AGW level* 470**	*AEGL-2* -	*ERPG-2* *810*	
***LBW level* 1400**	*AEGL-3* -	*ERPG-3* *1210*	

[17] Hotchkiss, J.A., Anrus, A.K., Johnson, K.A., Krieger, S.M., Woolhiser, M.R., Maurissen, J.P. 2010. Acute toxicologic and neurotoxic effects of inhaled 1,2-dichloroethane in adult Fischer 344 rats. Food and Chemical Toxicology 48 (2010) 470-481.
[18] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 75-35-4

1,1-Dichlooretheen

$CH_2=CCl_2$

VN-nr: 1303

GEVI: 339

Synoniemen: vinylideenchloride, 1,1-dichloorethyleen, VDC (Engels: vinylidene chloride)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	110	78	62	49	39	28
Levensbedreigende waarden	LBW (mg/m³)	3800	2600	2100	1700	1300	660

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,248 ppm; 1 ppm = 4,031 mg/m³

Explosiegrens: 5,6% ≈ 230.000 mg/m³

Geur: karakteristieke chloroformachtig

LOA: 12022 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze, vluchtige vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,5

Molecuulmassa:	96,9 g/mol
Zuurgraad:	-
LogKow:	2,1
Wateroplosbaarheid:	0,25 g/100 ml (slecht)
Verzadigde dampdruk:	665 mbar

Overige informatie

Publieke grenswaarde: geen

MAK: 8,0 mg/m³

TLV-TWA: 20 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW**:* prikkeling van ogen en keel

AGW → LBW: keelpijn en hoesten, duizeligheid, misselijkheid, hoofpijn, sufheid, effecten op ongeboren vrucht

Boven LBW: bewustzijnsdaling, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof veroorzaakt irritatie van de slijmvliezen
- Na absorptie kunnen cardiovasculaire en CZS-effecten worden verwacht: soms met een korte excitatiefase, gevolgd door depressie.
- 1,1-dichlooretheen kan embryotoxiciteit veroorzaken.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn

Oogcontact: roodheid en pijn

Carcinogeniteit

IARC classificatie: 3

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken en spoelen en wassen met water en zeep.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 75-35-4 **Vinylidene chloride** **$CH_2=CCl_2$** **UN-nr: 1303**

Basis for the Dutch Intervention Values

VRW: Not recommended in accordance with the ERPG-document

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added

LBW: Based on additional information to that described in ERPG-document, different values are derived, other time points added.

Date:31-10-2017 ERPG 2006

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	110	78	62	49	39	28	Developmental toxicity in rabbits and rats
LBW	3800	2600	2100	1700	1300	660	Lethality data in rats

Derivation of the Dutch Intervention Values

VRW: VRW values are not recommended, because there are no exposure-response data in humans or animals consistent with VRW-level effects.

AGW: In an embryotoxicity and fetotoxicity study in rats and rabbits some signs of toxicity were observed due to inhalation exposure to vinylidene chloride. Both rats and rabbits were exposed to 20 (rats only), 80 or 160 ppm for 7 hr/day from GD6 to GD15. Concentrations correspond to 81, 322 and 645 mg/m^3. A significantly increased incidence of resorptions was observed in rabbits at 645 mg/m^3. In rabbit pups from dams exposed to 645 mg/m^3, there was an increased incidence of the 13th pairs of ribs. In rats inhalation exposure to vinylidene chloride resulted in marginal embryotoxicity or fetotoxicity (minor skeletal alterations: increased incidence of delayed ossification of skull bones and of wavy ribs) at 322 mg/m^3 and 645 mg/m^3. The effects in pups were seen in the presence of maternal toxicity (decrease in body weight gain, decrease in food consumption, increased water consumption and increased liver weight (in rats at 322 mg/m^3). The effects were more marked at 645 mg/m^3. Though it is uncertain whether these effects can be the result of a single exposure, In the absence of further data the increased incidence of resorptions observed in rabbits exposed to 645 mg/m^3, the exposure to 322 mg/m^3 for 7 hours was considered a suitable point of departure for derivation of the AGW values. This PoD is supported by the results of a subchronic inhalation study in rats, guinea pigs, rabbits and monkeys (8 hrs/day, 5 days/wk, 6 wks), where no overt signs of toxicity at the highest concentration tested of 100 ppm (403 mg/m^3) were observed. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$ with the default n=1 and n=3, to calculate to longer and shorter durations, respectively.

LBW: LWB values are based on an acute inhalation toxicity study in rats as reported for this substance in the publically available REACH registration dossier on ECHA's website. The original publication was not available and the data were not included in the ERPG document. The owner of the study report confirmed that the summary as provided on the REACH website is correct (see additional toxicological information for more study data). Rats (10/sex/concentration) were exposed, whole body, for 4 hour to analytical vapour concentrations of 1970, 4730, 9000 or 13850 ppm, reported to correspond to 7820, 18770, 35710, or 54960 mg/m^3. A 4-hour LC_{01} of 13100 mg/m^3 and a 4-hour LC_{50} of 34130 mg/m^3 were calculated using DoseResp. The LC_{01} value of 13100 mg/m^3 was used as point of departure to calculate the LBW values. The value is supported by mortality data observed in rats in a 4-hour inhalation study with only two concentration levels; 4900 ppm (19750 mg/m^3) killed 1/16 animals and 6150 ppm (24788 mg/m^3) killed 7/16 animals. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$ with the default n = 1 and n= 3, to calculate to longer and shorter durations, respectively. It is noted that lethality data for mice are much lower. This is the consequence of a different metabolism depending on glutathione. Glutathione levels in humans resemble those in rats, not those in mice.

Additional toxicological information (including relevant results of a general literature search, if any)

VDC is metabolized via mixed function oxidase enzymes to form an oxirane intermediate, 1,1-dichloroethylene oxide, and then reacts with glutathione or rearranges to form chloroacetyl chloride. Lethality data in several species show that mice are more sensitive to 1,1-dicholorethylene. The differences among species are attributed to the glutathione availability, with the mouse being extremely limited in rapid regeneration of glutathione. Man responds more like the rat in glutathione regeneration.

The substance is not toxic for fertility. In an embryotoxicity and fetotoxicity study of inhaled or ingested vinylidene chloride in rats and rabbits some toxicity to both dams and developing embryos was observed among rats inhaling 80 or 160 ppm (322 or 645 mg/m^3) and among rabbits inhaling 160 ppm (645 mg/m^3). In rabbits exposed to 645 mg/m^3 a significantly increased incidence of resorptions was observed. In rat dams exposed to 322 and 645 mg/m^3 increases in liver to body weight ratio were observed and pups exposed to 322 or 645 mg/m^3 exhibited delayed ossification of skull bones and wavy ribs. In rabbits, pups from dams exposed to 645 mg/m^3, there was an increased incidence of the 13th pair of ribs.

In the publically available REACH registration dossier on ECHAs website, an acute inhalation toxicity study was summarised that was not referenced by the ERPG committee. According to the summary of the registrant, the study was performed according to OECD TG 403. In this study Sprague-Dawley rats were exposed, whole body in a steel/glass inhalation room, for 4 hour to analytical vapour concentrations of 1970, 4730, 9000 and 13850 ppm, reported to correspond to 7820, 18770, 35710, and 54960 mg/m^3. Lethality was observed in the three highest exposure groups: males 0/2, 2/10, 6/10, 10/10 and females 0/10, 1/10, 0/10, 10/10. Animals were observed for a 14 day period after exposure. Clinical signs observed in surviving animals were narcosis and apathy and shock. Other findings included acute contraction of ventricle of the heart and pulmonary bleeding/local inflammation.

H332 (harmful if inhaled) and H351 (suspected of causing cancer).

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to carcinogenicity to humans)

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: sweet chloroform like

OT= The odour threshold lies between 190 ppm (766 mg/m^3) (Amoore, 1983) and 2000 mg/m^3 (496 ppm) (Ruth, 1986)

LOA = 11.8 * OT * 1.33 = 11.8 * 766 * 1.33= 12022 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value)

The odour threshold lies above all intervention values.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated) [19]

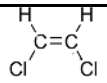
VRW level **NR**	*AEGL-1* -	*ERPG-1* ID (=insufficient data)		*IDLH: -*
AGW level **62**	*AEGL-2* -	*ERPG-2* 100[20]		
LBW level **2100**	*AEGL-3* -	*ERPG-3* 300[b]		

[19] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.
[20] ERPG states values in ppm and mg/m^3 that do not match. It is unclear which values should apply.

Stofdocument deel A

CAS-nr: 156-59-2 (*cis*)
$C_2H_2Cl_2$

cis-1,2-Dichloorethyleen[21]



VN-nr: 1150
GEVI: 33

Synoniemen: (cis-)1,2-dichlooretheen, (cis-)1,2-DCE (Engels: *cis*-1,2-dichloroethene)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	550	550	550	550	550	550
Alarmeringsgrenswaarden	AGW (mg/m³)	1.700	1.700	1.700	1.700	1.400	900
Levensbedreigende waarden	LBW (mg/m³)	3.900	3.900	3.900	3.900	3.100	1.600

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,248 ppm; 1 ppm = 4,031 mg/m³

Explosiegrens: 6,2-16 volume% ≈ 250.000-640.000 mg/m³

Geur: typerende geur

LOA: 1083 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,5

Molecuulmassa:	96,9 g/mol
Zuurgraad:	geen data
LogKow:	1,86
Wateroplosbaarheid:	0,35 g/100 ml (slecht)
Verzadigde dampdruk:	240 mbar

Overige informatie

Publieke grenswaarde: niet vastgesteld

MAK: 800 mg/m³ (afgeleid voor mengsel)

TLV-TWA: 800 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: hoesten
VRW → AGW: duizeligheid, sufheid, prikkeling van ogen en keel
AGW → LBW: hoofdpijn, sufheid, duizeligheid, tranende ogen, keelpijn, misselijkheid
Boven LBW: bewustzijnsdaling, narcose, cardiovasculaire collaps, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt irriterend op de ogen en luchtwegen.
- De stof kan inwerken op het CZS.
- De narcotische effecten kunnen al optreden bij concentraties die nog niet als irriterend voor de ogen en luchtwegen worden ervaren.
- Blootstelling kan verlaging van bewustzijn veroorzaken en schade aan de longen, lever en hartspier.
- In ernstige gevallen kans op bewusteloosheid en sterfte

Effecten bij blootstelling aan vloeistof

Huidcontact: droge huid, roodheid en pijn
Oogcontact: roodheid en pijn, slecht zien en hoornvliesbeschadiging.

Carcinogeniteit

IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust en onmiddellijk arts raadplegen.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), bij aanhoudende irritatieklachten (oog)arts brengen.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

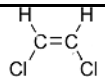
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

[21] Er zijn geen afzonderlijke interventiewaarden afgeleid voor mengsels van *cis*- en *trans*-1,2-dichloorethyleen (CAS nummer voor mengsels: 540-59-0), vanwege wisselende samenstellingen. De interventiewaarden voor *cis*-1,2-dichloorethyleen gelden daarom ook voor alle *cis-trans*-mengsels.

Stofdocument deel B

CAS-nr: 156-59-2
$C_2H_2Cl_2$

cis-1,2-dichloroethene[22]



UN-nr: 1150

Basis for the Dutch Intervention Values

VRW: AEGL values adopted, 2 hour value added.

AGW: Different PoD as for AEGL for 10 min-1 hour values, 4-8 hour values adopted, 2h value added.

LBW: Different point of departure as for AEGL values, 2hr value added.

Date: 16-10-2018	AEGL document: Final, 2010

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	550	550	550	550	550	550	Threshold for eye irritation in humans
AGW	1,700	1,700	1,700	1,700	1,400	900	Narcosis in rats
LBW	3,900	3,900	3,900	3,900	3,100	1,600	Threshold for lethality in rats

Derivation of the Dutch Intervention Values

1,2-dichloroethene can exist both as a *cis*- and a *trans*-isomer as well as in different mixtures. For the mixtures no data were reported in the AEGL document. The *trans*-isomer data package is more extensive than the *cis*-isomer data package. The reported studies indicate that the *cis*-isomer is more acutely toxic than the *trans*-isomer.

VRW: Though the *cis*-isomer of 1,2-dichloroethene is more potent, the toxicity profiles of both isomers is similar. The data package for the *trans*-isomer is more extensive. Therefore, the VRW values for *trans*-1,2-dichloroethene will be used to derive VRW values for *cis*-1,2-dichlorethene. The acute lethality data and data on narcosis suggests use of a modifying factor of 2 to cover for the difference in toxic potency.

Derivation of VRW-values for trans-1,2-dichloroethene

The VRW for *trans*-1,2-dichloroethene is based on data from a human volunteer study (n=2). Subjects were exposed to *trans*-1,2-dichloroethene for 5 minutes to 275, 950, 1,700 and 2,200 ppm (corresponding with 1,108, 3,829, 6,852 and 8,867 mg/m^3, respectively), 10 minutes to 825 and 1,200 ppm (corresponding with 3,325 and 4,836 mg/m^3, respectively) and 30 minutes to 1000 ppm (corresponding with 4,031 mg/m^3). In this study *trans*-1,2-dichloroethene at a concentration of 1108 mg/m^3 for 5 minutes showed no effects. A concentration of 3,325 mg/m^3 caused slight dizziness after 5 minutes during a 10 minute exposure and slight eye irritation was observed at a concentration of 3,829 mg/m^3 for 5 minutes. Dizziness and slight burning of the eyes was reported after 10 minutes in a 30 minute exposure regimen to 1,000 ppm (corresponding with 4,031 mg/m^3). The NOAEC for eye irritation of 3,325 mg/m^3 was used as point of departure. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was not applied as eye irritation is considered to be concentration-dependent rather than concentration × time-dependent. The results are supported by data from a rat developmental study, where *trans*-1,2-dichloroethene exposed pregnant rats showed clear ocular discharge (13/24) and periocular wetness (3/24) at 2,000 ppm (8,061 mg/m^3). At 6,000 ppm (24,184 mg/m^3) increased incidences of both effects were observed and at 1,200 ppm (48,368 mg/m^3) all animals showed both effects, but not more severe eye effects were reported.

AGW: Though the *cis*-isomer of 1,2-dichloroethene is more potent, the toxicity profiles of both isomers is similar. The data package for the *trans*-isomer is more extensive. Therefore, the AGW values for *trans*-1,2-dichloroethene will be used to derive AGW values for *cis*-1,2-dichlorethene. The acute lethality data suggests use of a modifying factor of 2 to cover for the difference in toxic potency.

Derivation of AGW-values for trans-1,2-dichloroethene

[22] No separate intervention values have been derived for mixtures of *cis*- and *trans*-1,2-dichloorethylene (CAS: 540-59-0), because of differing compositions. Intervention values for *cis*-1,2-dichloorethyleen apply to all *cis*-*trans*-mixtures.

The AGWs for 2, 4 and 8 hours are based on a developmental toxicity study. Pregnant rats were exposed to *trans*-1,2-dichloroethene at concentrations of 2,000, 6,000 and 12,000 ppm, equivalent with 8,061, 24,184 and 48,368 mg/m^3, for 6 hours during GD7-16. Rats exposed to 48,368 mg/m^3 showed narcotic effects. The level of 24,184 mg/m^3 was used as point of departure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was performed using the equation $C^n \times t = k$, using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively, except for the 10, 30 and 60 min exposure durations. Extrapolation using n=3 to these values would lead to exposure time and duration at which healthy adult humans responded with symptoms reaching a level of severe dizziness. Dizziness was seen in humans after exposure at 1,000 ppm (4,031 mg/m^3) for 10 minutes, during an exposure lasting for 30 minutes. Not to come into conflict with human data, the 10- and 30-minute and 1 hour values were set equal to the 2 hour value of 3,500 mg/m^3.

LBW: Though the *cis*-isomer of 1,2-dichloroethene is more potent, the toxicity profiles of both isomers is similar. Though lethality data for the *cis*-isomer are available, the data were insufficient to derive reliable LC_{01} values. Comparison of the calculated LC_{50} values from the *cis*- and *trans*-isomer does indicate that the *cis*-isomer is twice as potent as the *trans*-isomer. Therefore, the LBW values for *trans*-1,2-dichloroethene will be used to derive LBW values for *cis*-1,2-dichlorethene, using a modifying factor of 2 to cover for the difference in toxic potency.

Derivation of LBW-values for trans-1,2-dichloroethene
The LBWs were primarily based on a 4 hour rat lethality study. Rats (5/sex/conc) were exposed to 12,300, 22,500, 28,100, and 34,100 ppm *trans*-1,2-dichloroethene, equivalent with 49,577, 90,690, 113,262 and 137,446 mg/m^3, leading to lethality of 0/10, 4/10, 7/10 and 10/10 animals, respectively. Older lethality studies with mice (3/concentration) reported a.o.100% death after 21-32 minutes exposure to 105,000 mg/m^3, 100% death between 66-92 minutes of exposure to 80,000 mg/m^3, and 100% death 121-142 minutes exposure to 75,000 mg/m^3
The 4 hour LC_{01} of 62,220 mg/m^3 calculated with DoseResp, was used as point of departure for deriving LBW values. The default total uncertainty factor of 10 (3×3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was performed using the equation $C^n \times t = k$, using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. Using n=3 to calculate the 10 and 30 min and 1 hour exposures would lead to LBWs of 18,000, 12,000, and 9,900 mg/m^3. Not to come into conflict with the lethality data in mice (all animals dying within 75-114 minutes exposure 16 250 ppm (65 000 mg/m^3) *cis*-1,2-dichloroethene and after 121-142 minutes exposure to 18 750 ppm (75 000 mg/m^3) *trans*-1,2-dichlooroethene), the 10 and 30 min and 1 hour LBWs are set equal to the 2 hour value of 7,800 mg/m^3.

Additional toxicological information (including relevant results of a general literature search, if any)

1,2-Dichloroethene is a flammable, colourless liquid existing in both *cis* and *trans*-isomers and as a mixture of these two isomers. The *trans*-isomer is commercially isolated by distillation and sold as a highly purified product that is used in precision cleaning of electronic equipment.

Nonlethal toxicity and lethality data indicate that 1,2-dichloroethene has a narcotic effect and that the *cis*-isomer is about two times more potent than the *trans*-isomer with respect to narcosis. In general animal exposure to the *trans*-isomer took 2 – 3 times longer to lose equilibrium than when exposed to the same concentration of the *cis*-isomer. Furthermore, a minimum alveolar concentration of 0.0183 % of the *trans*-isomer was needed for induction of anaesthesia, whereas a concentration of 0.0071% was needed with the *cis*-isomer. Narcotic observations indicated a progression from equilibrium effects, followed by lethargy, light narcosis (loss of limb reflex, maintenance of corneal reflex), finally deep narcosis (loss of corneal reflex), and in some cases death. Dose-related ocular irritation was observed in rats. Lethality data (comparison of 4 hour LC_{50} values) also indicate that the *cis*-isomer (LC_{50} 13 700 ppm) is twice as potent as the *trans*-isomer (LC_{50} 24 100 ppm.
No data on developmental and reprotoxic effects in humans were located for *cis*-1,2-dichloroethene. A reproductive study in rats with *trans*-1,2-dichloroethene shows a decrease in foetal body weight in the offspring.

H332: Harmful if inhaled

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not evaluated	Odour: characteristic odour (AEGL: ethereal,

No carcinogenic risk potency (CRP) was derived	slightly acrid) OT: 69 mg/m^3 [AEGL, 2010; O'Neil et al, 2001] LOA = 11.8 * 69 * 1.33 = 1083 mg/m^3 (The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value) The LOA is comparable with the VRW values.

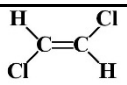
***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*[23]				
VRW level **550**	*AEGL-1* 554	*ERPG-1* -		*IDLH:* 1,000 ppm (4,031 mg/m^3) (30 minutes) *(for mixtures of 1,2-dichloroethenes)*
AGW level **1,700**	*AEGL-2* 1,980	*ERPG-2* -		
LBW level **3,900**	*AEGL-3* 3,366	*ERPG-3* -		

[23] Note that the AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL.

Stofdocument deel A

CAS-nr: 156-60-5 (*trans*)
$C_2H_2Cl_2$

trans-1,2-Dichloorethyleen[24]



VN-nr: 1150
GEVI: 33

Synoniemen: (E)-dichlooretheen, (trans)-1,2-dichloorethyleen, trans-dioform, acetyleendichloride (Engels: *trans*-1,2-dichloroethene)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	1.100	1.100	1.100	1.100	1.100	1.100
Alarmeringsgrenswaarden	AGW (mg/m³)	3.500	3.500	3.500	3.500	2.800	1.800
Levensbedreigende waarden	LBW (mg/m³)	7.800	7.800	7.800	7.800	6.200	3.100

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,248 ppm; 1 ppm = 4,031 mg/m³

Explosiegrens: 6,1-12,8 volume% ≈ 250.000-520.000 mg/m³

Geur: typerende geur

LOA: 1083 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,8

Molecuulmassa:96,9 g/mol

Zuurgraad: geen data
LogKow: 2,1 (berekend)
Wateroplosbaarheid: 0,63 g/100 ml(slecht)
Verzadigde dampdruk: 353 mbar

Overige informatie

Publieke grenswaarde: niet vastgesteld
MAK: 800 mg/m³ (afgeleid voor mengsel)
TLV-TWA: 800 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: hoesten
VRW → AGW: duizeligheid, sufheid, prikkeling van ogen en keel
AGW → LBW: hoofdpijn, sufheid, duizeligheid, tranende ogen, keelpijn, misselijkheid
Boven LBW: bewustzijnsdaling, narcose, cardiovasculaire collaps, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt irriterend op de ogen en luchtwegen.
- De stof kan inwerken op het CZS.
- De narcotische effecten kunnen al optreden bij concentraties die nog niet als irriterend voor de ogen en luchtwegen worden ervaren.
- Blootstelling kan verlaging van bewustzijn veroorzaken en schade aan de longen, lever en hartspier.
- In ernstige gevallen kans op bewusteloosheid en sterfte.

Effecten bij blootstelling aan vloeistof

Huidcontact: droge huid, roodheid en pijn

Oogcontact: roodheid en pijn, slecht zien en hoornvliesbeschadiging.

Carcinogeniteit

IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust en onmiddellijk arts raadplegen.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), bij aanhoudende irritatieklachten (oog)arts brengen.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen*.

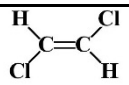
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen.

[24] Voor *cis*-1,2-dichloorethyleen (CAS: 156-59-2), welke als meer potent wordt beschouwd, zijn lagere Interventiewaarden afgeleid, die ook gelden voor de verschillende *cis-trans* mengsels (CAS: 156-59-0). Zie hiervoor het stofdocument voor *cis*-1,2-dichloorethyleen.

Stofdocument deel B

CAS-nr: 156-60-5
$C_2H_2Cl_2$

trans-1,2-dichloroethene[25]



UN-nr: 1150

Basis for the Dutch Intervention Values

VRW: AEGL values adopted, 2h value added.

AGW: Different PoD as for AEGL for 10 min-1 hour values, 4-8 hour values adopted, 2h value added.

LBW: Different point of departure as for AEGL values, 2h value added.

Date: 16-10-2018 | AEGL document: Final, 2010

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	1,100	1,100	1,100	1,100	1,100	1,100	Threshold for eye irritation in humans
AGW	3,500	3,500	3,500	3,500	2,800	1,800	Narcosis in rats
LBW	7,800	7,800	7,800	7,800	6,200	3,100	Threshold for lethality in rats

Derivation of the Dutch Intervention Values

1,2-dichloroethene can exist both as a *cis*- and a *trans*-isomer as well as in different mixtures. For the mixtures no data were reported in the AEGL document. The *trans*-isomer data package is more extensive than the *cis*-isomer data package. The reported studies indicate that the *cis*-isomer is more acutely toxic than the *trans*-isomer.

VRW: The VRW is based on data from a human volunteer study (n=2). Subjects were exposed to *trans*-1,2-dichloroethene for 5 minutes to 275, 950, 1,700 and 2,200 ppm (corresponding with 1,108, 3,829, 6,852 and 8,867 mg/m³, respectively), 10 minutes to 825 and 1,200 ppm (corresponding with 3,325 and 4,836 mg/m³, respectively) and 30 minutes to 1000 ppm (corresponding with 4,031 mg/m³). In this study *trans*-1,2-dichloroethene at a concentration of 1108 mg/m³ for 5 minutes showed no effects. A concentration of 3,325 mg/m³ caused slight dizziness after 5 minutes during a 10 minute exposure and slight eye irritation was observed at a concentration of 3,829 mg/m³ for 5 minutes. Dizziness and slight burning of the eyes was reported after 10 minutes in a 30 minute exposure regimen to 1,000 ppm (corresponding with 4,031 mg/m³). The NOAEC for eye irritation of 3325 mg/m³ was used as point of departure. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was not applied as eye irritation is considered to be concentration-dependent rather than concentration × time-dependent. The results are supported by data from a rat developmental study, where *trans*-1,2-dichloroethene exposed pregnant rats showed clear ocular discharge (13/24) and periocular wetness (3/24) at 2,000 ppm (8,061 mg/m³). At 6,000 ppm (24,184 mg/m³) increased incidences of both effects were observed and at 12,000 ppm (48,368 mg/m³) all animals showed both effects, but not more severe eye effects were reported.

AGW: The AGWs for 2, 4 and 8 hours are based on a developmental toxicity study. Pregnant rats were exposed to *trans*-1,2-dichloroethene at concentrations of 2,000, 6,000 and 12,000 ppm, equivalent with 8,061, 24,184 and 48,368 mg/m³, for 6 hours during GD7-16. Rats exposed to 48,368 mg/m³ showed narcotic effects. The level of 24,184 mg/m³ was used as point of departure. The default total uncertainty factor of 10 (3×3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was performed using the equation $C^n \times t = k$, using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively, except for the 10, 30 and 60 min exposure durations. Extrapolation using n=3 to these values would lead to exposure time and duration at which healthy adult humans responded with symptoms reaching a level of severe dizziness. Dizziness was seen in humans after exposure at 1,000 ppm (4,031 mg/m³) for 10 minutes, during an exposure lasting for 30 minutes. Not to come into conflict with human data, the 10- and 30-minute and 1 hour values were set equal to the 2 hour value of 3,500 mg/m³.

[25] For *cis*-1,2-dichloroethene (CAS: 156-59-2), which is considered to be more potent than the *trans*-isomer, lower intervention values have been derived. These values also apply to the different *cis-trans* mixtures (CAS: 156-59-0). See support document for *cis*-1,2-dichloroethylene.

LBW: The LBWs were primarily based on a 4 hour rat lethality study. Rats (5/sex/conc) were exposed to 12,300, 22,500, 28,100, and 34,100 ppm *trans*-1,2-dichloroethene, equivalent with 49,577, 90,690, 113,262 and 137,446 mg/m^3, leading to lethality of 0/10, 4/10, 7/10 and 10/10 animals, respectively. Older lethality studies with mice (3/concentration) reported a.o.100% death after 21-32 minutes exposure to 105,000 mg/m^3, 100% death between 66-92 minutes of exposure to 80,000 mg/m^3, and 100% death 121-142 minutes exposure to 75,000 mg/m^3.
The 4 hour LC_{01} of 62,220 mg/m^3 calculated with DoseResp, was used as point of departure for deriving LBW values. The default total uncertainty factor of 10 (3×3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was performed using the equation $C^n \times t = k$, using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. Using n=3 to calculate the 10 and 30 min and 1 hour exposures would lead to LBWs of 18,000, 12,000, and 9,900 mg/m^3. Not to come into conflict with the lethality data in mice (all animals dying within 75-114 minutes exposure 16 250 ppm (65 000 mg/m^3) *cis*-1,2-dichloroethene and after 121-142 minutes exposure to 18 750 ppm (75 000 mg/m^3) *trans*-1,2-dichlooroethene), the 10 and 30 min and 1 hour LBWs are set equal to the 2 hour value of 7,800 mg/m^3.

Additional toxicological information (including relevant results of a general literature search, if any)

1,2-Dichloroethene is a flammable, colourless liquid existing in both *cis*- and *trans*-isomers and as a mixture of these two isomers. The *trans*-isomer is commercially isolated by distillation and sold as a highly purified product that is used in precision cleaning of electronic equipment.

Nonlethal toxicity and lethality data indicate that 1,2-dichloroethene has a narcotic effect and that the *cis*-isomer is more potent than the *trans*-isomer with respect to narcosis. In general animal exposure to the *trans*-isomer took 2 – 3 times longer to lose equilibrium than when exposed to the same concentration of the *cis*- isomer. Furthermore, a minimum alveolar concentration of 0.0183 % of the *trans*- isomer was needed for induction of anaesthesia, whereas a concentration of 0.0071% was needed with the *cis*-isomer. Narcotic observations indicated a progression from equilibrium effects, followed by lethargy, light narcosis (loss of limb reflex, maintenance of corneal reflex), finally deep narcosis (loss of corneal reflex), and in some cases death. Dose-related ocular irritation was observed in rats. Lethality data (comparison of 4 hour LC_{50} values) also indicate that the *cis*-isomer (LC_{50} 13 700 ppm) is twice as potent as the *trans*-isomer (LC_{50} 24 100 ppm.

No data on developmental and reprotoxic effects in humans were located. A reproductive study in rats with the *trans*-isomer shows a decrease in fetal body weight in the offspring.

H332: Harmful if inhaled

Carcinogenicity and derivation of the CRP value

IARC classification: not evaluated

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: characteristic odour (AEGL: ethereal, slightly acrid)

OT: 69 mg/m^3 [AEGL, 2010; O'Neil et al, 2001]
LOA = 11.8 * 69 * 1.33 = 1083 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is comparable with the VRW values.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)[26]

VRW level **1,100**	*AEGL-1* 1,109	*ERPG-1* -		*IDLH:* 1,000 ppm (4,031 mg/m^3) (30 minutes) *(for mixtures of 1,2-dichloroethenes)*
AGW level **3,500**	*AEGL-2* 3,960	*ERPG-2* -		
LBW level **7,800**	*AEGL-3* 6,732	*ERPG-3* -		

[26] Note that the AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL.

Stofdocument deel A

CAS-nr: 75-54-7

Dichloormethylsilaan CH_4Cl_2Si

VN-nr: 1242
GEVI: X338

Synoniemen: methyldichloorsilaan,methylsiliciumdichloride, methylsilyldichloride (Engels: methyl dichlorosilane)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	4,3	4,3	4,3	4,3	4,3	4,3
Alarmeringsgrenswaarden	AGW (mg/m³)	270	130	80	50	31	31
Levensbedreigende waarden	LBW (mg/m³)	810	380	240	150	94	94

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,209 ppm; 1 ppm = 4,784 mg/m³

Explosiegrens: 2,4 vol% ≈ 115000 mg/m³

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze, rokende vloeistof
Brand: Zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,4

Molecuulmassa:	115,0 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	Reactie
Verzadigde dampdruk:	463 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW	geen informatie
VRW → AGW:	irritatie van ogen en luchtwegen, tranenvloed, hoesten, lichte benauwdheid
AGW → LBW:	ernstige irritatie van ogen en luchtwegen, pijn op de borst, benauwdheid, longontsteking, longoedeem
Boven LBW:	ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Chloorsilanen reageren zeer snel met water onder vorming van chloorwaterstof (HCl). De acute toxiciteit van dimethyldichloorsilaan wordt veroorzaakt door chloorwaterstof.
- Inhalatie van chloorwaterstof veroorzaakt een type I inhalatie intoxicatie.
- Chloorwaterstof veroorzaakt irritatie van de slijmvliezen van ogen en luchtwegen.
- Chloorwaterstof kan bij inhalatie longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, brandwonden

Oogcontact: bijtend, roodheid en pijn, slecht zien, hoornvliesbeschadiging, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen:	frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten
ogen:	minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid:	kleding uittrekken (NIET lostrekken), direct spoelen met veel water (minimaal 20 min.), dan pas eventueel aan de huid vastgeplakte kleding verwijderen en verder spoelen, en direct spoedeisende medische hulp inzetten.
ogen:	minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken:	mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken, direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 75-54-7 **Methyl dichlorosilane** **CH_4Cl_2Si** **UN-nr: 1242**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same rationale as AEGL (analogy with HCl), 2h value added

LBW: Same rationale as AEGL (analogy with HCl), 2h value added

Date: 06-10-2016 | AEGL document: Final, 2012

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	4.3	4.3	4.3	4.3	4.3	4.3	Based on HCl (Threshold of irritation in humans)
AGW	270	130	80	50	31	31	Based on HCl (one-third of LBW)
LBW	810	380	240	150	94	94	Based on HCl (Threshold of lethality in animals)

Derivation of the Dutch Intervention Values

VRW: Since no appropriate data exist for methyl dichlorosilane, VRW values for hydrogen chloride will be used (on ppm-basis) to derive VRW values for methyl dichlorosilane. The use of hydrogen chloride as a surrogate for methyl dichlorosilane was deemed appropriate since it is believed that the hydrolysis product, HCl, is responsible for the adverse effects. Because two moles of hydrogen chloride are produced for every mole of methyl dichlorosilane, a molar adjustment factor of 2 was applied to the hydrogen chloride VRW values.

Derivation of VRW values for HCl

The hydrogen chloride VRW values were based on a no-adverse-effect-level of 1.8 ppm (2.73 mg/m³) in exercising asthmatics with an exposure duration of 45 min. Because the test subjects were considered a sensitive subpopulation and the endpoint was essentially a no-effect level, no uncertainty factor was applied to account for sensitive human subpopulations. The VRW values were held constant for all specified exposure periods since mild irritant effects represent threshold effects and generally do not vary over time.

AGW: Since no appropriate data exist for methyl dichlorosilane, AGW values for hydrogen chloride will be used (on ppm-basis) to derive AGW values for methyl dichlorosilane. Because two moles of hydrogen chloride are produced for every mole of methyl dichlorosilane, a molar adjustment factor of 2 was applied to the hydrogen chloride AGW values.

Derivation of AGW values for HCl

The AGW values of HCl for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data. The only study of HCl that addressed effects that meet the definition of an AGW, severe nasal lesions, was a study on hydrogen halides by Stavert et al. (1991). Nevertheless, this study was not considered a suitable basis for derivation of AGW values because 6% of the animals died after exposure to HCl at 1300 ppm (1974 mg/m³), only one concentration was tested and the number of animals tested was inconsistent.

LBW: Since no appropriate data exist for methyl dichlorosilane, LBW values for hydrogen chloride will be used (on ppm-basis) to derive LBW values for methyl dichlorsilane. Because two moles of hydrogen chloride are produced for every mole of methyl dichlorosilane, a molar adjustment factor of 2 was applied to the hydrogen chloride LBW values.

Derivation of LBW values for HCl

The LBW values were based on a lethality study in rats. The rat study included six exposure durations and various concentrations. Probit analyses using DoseResp was performed and yielded LC_{01} values for the 10 min, 30 min, 1-, 2-,4-, and 8hrs exposure durations of 3370, 1602, 1002, 627, 393 and 246 ppm (5116, 2433, 1522, 952, 596, and 373 mg/m³), respectively, which were used as

point of departure for LBW derivation. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The probit analyses yielded an n-value of 1.48, which was supported by the n-value of 1.59 calculated by Arts *et al.* (2000) from the C*t study. To maintain consistency with other hydrogen halogenides, the 8 hour value was set equal to the 4 hour value, as performed for the most potent hydrogen halogenide HF.

Additional toxicological information (including relevant results of a general literature search, if any)

No data concerning lethality and nonlethal toxicity in humans from dimethyldichlorosilane exposure were located in the available literature.

Chlorosilanes react violently with water to produce hydrogen chloride gas. Data suggest that the acute toxicity of chlorosilanes is due to the hydrogen chloride hydrolysis product; acute toxicity of the chlorosilanes is both qualitatively (based on clinical signs) and quantitatively (based on molar equivalents of hydrogen chloride) similar to that of HCl.

Although toxicity data are limited for individual chlorosilanes, well-conducted 1-hr inhalation toxicity studies in rats are available for a series of chlorosilanes. In general, LC_{50} values for monochlorosilanes were approximately twice the LC_{50} values for dichlorosilanes and three times the LC_{50} values for trichlorosilanes. Clinical signs were consistent with hydrogen chloride exposure and included lacrimation, salivation, dried material around or on the eyes and/or nose, green staining around the nose and mouth, and perineal urine staining. Labored breathing, rales, hypoactivity, closed or partially closed eyes, prostration, corneal opacity or opaqueness, and swollen and/or necrotic paws were also observed. Hemorrhage, congestion and/or consolidation of the lungs, ectasia of the lungs, gaseous distension of the gastrointestinal tract, absence of body fat, obstruction of nostrils, dried and/or firm nares, alopecia around the eyes and discoloration of hair were observed at necropsy

No data concerning developmental/reproductive toxicity for exposure to dimethyldichlorosilane were located in the available literature.

No harmonized H-statements for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

Derivation of the carcinogenic risk potency (CRP): No carcinogenic risk potency (CRP) was derived.

No data concerning the carcinogenicity of methyldichlorosilane in humans or experimental animals were identified in the available literature.

Odour and derivation of the LOA value

Odour: sharp odour

No LOA was derived due to lack of reliable data.

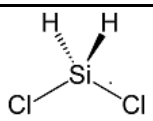
***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **4.3**	*AEGL-1* 4.3	*ERPG-1* -		*IDLH: not derived*
AGW level **80**	*AEGL-2* 52	*ERPG-2* -		
LBW level **240**	*AEGL-3* 240	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 4109-96-0
Cl_2H_2Si

Dichloorsilaan



VN-nr: 2189
GEVI: 263

Synoniemen: DCS (Engels: dichlorosilane)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	3,8	3,8	3,8	3,8	3,8	3,8
Alarmeringsgrenswaarden	AGW (mg/m³)	240	110	70	45	28	28
Levensbedreigende waarden	LBW (mg/m³)	710	340	210	130	83	83

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,238 ppm; 1 ppm = 4,202 mg/m³

Explosiegrens: LEL = 4,1 vol% ≈ 172.282 mg/m³

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 3,48

Molecuulmassa: 101,01 g/mol
Zuurgraad: Geen data
LogKow: Geen data
Wateroplosbaarheid: reactie
Verzadigde dampdruk: 1636 mbar

Overige informatie

Publieke grenswaarde:
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW geen informatie

VRW → AGW: irritatie van ogen en luchtwegen, tranenvloed, hoesten, lichte benauwdheid

AGW → LBW: ernstige irritatie van ogen en luchtwegen, pijn op de borst, benauwdheid, longontsteking, longoedeem

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Chloorsilanen reageren zeer snel met water onder vorming van chloorwaterstof (HCl). De acute toxiciteit van dichloorsilaan wordt veroorzaakt door chloorwaterstof.
- Inhalatie van chloorwaterstof veroorzaakt een type I inhalatie intoxicatie.
- Chloorwaterstof veroorzaakt irritatie van de slijmvliezen van ogen en luchtwegen.
- Chloorwaterstof kan bij inhalatie longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, brandwonden

Oogcontact: bijtend, roodheid en pijn, slecht zien, hoornvliesbeschadiging, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: kleding uittrekken (NIET lostrekken), direct spoelen met veel water (minimaal 20 min.), dan pas eventueel aan de huid vastgeplakte kleding verwijderen en verder spoelen, en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken, direct spoedeisende medische hulp inzetten.

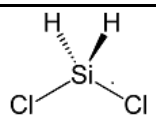
***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 4109-96-0
Cl_2H_2Si

Dichlorosilane



UN-nr: 2189

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same rationale as AEGL (analogy with HCl), 2h value added

LBW: Same rationale as AEGL (analogy with HCl), 2h value added

Date: 16-10-2018 | AEGL document: Final, 2012

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	3.8	3.8	3.8	3.8	3.8	3.8	Based on HCl (Threshold for irritation in humans)
AGW	240	110	70	45	28	28	Based on HCl (one-third of LBW)
LBW	710	340	210	130	83	83	Based on HCl (Threshold for lethality in animals)

Derivation of the Dutch Intervention Values

VRW: Since no appropriate data exist for dichlorosilane, VRW values for hydrogen chloride will be used (on ppm-basis) to derive VRW values for dichlorosilane. The use of hydrogen chloride as a surrogate for dichlorosilane was deemed appropriate since it is believed that the hydrolysis product, HCl, is responsible for the adverse effects. Because two moles of hydrogen chloride are produced for every mole of methyl dichlorosilane, a molar adjustment factor of 2 was applied to the hydrogen chloride VRW values.

Derivation of VRW values for HCl

The hydrogen chloride VRW values were based on a no-adverse-effect-level of 1.8 ppm (2.73 mg/m^3 for HCl, corresponding to 3.8 mg/m^3 for dichlorosilane) in exercising asthmatics with an exposure duration of 45 min. Because the test subjects were considered a sensitive subpopulation and the endpoint was essentially a no-effect level, no uncertainty factor was applied to account for sensitive human subpopulations. The VRW values were held constant for all specified exposure periods since mild irritant effects represent threshold effects and generally do not vary over time.

AGW: Since no appropriate data exist for dichlorosilane, AGW values for hydrogen chloride will be used (on ppm-basis) to derive AGW values for dichlorosilane. The AGW values were derived by dividing the LBW values by a factor of 3.

LBW: Since no appropriate data exist for dichlorosilane, LBW values for hydrogen chloride will be used (on ppm-basis) to derive LBW values for dichlorosilane. Because two moles of hydrogen chloride are produced for every mole of dichlorosilane, a molar adjustment factor of 2 was applied to the hydrogen chloride LBW values.

Derivation of LBW values for HCl

The LBW values were based on a lethality study in rats. The rat study included six exposure durations and various concentrations. Probit analyses using DoseResp was performed and yielded LC_{01} values for the 10 min, 30 min, 1-, 2-, 4-, and 8hrs exposure durations of 3370, 1602, 1002, 627, 393 and 246 ppm (5116, 2433, 1522, 952, 596, and 373 mg/m^3 for HCl, corresponding to 7080, 3366, 2105, 1317, 826 and 517 mg/m^3 for dichlorosilane), respectively, which were used as point of departure for LBW derivation. The default total uncertainty factor of 10 (3×3) was considered sufficient to account for inter- and intraspecies differences. The probit analyses yielded an n-value of 1.48, which was supported by the n-value of 1.59 calculated by Arts *et al.* (2000) from the C*t study. To maintain consistency with other hydrogen halogenides, the 8 hour value was set equal to the 4 hour value.

Additional toxicological information (including relevant results of a general literature search, if any)

No data concerning lethality and nonlethal toxicity in humans from dichlorosilane exposure were located in the available literature.

Chlorosilanes react violently with water to produce hydrogen chloride gas. Data suggest that the acute toxicity of chlorosilanes is due to the hydrogen chloride hydrolysis product; acute toxicity of the chlorosilanes is both qualitatively (based on clinical signs) and quantitatively (based on molar equivalents of hydrogen chloride) similar to that of HCl.

Although toxicity data are limited for individual chlorosilanes, well-conducted 1-hr inhalation toxicity studies in rats are available for a series of chlorosilanes. In general, LC_{50} values for monochlorosilanes were approximately twice the LC_{50} values for dichlorosilanes and three times the LC_{50} values for trichlorosilanes. Clinical signs were consistent with hydrogen chloride exposure and included lacrimation, salivation, dried material around or on the eyes and/or nose, green staining around the nose and mouth, and perineal urine staining. Labored breathing, rales, hypoactivity, closed or partially closed eyes, prostration, corneal opacity or opaqueness, and swollen and/or necrotic paws were also observed. Hemorrhage, congestion and/or consolidation of the lungs, ectasia of the lungs, gaseous distension of the gastrointestinal tract, absence of body fat, obstruction of nostrils, dried and/or firm nares, alopecia around the eyes and discoloration of hair were observed at necropsy

No data concerning developmental/reproductive toxicity for exposure to dichlorosilane were located in the available literature.

No harmonised H-statements for human health.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not evaluated Derivation of the carcinogenic risk potency (CRP): No carcinogenic risk potency (CRP) was derived. No data concerning the carcinogenicity of dichlorosilane in humans or experimental animals were identified in the available literature.	Odour: sharp odour No LOA was derived due to lack of reliable data.

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)*** [27]

VRW level **3.8**	*AEGL-1* 3.8	*ERPG-1* -		*IDLH: not derived*
AGW level **70**	*AEGL-2* 46	*ERPG-2* -		
LBW level **210**	*AEGL-3* 210	*ERPG-3* -		

[27] Note that the AEGL values as presented here (in mg/m³) are derived using the conversion factors of the AEGL.

Stofdocument deel A

CAS-nr: 460-19-5 **Dicyaan** **NC-CN** **VN-nr: 1026**

GEVI: 263

Synoniemen: cyanogeen, oxalonitril, ethaandinitril (Engels: cyanogen) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	5,4	5,4	4,3	3,4	2,7	2,2
Alarmeringsgrenswaarden	AGW (mg/m³)	110	36	18	9,0	9,0	9,0
Levensbedreigende waarden	LBW (mg/m³)	320	110	54	27	27	27

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,462 ppm; 1 ppm = 2,16 mg/m³

Explosiegrens:
LEL: 6,6% ≈ 143.000 mg/m³

Geur: Stekende, amandelachtige geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,8

Molecuulmassa: 52,03 g/mol

Zuurgraad: Geen data

LogKow: 0,07

Wateroplosbaarheid: 0,97 g/100 ml

Verzadigde dampdruk: 5.730 mbar

Overige informatie

Publieke grenswaarde:
Voor cyaniden geldt:
1 mg/m³ (TGG 8 uur),
10 mg/m³ (TGG 15 min)
MAK: 11 mg/m³, H notatie
TLV-TWA: 21.6 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte irritatie van ogen en neus

VRW → AGW: matige irritatie van ogen en neus, hoofdpijn

AGW → LBW: hoesten, ernstige irritatie, misselijkheid, braken, duizeligheid, spierzwakte, verwardheid

Boven LBW: convulsies, ademnood, coma, ademstilstand, hartstilstand, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof reageert met zuren tot de vorming van cyaanwaterstof.
- Cyanide blokkeert de ademhalingsketen in de cel. Hierdoor wordt de energiehuishouding verstoord en kan uiteindelijk lactaatacidose ontstaan.
- Primaire systemische doelorganen zijn het centrale zenuwstelsel en het cardiovasculaire systeem.
- De stof werkt irriterend op de ogen, en de luchtwegen.
- Snelle verdamping kan bevriezingsverschijnselen veroorzaken.

Effecten bij blootstelling aan vloeistof

Huidcontact: *vloeistof*: bevriezingsletsel

Oogcontact: *gas*: roodheid en pijn, *vloeistof*: bevriezingsletsel

Carcinogeniteit

IARC classificatie: Niet geclassificeerd

CRP: Niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust, halfzittende houding, GEEN mond-op-mondbeademing, 100% zuurstof, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, specifieke behandeling, *in geval van bevriezingswonden*: aan de huid vastgevroren kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen, en direct spoedeisende medische hulp inzetten.

ogen: *in geval van bevriezingswonden*: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas)

Specifieke behandeling en materialen: Bij vergiftiging is specifieke eerste hulp noodzakelijk; specifieke antidota (zoals 100% zuurstof, natriumthiosulfaat en hydroxocobalamine) moeten met gebruiksaanwijzing ter plekke beschikbaar zijn.

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor verdere informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 460-19-5 **Cyanogen** **NC-CN** **UN-nr: 1026**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same rationale for AEGL (one-third of LBW), 2h value added

LBW: AEGL value is adopted, 2h value added using different rationale (time-scaling based on 1-hour LBW value)

Date: November 2015 | AEGL document: Final, 2014

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	5.4	5.4	4.3	3.4	2.7	2.2	VRW values for hydrogen cyanide were adopted; mild headache in humans.
AGW	110	36	18	9.0	9.0	9.0	One-third of the LBW values
LBW	320	110	54	27	27	27	Lethality threshold in rats.

Derivation of the Dutch Intervention Values

VRW: Because no human exposure data for cyanogen for durations longer than 8 min were available and because the cyanide metabolite has the potential to cause the systemic effects reported for cyanogen, the VRW values for hydrogen cyanide were adopted as VRW values for cyanogen.
The VRW levels for hydrogen cyanide were based on data from monitoring studies in workers. Although the exposures were of chronic duration, they represent the best available human data. Exposure in a cyanide-salt production facility (exposure duration 1-40 years) to a geometric mean concentration of 0.03-0.96 ppm (0.034- 1.08 mg/m^3) (+ possible excursions up to 6 ppm (6.7 mg/m^3)) in 63 male workers did not result in exposure-related health effects as compared to 100 referent workers. As point of departure, an 8 hour exposure to 1 ppm (1.123 mg/m^3) hydrogen cyanide was used. Mild headache was considered a suitable critical endpoint. Using this point of departure no intraspecies uncertainty factor was used because it is the lowest NOAEL observed. The data were scaled across time using the relationship C^n x t = k, with default values n=3 when extrapolating to shorter exposure durations.

The approach is supported by a study with cyanogen in which seven human subjects were exposed to cyanogen in three separate tests. These tests resulted in a NOEL for irritation in humans of 8 ppm (17.3 mg/m^3) for 6 min. Ocular and nasal irritation was reported at the next highest concentration tested, namely 16 ppm for 6 min (34.6 mg/m^3). Applying the default uncertainty factor of 3 to account for intraspecies differences, would result in a threshold for irritation of 2.7 ppm (5.8 mg/m^3). To ensure that the VRW values based on hydrogen cyanide are all protective of both irritation and potential systemic cyanide effects, the 10 min value was set equal to the 30 min value in order to stay below the cyanogen irritation threshold of 2.7 ppm (5.8 mg/m^3).

AGW: No appropriate data for derivation of AGW values are found for cyanogen. The AGW values were derived by dividing the LBW values for cyanogen by a factor of 3. That approach is justified by the steep concentration-response curve for cyanogen, e.g. mortality in rats:
- 0/6 at 1,000 ppm (2,164 mg/m^3) for 15 min versus 6/6 at 1,000 ppm for 30 min
- 0/6 at 500 ppm (1,082 mg/m^3) for 30 min versus 6/6 at 500 ppm for 45 min
- 0/6 at 400 ppm (866 mg/m^3) for 45 min versus 6/6 at 400 ppm for 60 min
- 3/6 at 4,000 ppm (8640 mg/m^3) for 7.5 min versus 6/6 at 4,000 ppm for 15 min
- 0/6 at 2,000 ppm (4320 mg/m^3) for 7.5 min versus 6/6 at 2,000 ppm for 15 min

LBW: Experimental concentrations causing no deaths in rats were used as points of departure for the 10-min, 30-min, and 1-h LBW values. The 10-min exposure at 1530 ppm (3305 mg/m^3) was used as the point of departure for the 10-min LBW value, the 30-min exposure at 500 ppm (1,082 mg/m^3) was used as the point of departure for the 30-min LBW value, and the 1-h exposure at 250 ppm (541 mg/m^3) was used as the point of departure for the 1-h LBW value. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The 2-h LBW value was based on the 1-h LBW value using the equation $C^n \times t = k$, with a default value of n = 1. The 4- and 8-h LBW values were set equal to the 2-h LBW value. That approach was used because time scaling using the equation $C^n \times t = k$, with a default value of n = 1, yielded possible 4- and 8-h LBW values of 6.3 and 3.2 ppm (13.5 and 6.8 mg/m^3), respectively. Those values are inconsistent

with the repeated-exposure data in both monkey and rat studies. Rats experienced only decreased body weight, and monkeys similarly exposed showed only marginal behavioral effects. No effects were noted in either species exposed at 11 ppm (23.8 mg/m^3).

Additional toxicological information (including relevant results of a general literature search, if any)

The mechanism of toxicity of cyanogen is similar to that of hydrogen cyanide. Hydrogen cyanide acts on the central nervous system. It interrupts cellular respiration by inhibiting cytochrome oxidase, thus blocking electron transfer to oxygen. Tissue oxygen concentrations rise, resulting in increased tissue oxygen tension and a decreased unloading for oxyhemoglobin. As a consequence, oxidative metabolism may slow to a point where it cannot meet metabolic demands. That is particularly critical in the brainstem nuclei where lack of an energy source results in central respiratory arrest and death. Cyanide can inhibit many other enzymes, particularly those that contain iron or copper, but cytochrome oxidase appears to be the most sensitive enzyme. Cyanide also stimulates the chemoreceptors of the carotid and aortic bodies to produce a brief period of hyperpnea. Cardiac irregularities may occur, but death is due to respiratory arrest. Brain lesions have been associated with exposure of animals to hydrogen cyanide at high concentrations.

The substance is also irritating to the eyes and the respiratory tract. Rapid evaporation of the liquid may cause frostbite.

No reproductive or developmental data were located for cyanogen. For hydrogen cyanide, no information on the reproductive or developmental toxicity via the inhalation route is available. The teratogenic potential of hydrogen cyanide was studied by infusing sodium cyanide to hamsters. Based on the results of this study and the results of studies with sodium cyanide, aliphatic nitriles and cyanogenic glycosides it can be concluded that the teratogenic activities can be attributed to the cyanide released through metabolism of the parent compounds: in each case, developmental toxicity was observed only at dose levels also inducing signs of maternal cyanide intoxication.

H330: Fatal if inhaled; H319: Causes serious eye irritation; H335: May cause respiratory irritation.

Carcinogenicity and derivation of the CRP value

IARC classification: Not classified.

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: pungent, penetrating, almond-like odour

Odour threshold: 509 mg/m^3 [Ruth, 1986]

No LOA was derived (due to lack of reliable data)

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **4.3**	*AEGL-1* 4.3	*ERPG-1* Not Derived		*IDLH: Not Derived*
AGW level **18**	*AEGL-2* 18	*ERPG-2* Not Derived		
LBW level **54**	*AEGL-3* 54	*ERPG-3* Not Derived		

Stofdocument deel A

CAS-nr: 77-73-6

Dicyclopentadieen

$C_{10}H_{12}$

VN-nr: 2048

GEVI: 30

Synoniemen: DCPD, tricyclo(5,2,1,0)-3,8-decadieen (Engels: dicyclopentadiene)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	5,5	5,5	5,5	5,5	5,5	5,5
Alarmeringsgrenswaarden	AGW (mg/m³)	84	58	46	36	29	19
Levensbedreigende waarden	LBW (mg/m³)	180	120	97	77	61	40

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,182 ppm; 1 ppm = 5,50 mg/m³

Explosiegrens: LEL = 0,8 vol% ≈ 44.000 mg/m³

Geur: typerende kamfer-achtige geur

LOA: 0,26 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot gelige kristallen of poeder

Brand: Brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,02

Molecuulmassa: 132,2 g/mol

Zuurgraad: Niet bekend

LogKow: 2,8

Wateroplosbaarheid: 0,002 g/100 ml (zeer slecht)

Verzadigde dampdruk: 3 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid.

MAK: 2,7 mg/m³

TLV-TWA: 27,5 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: irritatie van ogen, keel en luchtwegen,

AGW → LBW: hoofdpijn, duizeligheid, coördinatiestoornissen, sufheid, ademnood

Boven LBW: convulsies, bewusteloosheid en sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De damp veroorzaakt irritatie van ogen, keel en luchtwegen.
- Bij hogere blootstelling werkt de stof in op het centrale zenuwstelsel met als gevolg functiestoornissen tot in ernstige gevallen convulsies en diepe bewusteloosheid.

Effecten bij blootstelling aan vloeistof

Huidcontact: prikkeling, roodheid

Oogcontact: roodheid en pijn, branderig gevoel

Carcinogeniteit

IARC classificatie: niet geclassificeerd.

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: overmaat stof droog verwijderen of opdeppen, verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 77-73-6 **Dicyclopentadiene** $C_{10}H_{12}$ **UN-nr: 2048**

Basis for the Dutch Intervention Values

VRW: Based on information as described in ERPG-document, different values are derived, other time-points added

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017 | ERPG 2006

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	5.5	5.5	5.5	5.5	5.5	5.5	Eye and throat irritation in humans
AGW	84	58	46	36	29	19	Impaired ability to escape in mice
LBW	180	120	97	77	61	40	Lethality in mice

Derivation of the Dutch Intervention Values

VRW: VRW values are based on a human volunteer study in which 2 volunteers inhaled concentrations of 1 ppm (5.5 mg/m³) and 5.5 ppm (30.3 mg/m³) for 30 minutes. One volunteer reported light eye and throat irritation after 7 minutes of exposure to 5.5 mg/m³ and one volunteer reported eye irritation after 10 minutes of exposure to 30.3 mg/m³. There was a wide spread of findings among all human studies. In one study human volunteer workers exposed to 50-448 ppm (275-2464 mg/m³) for 2 minutes reported only slight odour to faint irritation. Whereas in a study with human volunteers exposed to 0.18 to 4.14 ppm (1-23 mg/m³) unpleasant odour to nauseating odour was reported. The concentration of 5.5 mg/m³ was used as the point of departure for derivation of the VRW values. Considering that this falls in the lower range of concentrations with reported effects an uncertainty factor of 1 was considered sufficient to account for intra-species differences. Irritation is considered to be concentration rather than concentration x time dependent and therefore the same VRW value was applied across all time points.

AGW: AGW values are based on signs of irregular breathing, loss of coordination and inactivity in mice after single inhalation exposure. Groups of six mice per sex were exposed to 46, 130, 260, and 557 ppm (253, 715, 1430 and 3063 mg/m³) during 6 hours, followed by a 14-day observation period. At 715 mg/m³ mice exhibited irregular breathing, loss of coordination, and slight tremors and 2/6 males and 3/6 females were found dead on the day following exposure; at 253 mg/m³ no effects were observed. In a similar study mice were exposed during 6 hours to 50, 99, 213, 431 and 576 ppm (275, 544, 1171, 2370, and 3167 mg/m³) followed by a 14-day observation period. At the lowest concentration tested (275 mg/m³), all mice showed inactivity and partially closed eyes. Activity returned upon removal from the exposure. At the next higher concentration most animals exhibited inactivity and partially closed eyes and some mice (number unclear) showed excessive lacrimation. One female mouse died on the day following exposure. As the observed effects can be considered to impair the ability to escape, the NOAEL of 253 mg/m³ for 6 hours was used as a point of departure for AGW effects. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intra-species differences. Time scaling was performed using $C^n * t = k$, with the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively.

LBW: LBW values are based on a lethality study in mice. Male and female mice (10 animals per sex) were exposed for 6 hours to 50, 99, 213, 431 and 576 ppm (275, 544, 1171, 2370, and 3167 mg/m³), followed by a 14-day observation period. Mortality rates were 0/10, 0/10, 10/10, 10/10 and 10/10 for male mice, and 0/10, 1/10, 10/10, 10/10 and 10/10 for female mice, respectively. Data were analysed with Doseresp and the resulting 6-hour LC_{01} and LC_{50} values were 535 and 557 mg/m³, respectively, for combined analysis of male and female data. In another study, mice (6 animals per sex) were exposed to 46, 130, 260, and 557 ppm (253, 715, 1430 and 3063 mg/m³) during 6 hours, followed by a 14-day observation period in which mortality occurred at higher concentrations.

Mortality rates were 0/6, 2/6, 6/6 and 6/6 for male mice, and 0/6, 3/6, 6/6 and 6/6 for female mice, respectively (no solution possible in dose-resp; 6-hour LC_{50} values were reported in the study at 786 mg/m^3 for male mice and 690 mg/m^3 for female mice). The 6-hour LC_{01} value of 535 mg/m^3 was used as the point of departure for the derivation of the LBW values. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the default values of n=1 and n=3 when extrapolating to longer and shorter durations, respectively. The use of mouse lethality data is supported by LC_{50} values from different inhalation studies in rats, mice, guinea pigs, rabbits and dogs, which indicated that the mouse is the most sensitive species.

Additional toxicological information (including relevant results of a general literature search, if any)

Dicyclopentadiene is rapidly absorbed and mainly excreted through the urine in laboratory animals. Symptoms of acute toxicity follow a general pattern of eye irritation, loss of coordination, and death preceded by convulsions.

Animal studies indicate no evidence for reproductive toxicity of dicyclopentadiene.

H302: Harmful if swallowed; H315: Causes skin irritation; H319: Causes serious eye irritation; H332: Harmful if inhaled; H335: May cause respiratory irritation

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: typical, campher-like odour

OT: 0.017 mg/m^3 [AIHA 1989]
LOA = 11.8 * OT_{50} * 1.33 = 0.26 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies below VRW level.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [28]

VRW level **5.5**	*AEGL-1* -	*ERPG-1* 0.11[29]		*IDLH: not derived*
AGW level **46**	*AEGL-2* -	*ERPG-2* 27		
LBW level **97**	*AEGL-3* -	*ERPG-3* 406		

[28] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.
[29] Note that the ERPG-1 value of 0.11 mg/m^3 as presented in the ERPG-document does not match with the conversion of ppm-values to mg/m^3-values. According to the ERPG-document, 1 ppm = 5.4 mg/m^3. This would lead to the following values for ERPG-1: 0.01 ppm * 5.4 = 0.054 mg/m3.

Stofdocument deel A

CAS-nr: 92-52-4 **Difenyl** **C12H10** **VN-nr: 3077 n.e.g.** **GEVI: 90**

Synoniemen: fenylbenzeen, dibenzeen (Engels: biphenyl) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	6,4	4,4	3,5	2,8	2,2	1,4
Alarmeringsgrenswaarden	AGW (mg/m³)	210	150	120	58	29	14
Levensbedreigende waarden	LBW (mg/m³)	630	440	350	170	87	43

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,156 ppm; 1 ppm = 6,414 mg/m³

Explosiegrens: 0,6 vol% ≈ 38000 mg/m³

Geur: typerende, sterke geur

LOA: 0,94 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: witte/lichtgele kristallen, witte schilfers

Brand: moeilijk brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,0

Molecuulmassa: 154,2 g/mol

Zuurgraad: Geen data

LogKow: 3,8

Wateroplosbaarheid: Niet

Verzadigde dampdruk: 0,04 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 1,28 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: irritatie van de slijmvliezen van ogen en luchtwegen, hoesten, hoofdpijn, duizeligheid, misselijkheid

AGW → LBW: ernstige irritatie van ogen en luchtwegen, hoestaanvallen, braken

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Difenyl is een irriterende stof voor neus, ogen en luchtwegen

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn

Oogcontact: roodheid en pijn

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, en bij aanhoudende klachten arts raadplegen

Ontsmetting vloeistof

huid: overmaat stof droog verwijderen, verontreinigde kleding uittrekken, spoelen en wassen met water en zeep.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), en onmiddellijk arts raadplegen. Niet laten braken

Specifieke behandeling en materialen*: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 92-52-4 **Biphenyl** **C12H10** **UN-nr: 3077 n.o.s.**

Basis for the Dutch Intervention Values

VRW: In contrast to the AEGL-1, VRW values are derived

AGW: Different point of departure than AEGL, 2h value added

LBW: In contrast to the AEGL-3, LBW values are derived.

Date: 06-10-2016 | AEGL Interim 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	6.4	4.4	3.5	2.8	2.2	1.4	Rapid, shallow breathing; hyperactivity in rats and mice.
AGW	210	150	120	58	29	14	1/3 LBW
LBW	630	440	350	170	87	43	Highest non-lethal level rats

Derivation of the Dutch Intervention Values

VRW: The highest dose level of an acute toxicity study (1x 6 hr, to 0.8 ppm or 3.0 ppm, equivalent with 5.1 or 19.2 mg/m³) in rats was chosen as point of departure for the VRW. Though no effects were observed in the study, the effects observed in other studies in rats and mice at higher concentration levels support the choice of this PoD (nasal discharge in rats at 6.0 and 48 ppm, equivalent with 38.5 and 308 mg/m³ in repeated dose studies and hyperactivity and shallow respiration in mice after 4 hour exposure to 14 ppm, or 89.8 mg/m³).
The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. For time-scaling $C^n \times t = k$ was used, using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively.

AGW: In de absence of adequate data to derive AGW values, the LBW values were divided by 3.

LBW: LBW-values are based on results from an acute inhalation toxicity study in rats (see 'Additional toxicological information'). Rats (n=8) were exposed one hour to 960 and 3470 mg/m³ biphenyl. The highest non-lethal level (3470 mg/m³) was used as point of departure for LBW. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. For time-scaling $C^n \times t = k$ was used, using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Biphenyl is a direct acting irritant to the nose, eyes and respiratory tract.
In addition to data available in the AEGL TSD, an additional acute inhalation toxicity study in rats was included in the evaluation and used as basis for LBW derivation (Haley et al., 1959). Rats were exposed via whole body inhalation for one hour to 0, 960 or 3470 mg/m³ diphenyl. After a 14-day post-exposure observation period, none of the animals died. Non-lethal effects included tracheal edema (reversible after one week), acute tracheal necrosis and chronic tracheitis. It is noted that ocular irritation and labored breathing were not observed upon exposure to this compound.

There is no information on the reproductive and developmental toxicity via the inhalation route in the available literature (search up to 2015).

H315: Causes skin irritation, H319: Causes serious eye irritation, H335: May cause respiratory irritation

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

Derivation of the carcinogenic risk potency (CRP): not derived

Odour and derivation of the LOA value

Odour: typical, strong odour or pleasant, butter like odour

Odour threshold (ODT): 0.06 mg/m³ (AIHA 1995)

LOA = 11.8 * ODT * 1.33 = 0.94 mg/m³

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 *

	log (C/ODT) + 0.5. A correction factor of 1.33 is applied to this value) The LOA is below the AGW, but there are no adequate data to determine whether subjects can be aware of the odour below the level where health effects may be expected. .

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)***				
VRW level **3.5**	*AEGL-1* NR	*ERPG-1* -		*IDLH: 100 mg/m³*
AGW level **120**	*AEGL-2* 62	*ERPG-2* -		
LBW level **350**	*AEGL-3* NR	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 80-10-4 **Difenyldichloorsilaan** $C_{12}H_{10}Cl_2Si$ **VN-nr: 1769**

GEVI: X80

Synoniemen: dichloordifenylsilaan (Engels: diphenyl dichlorosilane) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	9,5	9,5	9,5	9,5	9,5	9,5
Alarmeringsgrenswaarden	AGW (mg/m³)	590	280	180	110	69	69
Levensbedreigende waarden	LBW (mg/m³)	1.800	840	530	330	210	210

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,095 ppm; 1 ppm = 10,5 mg/m³

Explosiegrens: geen data

Geur: scherpe geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: geen informatie

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa: 253,2 g/mol

Zuurgraad: geen data

LogKow: geen data

Wateroplosbaarheid: reactie

Verzadigde dampdruk: geen data

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW geen informatie

VRW → AGW: oog- en luchtwegirritatie, tranenvloed, hoesten, lichte benauwdheid

AGW → LBW: ernstige oog- en luchtwegirritatie, pijn op de borst, benauwdheid, longontsteking, longoedeem

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Chloorsilanen reageren zeer snel met water onder vorming van chloorwaterstof (HCl). De acute toxiciteit van difenyldichloorsilaan wordt veroorzaakt door chloorwaterstof.
- Inhalatie van chloorwaterstof veroorzaakt een type I inhalatie intoxicatie.
- Chloorwaterstof veroorzaakt irritatie van de slijmvliezen van ogen en luchtwegen.
- Chloorwaterstof kan bij inhalatie longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, brandwonden.

Oogcontact: bijtend, roodheid en pijn, hoornvliesbeschadiging, ernstige brandwonden.

Carcinogeniteit

IARC classificatie: niet geclassificeerd.

CRP: niet afgeleid.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust; in geval van rode ogen halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken (voorzichtig i.v.m mogelijk reeds beschadigde huid), minimaal 20 min. spoelen met veel water of douchen, en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen:.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 80-10-4 **Diphenyl dichlorosilane** **$C_{12}H_{10}Cl_2Si$** **UN-nr: 1769**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same rationale as AEGL (analogy with HCl), 2h value added

LBW: Same rationale as AEGL (analogy with HCl), 2h value added

Date: November 2015 | AEGL document: Final, 2012

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	9.5	9.5	9.5	9.5	9.5	9.5	Based on HCl (Threshold for irritation in humans)
AGW	590	280	180	110	69	69	Based on HCl (one-third of LBW)
LBW	1,800	840	530	330	210	210	Based on HCl (Calculated threshold for lethality in animals)

Derivation of the Dutch Intervention Values

VRW: Since no appropriate data exist for diphenyl dichlorosilane, VRW values for hydrogen chloride will be used (on ppm-basis) to derive VRW values for diphenyl dichlorosilane. The use of hydrogen chloride as a surrogate for diphenyl dichlorosilane was deemed appropriate since it is believed that the hydrolysis product, HCl, is responsible for the adverse effects. Because two moles of hydrogen chloride are produced for every mole of diphenyl dichlorosilane, a molar adjustment factor of 2 was applied to the hydrogen chloride VRW values.

Derivation of VRW values for HCl

The hydrogen chloride VRW values were based on a no-adverse-effect-level of 1.8 ppm (2.73 mg/m³) in exercising asthmatics with an exposure duration of 45 min. Because the test subjects were considered a sensitive subpopulation and the endpoint was essentially a no-effect level, no uncertainty factor was applied to account for sensitive human subpopulations. The VRW values were held constant for all specified exposure periods since mild irritant effects represent threshold effects and generally do not vary over time.

AGW: Since no appropriate data exist for diphenyl dichlorosilane, AGW values for hydrogen chloride will be used (on ppm-basis) to derive AGW values for diphenyl dichlorosilane. Because two moles of hydrogen chloride are produced for every mole of diphenyl dichlorosilane, a molar adjustment factor of 2 was applied to the hydrogen chloride AGW values.

Derivation of AGW values for HCl

The AGW values of HCl for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data. The only study of HCl that addressed effects that meet the definition of an AGW, severe nasal lesions, was a study on hydrogen halides by Stavert et al. (1991). Nevertheless, this study was not considered a suitable basis for derivation of AGW values because 6% of the animals died after exposure to HCl at 1300 ppm (1974 mg/m³), only one concentration was tested and the number of animals tested was inconsistent.

LBW: Since no appropriate data exist for diphenyl dichlorosilane, LBW values for hydrogen chloride will be used (on ppm-basis) to derive LBW values for diphenyl dichlorsilane. Because two moles of hydrogen chloride are produced for every mole of diphenyl dichlorosilane, a molar adjustment factor of 2 was applied to the hydrogen chloride LBW values.

Derivation of LBW values for HCl

The LBW values were based on a lethality study in rats. The rat study included six exposure durations and various concentrations. Probit analyses using DoseResp was performed and yielded LC_{01} values for the 10 min, 30 min, 1-, 2-,4-, and 8hrs exposure durations of 3370, 1602, 1002, 627, 393 and 246 ppm (5116, 2433, 1522, 952, 596, and 373 mg/m³), respectively, which were used as point of departure for LBW derivation. The default total uncertainty factor of 10 (3x3) was considered

sufficient to account for inter- and intraspecies differences. The probit analyses yielded an n-value of 1.48, which was supported by the n-value of 1.59 calculated by Arts *et al.* (2000) from the C*t study. To maintain consistency with other hydrogen halogenides, the 8 hour value was set equal to the 4 hour value, as performed for the most potent hydrogen halogenide HF.

Additional toxicological information (including relevant results of a general literature search, if any)

No data concerning lethality or nonlethal toxicity in humans from diphenyl dichlorosilane were located in the available literature.

Chlorosilanes react violently with water to produce hydrogen chloride gas. Data suggest that the acute toxicity of chlorosilanes is due to the hydrogen chloride hydrolysis product; acute toxicity of the chlorosilanes is both qualitatively (based on clinical signs) and quantitatively (based on molar equivalents of hydrogen chloride) similar to that of HCl.

Although toxicity data are limited for individual chlorosilanes, well-conducted 1-hr inhalation toxicity studies in rats are available for a series of chlorosilanes. In general, LC_{50} values for monochlorosilanes were approximately twice the LC_{50} values for dichlorosilanes and three times the LC_{50} values for trichlorosilanes. Clinical signs were consistent with hydrogen chloride exposure and included lacrimation, salivation, dried material around or on the eyes and/or nose, green staining around the nose and mouth, and perineal urine staining. Labored breathing, rales, hypoactivity, closed or partially closed eyes, prostration, corneal opacity or opaqueness, and swollen and/or necrotic paws were also observed. Hemorrhage, congestion and/or consolidation of the lungs, ectasia of the lungs, gaseous distension of the gastrointestinal tract, absence of body fat, obstruction of nostrils, dried and/or firm nares, alopecia around the eyes and discoloration of hair were observed at necropsy.

No data concerning developmental/reproductive toxicity for exposure to diphenyl dichlorosilane were located in the available literature.

No harmonized H-sentences for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified.

No carcinogenic risk potency (CRP) was derived

No data concerning carcinogenicity for exposure to diphenyl dichlorosilane were located in the available literature.

Odour and derivation of the LOA value

Odour: pungent odour

No LOA was derived due to lack of data.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **9.5**	*AEGL-1* 9.5	*ERPG-1* not derived		*IDLH:* not derived
AGW level **180**	*AEGL-2* 120	*ERPG-2* not derived		
LBW level **530**	*AEGL-3* 530	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 101-68-8

Difenylmethaan-4,4'-diisocyanaat

$C_{15}H_{10}N_2O_2$

VN-nr: 2206
GEVI: 60

Synoniemen: 4,4`-methyleendifenyldiisocyanaat, MDI, methyleen-bis(fenyl)isocyanaat (Engels: methylene diphenyl diisocyanate)

Status: geen

Interventiewaarden		10	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,20	0,20	0,20	0,20	0,20	0,20
Alarmeringsgrenswaarden	AGW (mg/m³)	15	10	8,1	4,0	2,0	1,0
Levensbedreigende waarden	LBW (mg/m³)	44	31	24	19	15	7,7

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,096 ppm; 1 ppm = 10,412 mg/m³

Explosiegrens: 0,4 vol % .≈ 4000 ppm = 42000 mg/m³

Geur: karakteristieke sinaasappelachtige geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: witte tot lichtgele schilfers of poeder; wordt donkerder bij blootstelling aan licht en lucht

Brand: moeilijk brandbaar. Bij vele reacties kans op brand en explosie.

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,00

Molecuulmassa:	250,3 g/mol
Zuurgraad:	Geen data
LogKow:	4,5
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	<0,00002mbar

Overige informatie

Publieke grenswaarde:
geen
MAK: 0,05 mg/m³
TLV-TWA: 0,052 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW:	irritatie aan ogen, neus en luchtwegen, keelpijn, hoesten, rhinitis, hoofdpijn, misselijkheid, piepende ademhaling
AGW → LBW:	ernstige luchtwegirritatie, onregelmatige ademhaling, benauwdheid, long oedeem
Boven LBW:	ademnood, sterfte

LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Difenylmethaan-4,4`-diisocyanaat is sterk irriterend voor de ogen en luchtwegen. Bij hoge concentraties werkt de stof bijtend.
- Bij inademing van hoge concentraties gaan vooral effecten op het alveolaire niveau overheersen, zoals longoedeem en Type IIA reacties
- Blootstelling kan een astmatische reactie veroorzaken.
- De stof is sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact. Kruisgevoeligheid met andere diisocyanaten is mogelijk.

Effecten bij blootstelling aan vloeistof/vaste stof

(smeltpunt van deze vaste stof rond 40 °C)
Huidcontact: roodheid en pijn, blaren
Oogcontact: roodheid en pijn

Carcinogeniteit

IARC classificatie: 3
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en onmiddellijk arts raadplegen.

Ontsmetting vloeistof
huid: overmaat stof opdeppen, verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen..
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: mond laten spoelen (uitspugen!), en onmiddellijk arts raadplegen.

***Specifieke behandeling en materialen**: geen.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 101-68-8 **methylene diphenyl diisocyanate** **$C_{15}H_{10}N_2O_2$** **UN-nr: 2206**

Basis for the Dutch Intervention Values

VRW: Based on information as described in ERPG-document, but in contrast to ERPG values are derived for all time-points.

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017 | ERPG 2011

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.20	0.20	0.20	0.20	0.20	0.20	Erythema and restlessness in rats
AGW	15	10	8.1	4.0	2.0	1.0	Ocular and respiratory irritation in rats
LBW	44	31	24	19	15	7.7	Rat lethality data (4 hr LC_{01})

Derivation of the Dutch Intervention Values

VRW: In a 1-hour acute inhalation toxicity study male rats (6/group) were exposed to 0.6, 80.8, 162, 171.5, 186.6, 562.5 or 1530 mg/m³ MDI. Clinical signs observed at 80.8 mg/m³ were salivation, lacrimation, nasal drip, nasal porphyrin discharge, dyspnea and escape behaviour. Clinical signs at 0.6 mg/m³ in the same study consisted of slight erythema and restlessness. This study was designed as an acute lethality study with a reported LC_{50} of 178 mg/m³. The effects observed at the next lowest level do not meet the criteria for AGW effects. The effects (erythema and restlessness) at 0.6 mg/m³ were considered VRW effects and this level was used as point of departure. An overall uncertainty factor of 3, instead of 3x3, was considered sufficient to account for inter- and intraspecies differences, because of the large dose-spacing between the NOAEL and LOAEL. Timescaling was not applied as local effects are considered to be concentration-dependent rather than time-dependent.

AGW: In a 1-hour acute inhalation toxicity study male rats (6/group) were exposed to 0.6, 80.8, 162, 171.5, 186.6, 562.5 or 1530 mg/m³ MDI. Clinical signs observed at 80.8 mg/m³ were salivation, lacrimation, nasal drip, nasal porphyrin discharge, dyspnea and escape behaviour. Clinical signs at 0.6 mg/m³ in the same study consisted of slight erythema and restlessness. This study was designed as an acute lethality study with a reported LC_{50} of 178 mg/m³. The effects observed at the lowest level do not meet the criteria for AGW effects. The effects (reversible excessive lacrimation) at 80.8 mg/m³ are slightly above the threshold for AGW effects and very near the threshold for lethality in this study. However, this level was considered to be most suitable as point of departure for derivation of the AGW. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$ with the default n = 1 and n = 3, to calculate to longer and shorter durations, respectively.

LBW: Two acute inhalation studies were performed in rats with methylene diphenyl diisocyanate (MDI) in monomeric form for 4 and 1 hour(s) in various concentrations. As the 1 hour exposure study (see AGW for description) resulted in LC_{01} and LC_{50} values unrealistically close to each other this study was not further considered for LWB derivation. In the 4 hour exposure study (a non-published report by Bayer, 2008) Wistar rats (5/sex/concentration) were exposed nose only to aerosolized concentrations of MDI (MMAD of <3 µm) at gravimetrical concentrations of 300, 354.2, 399.2, 500 and 553.8 mg/m³ for 4 hours. At 300 mg/m³ no animals died. Lethality was observed from 354.2 mg/m³ onwards: 2/10, 7/10, 3/10, 8/10 animals died at the respective concentration levels for both sexes combined. The reported LC_{50} and LC_{01} were 413 and 139 mg/m³, respectively. With DoseResp a 4h LC_{01}-value of 153 mg/m³ was calculated. This value is used as point of departure for LBW derivation. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$ with the default n = 1 and n = 3, to calculate to longer and shorter durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

The substance is a solid with a low vapour pressure. Inhalation exposure will occur via aerosols.

Methylene diphenyl diisocyanate is a corrosive substance, acting immediately at the point of contact. The degree of irritation seems to depend more on the exposure concentration, than the exposure-duration. Immediately after exposure, a decrease in respiratory rate can be detected in animals as well as humans. This rate becomes more graded after the initial exposure. Repeated exposure can induce asthmatic reactions in sensitized persons.

The substance has sensitizing properties.

Methylene diphenyl diisocyanate is not a developmental or reproductive toxicant.

H315: Causes skin irritation; H317: May cause an allergic skin reaction; H319: Causes serious eye irritation; H332: Harmful if inhaled; H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled; H335: May cause respiratory irritation; H351: Suspected of causing cancer; H373: May cause damage to the organs through prolonged or repeated exposure.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: 3 (not classifiable as to its carcinogenicity to humans) No carcinogenic risk potency (CRP) was derived.	Odour: orange-like odour According to the ERPG, 2010 odour threshold levels of 2-4 mg/m^3 have been reported. No LOA was derived due to the absence of reviewed data.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*[30]

VRW level **0.20**	*AEGL-1* -	*ERPG-1* NA		*IDLH:* 75 mg/m^3 (30 minutes)
AGW level **8.1**	*AEGL-2* -	*ERPG-2* 5		
LBW level **24**	*AEGL-3* -	*ERPG-3* 55		

[30] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 674-82-8 **Diketeen** $C_4H_4O_2$ **VN-nr: 2521**

GEVI: 663

Synoniemen: acetylketeen (Engels: Diketene) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	38	27	21	11	5,3	2,6
Levensbedreigende waarden	LBW (mg/m³)	120	80	63	32	16	7,9

Datum vaststelling: 16-12-2010 Conversiefactor: 1 mg/m³ = 0,286 ppm; 1 ppm = 3,50 mg/m³

Explosiegrens: LEL = 0,2 vol% ≈ 7000 mg/m³

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: brandgevaarlijk, kans op explosie bij vele reacties

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,02

Molecuulmassa: 84,1 g/mol
Zuurgraad: Geen data
LogKow: Geen data
Wateroplosbaarheid: reactie
Verzadigde dampdruk: 9,2 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: irriterende effecten niet uitgesloten

AGW → LBW: oog-, neus- en luchtwegirritatie, benauwdheid, longoedeem

Boven LBW: ademnood, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Diketeen is een irriterende stof voor de neus, ogen en luchtwegen.
- De stof kan longoedeem veroorzaken. De verschijnselen van longoedeem kunnen pas na enkele uren optreden en worden versterkt door lichamelijke inspanning.
- De stof heeft een steile concentratie-respons relatie.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, ernstige brandwonden

Oogcontact: bijtend, roodheid en pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 674-82-8 **Diketene** **$C_4H_4O_2$** **UN-nr: 2521**

Basis for the Dutch Intervention Values

VRW: Not recommended in accordance with AEGL

AGW: AEGL value adopted, 2 hr value added.

LBW: AEGL value adopted, 2 hr value added.

Date: 16-12-2010 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	38	27	21	11	5.3	2.6	One third of LBW value
LBW	120	80	63	32	16	7.9	Threshold for lethality in animals

Derivation of the Dutch Intervention Values

VRW: VRW values are not recommended for diketene due to insufficient data.

AGW: The AGW value is derived by taking one-third of the LBW value. The rationale for this approach is based on the steepness of concentration-response relationship for lethality. Furthermore, the experimental data from animal studies were not appropriate for deriving AGW values. Although rats exposed to 250 ppm (875 mg/m^3) for 1 hour showed clinical signs indicative of irritation to the eyes and respiratory tract and no deaths, the $BMDL_{05}$ for lethality used as the point of departure for deriving LBW values was less than the highest concentration causing no lethality in rats.

LBW: LBW values are derived from the mortality study where rats were exposed to 250, 500, or 750 ppm (875, 1750, or 2620 mg/m^3) diketene vapor for 1 hour. The $BMDL_{05}$ calculated using the log-probit model in EPA's Benchmark Dose Software (v. 1.3.2) is 181 ppm (633 mg/m^3) and the lethality threshold (LC_{01}) calculated by probit regression analysis is 276 ppm (966 mg/m^3); therefore, the $BMDL_{05}$ of 181 ppm (633 mg/m^3) is used as point of departure for deriving LBW values. A total uncertainty factor of 10 is applied, 3 for interspecies sensitivity and 3 for intraspecies variability. The interspecies and intraspecies uncertainty factors of 3 were selected because diketene appears to be a direct-acting irritant and the mode-of-action is not expected to differ among species or among individuals in the population. Time extrapolation was performed using $C^n \times t = k$, where the defaults n = 3 and n = 1 are applied for extrapolations to shorter and longer durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Diketene is a direct acting irritant to the nose, eyes and respiratory tract. It is known to cause pulmonary edema. Diketene is the dimeric form of ketene and is similar but less toxic than ketene.

No data were found on reproductive toxicity of diketene in humans or experimental animals.

H332: Harmful if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

No data were found on carcinogenicity of diketene in humans or experimental animals.

Odour and derivation of the LOA value

Odour: Pungent odour

No LOA was derived due to lack of data.

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)***				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* 3.5		*IDLH:* not derived
AGW level **21**	*AEGL-2* 21	*ERPG-2* 17		
LBW level **63**	*AEGL-3* 63	*ERPG-3* 170		

Stofdocument deel A

CAS-nr: 124-40-3 **Dimethylamine** **$(CH_3)_2$-NH** **VN-nr: 1032**

GEVI: 23

Synoniemen: DMA, N-methylmethaanamine (Engels: dimethylamine) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	19	19	19	19	19	19
Alarmeringsgrenswaarden	AGW (mg/m³)	240	160	120	97	76	59
Levensbedreigende waarden	LBW (mg/m³)	900	610	480	370	290	230

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,533 ppm; 1 ppm = 1,88 mg/m³

Explosiegrens: LEL = 2,8 vol% ≈ 53.000 mg/m³

Geur: scherp, vis- of ammoniak-achtig

LOA: 0,97 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos onder druk tot vloeistof verdicht gas

Brand: zeer brandgevaarlijk

Relatieve dichtheid van gas: 1,6

Molecuulmassa: 45,1 g/mol

Zuurgraad: pK_a 10,73 bij 25°C

LogKow: -0,3

Wateroplosbaarheid: volledig

Verzadigde dampdruk: 1700 mbar

Overige informatie

Publieke grenswaarde: 8,0 mg/m³ (8 uur)

MAK: 3,8 mg/m³

TLV-TWA: 9,4 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: mogelijk blauw en/of wazig zicht en het zien van halo's rond lichtbronnen

VRW → AGW: oog-, huid- en bovenste luchtwegirritatie, hoesten, niezen, tranenvloed

AGW → LBW: onderste luchtwegirritatie, benauwdheid, longoedeem, verlies van gezichtsvermogen, verminderde coördinatie, lethargie

Boven LBW: convulsies, ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Dimethylamine werkt irriterend tot bijtend op de ogen, de huid en de luchtwegen, waarschijnlijk door het sterk alkalische karakter van de stof.
- Depressie van het centraal zenuwstelsel kan ontstaan.
- Inademing kan, uitsluitend na verschijnselen van bijtende effecten op de slijmvliezen van de ogen en/of bovenste luchtwegen, longontsteking en/of longoedeem veroorzaken. Dit kan pas na enkele uren optreden en wordt versterkt door lichamelijke inspanning.
- Expositie van de ogen aan het gas kan cornea oedeem veroorzaken.
- In ernstige gevallen bestaat kans op verstikking door zwellingen in de keel.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, branderig gevoel, ernstige brandwonden, mogelijk ernstige bevriezings-verschijnselen zoals pijn, blaren, wonden.

Oogcontact: wazig en blauw zicht, bijtend, tranenvloed, slecht zien, ernstige brandwonden, permanent verlies van gezichtsvermogen

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: kort uitspoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen (zie opmerking hieronder).

Ontsmetting vloeistof

huid: spoelen met veel water / kleding uittrekken en onmiddellijk arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen:

Neem contact op met het NVIC (Tel: +31 (0)30 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 124-40-3 **Dimethylamine** **$(CH_3)_2$-NH** **UN-nr: 1032**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 16-12-2010 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	19	19	19	19	19	19	No signs of irritation in nasal passages or lesions in the lungs in rats
AGW	240	160	120	97	76	59	Nasal lesions in rats
LBW	900	610	480	370	290	230	Lethality threshold for mice

Derivation of the Dutch Intervention Values

VRW: The VRW was based on a study in which rats were exposed whole-body to 0, 10, 30, 100 ppm (0, 19, 56, 188 mg/m³) dimethylamine for 6 hours/day, 5 days/week, for 13 weeks (10 rats/sex/group). In rats exposed up to 100 ppm (188 mg/m³) dimethylamine, no histopathological lesions in the nasal passages and lungs of rats were observed. However, some other effects were seen. The 30 and/or 100 ppm rats had initially lower body weight gain, increased lung weights, and females had slightly increased weight of heart, liver, and kidneys. Although nasal lesions were not observed in this study, dimethylamine is an irritant. In a different study, rats were exposed to 175 ppm (328 mg/m³) dimethylamine 6 hours/day for 1, 2, 4 or 9 days. Acute exposure to 175 ppm (328 mg/m³) resulted in nasal pathology in rats independent of number of exposures. A total uncertainty factor of 10 was applied to the point of departure of 100 ppm (188 mg/m³), including 3 for interspecies uncertainty and 3 for human variability, because nasal irritation from an alkaline irritant gas is a direct surface-contact effect not involving metabolism, and is not likely to vary greatly between species or among humans. Because there is adaptation to the mild irritation that defines the VRW the resulting 10 ppm (19 mg/m³) concentration was applied to all VRW exposure durations.

AGW: The AGW was based on a study in which male rats were exposed to 175 ppm (328 mg/m³) dimethylamine for 6 hours (6/group). Rats had extensive nasal lesions and modified quantity, quality, and flow of mucus. Although reversibility was not addressed in this study, it should be noted that nasal and lung lesions were absent in rats following a 13-week repeated exposure to the next lowest concentration, 100 ppm (188 mg/m³) for 6 hours/day. A total uncertainty factor of 10 was applied to the point of departure of 175 ppm (328 mg/m³), including 3 for interspecies uncertainty and 3 for human variability, because nasal irritation from an alkaline irritant gas is a direct surface-contact effect not involving metabolism, and is not likely to vary greatly between species or among humans. An adjustment factor of 0.5 was applied because the endpoint was considered mild and reversible, based on the absence of nasal irritation and lung inflammation/lesions after 13 week repeated exposure to 100 ppm (188 mg/m³) 6 hours/day. Time scaling was performed using the equation $C^n \times t = k$ where n = 2.8, as calculated from rat lethality data (see LBW).

LBW: The LBW was based on a 2 hour $BMCL_{05}$ of 1978 ppm (3711 mg/m³) calculated from lethality data from a study in which mice (16 per group) were exposed to 815-26,100 ppm (1530-49,000 mg/m³; 8 concentrations tested). A total uncertainty factor of 10 was applied to the point of departure of 1978 ppm (3711 mg/m³), including 3 for interspecies uncertainty and 3 for human variability, because nasal irritation from an alkaline irritant gas is a direct surface-contact effect not involving metabolism, and is not likely to vary greatly between species or among humans. Time scaling was performed using the equation $C^n \times t = k$ where n = 2.8, as calculated from a linear regression of three LC_{50} studies with lethality data at five exposure durations, ranging from 6 minutes to 4 hours.

Additional toxicological information (including relevant results of a general literature search, if any)

The mechanism of dimethylamine toxicity has not been defined, although its irritant properties are likely related to its high alkalinity and corrosiveness to exposed tissues such as skin, eyes, and the respiratory

mucosa. Thus, dimethylamine has been reported to cause respiratory and ocular irritation in both humans and animals, which at sufficiently high concentrations caused breathing difficulties, lesions of the eyes and lungs, and death associated with lung lesions. Dimethylamine vapor is also associated with systemic effects in animals (neurotoxicity, lesions of liver and kidneys), the etiology of which is less clear.

A group of amines, including dimethylamine, has been reported to cause vision disturbances in workers exposed for several hours to concentrations too low to cause discomfort or disability. The workers complained of having blue vision or gray vision or seeing halos around objects. This phenomenon was due to edema of the corneal epithelium and/or light scatter from denatured proteins, which cleared spontaneously by the next day unless exposure was severe. In that case, the edema and blurred vision took several days to clear and was sometimes accompanied by photophobia and discomfort from roughness of the corneal surface.

No human data were located on potential reproductive or developmental toxicity of dimethylamine. Also in experimental animals, no inhalation developmental or reproductive toxicity studies were available. In a monkey exposed to 97 ppm (182 mg/m^3) and in two rabbits exposed to 183 ppm (343 mg/m^3) 7 hours/day, 5 days/week, for 18-20 weeks testicular tubular degeneration was found.

H315: Causes skin irritation; H318: Causes serious eye damage; H332: Harmful if inhaled; H335: May cause respiratory irritation.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Because the known human and animal carcinogen dimethylnitrosamine (DMNA) can be produced *in vitro* by reaction of dimethylamine and various N-O derivatives, there is concern about the potential carcinogenicity of dimethylamine *in vivo*. However, no human (or animal) studies to date have shown that dimethylamine is a carcinogen by any route of administration.

Odour and derivation of the LOA value

Odour: pungent, fishy odour, that becomes similar to that of ammonia at higher concentrations.

OT_{50}: 0.033 ppm (0.062 mg/m^3) [AEGL (2008); Ruijten (2005)]

LOA = 11.8 * OT_{50} * 1.33 = 0.97 mg/m^3

(The concentration Level leading to distinct Odour Awareness (l=3) is calculated using the formula: l = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is below the VRW; therefore subjects can be aware of the odour below the level where health effects may be expected.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **19**	*AEGL-1* 19	*ERPG-1* 1.1		*IDLH*: 938 (30 minutes)
AGW level **120**	*AEGL-2* 120	*ERPG-2* 190		
LBW level **480**	*AEGL-3* 470	*ERPG-3* 660		

Stofdocument deel A

CAS-nr: 75-78-5 **Dimethyldichloorsilaan** $C_2H_6Cl_2Si$ **VN-nr: 1162** **GEVI: X338**

Synoniemen: dimethylsiliciumdichloride, dichloordimethylsilaan (Engels: dimethyldichlorosilane) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	4,8	4,8	4,8	4,8	4,8	4,8
Alarmeringsgrenswaarden	AGW (mg/m³)	300	140	90	56	35	35
Levensbedreigende waarden	LBW (mg/m³)	900	430	270	170	110	110

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,186 ppm; 1 ppm = 5,37 mg/m³

Explosiegrens: LEL = 3,1 vol% ≈ 170.000 mg/m³

Geur: scherpe, bijtende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze, rokende vloeistof
Brand: Zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,5

Molecuulmassa: 129,1 g/mol
Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: Reactie
Verzadigde dampdruk: 153 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: irritatie van ogen en luchtwegen, tranenvloed, hoesten, lichte benauwdheid

AGW → LBW: ernstige irritatie van ogen en luchtwegen, pijn op de borst, benauwdheid, longontsteking, longoedeem

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Chloorsilanen reageren zeer snel met water onder vorming van chloorwaterstof (HCl). De acute toxiciteit van dimethyldichloorsilaan wordt veroorzaakt door chloorwaterstof.
- Inhalatie van chloorwaterstof veroorzaakt een type I inhalatie intoxicatie.
- Chloorwaterstof veroorzaakt irritatie van de slijmvliezen van ogen en luchtwegen.
- Chloorwaterstof kan bij inhalatie longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, brandwonden

Oogcontact: bijtend, roodheid en pijn, slecht zien, hoornvliesbeschadiging, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: n.v.t.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen, en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**:* geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 75-78-5 **Dimethyldichlorosilane** **$C_2H_6Cl_2Si$** **UN-nr: 1162**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same rationale as AEGL (analogy with HCl), 2h value added

LBW: Same rationale as AEGL (analogy with HCl), 2h value added

Date: November 2015 | AEGL document: Final, 2012

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	4.8	4.8	4.8	4.8	4.8	4.8	Based on HCl (Threshold of irritation in humans)
AGW	300	140	90	56	35	35	Based on HCl (one-third of LBW)
LBW	900	430	270	170	110	110	Based on HCl (Threshold of lethality in animals)

Derivation of the Dutch Intervention Values

VRW: Since no appropriate data exist for dimethyl dichlorosilane, VRW values for hydrogen chloride will be used (on ppm-basis) to derive VRW values for dimethyl dichlorosilane. The use of hydrogen chloride as a surrogate for dimethyl dichlorosilane was deemed appropriate since it is believed that the hydrolysis product, HCl, is responsible for the adverse effects. Because two moles of hydrogen chloride are produced for every mole of dimethyl dichlorosilane, a molar adjustment factor of 2 was applied to the hydrogen chloride VRW values.

Derivation of VRW values for HCl

The hydrogen chloride VRW values were based on a no-adverse-effect-level of 1.8 ppm (2.73 mg/m³) in exercising asthmatics with an exposure duration of 45 min. Because the test subjects were considered a sensitive subpopulation and the endpoint was essentially a no-effect level, no uncertainty factor was applied to account for sensitive human subpopulations. The VRW values were held constant for all specified exposure periods since mild irritant effects represent threshold effects and generally do not vary over time.

AGW: Since no appropriate data exist for dimethyl dichlorosilane, AGW values for hydrogen chloride will be used (on ppm-basis) to derive AGW values for dimethyl dichlorosilane. Because two moles of hydrogen chloride are produced for every mole of dimethyl dichlorosilane, a molar adjustment factor of 2 was applied to the hydrogen chloride AGW values.

Derivation of AGW values for HCl

The AGW values of HCl for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data. The only study of HCl that addressed effects that meet the definition of an AGW, severe nasal lesions, was a study on hydrogen halides by Stavert et al. (1991). Nevertheless, this study was not considered a suitable basis for derivation of AGW values because 6% of the animals died after exposure to HCl at 1300 ppm (1974 mg/m³), only one concentration was tested and the number of animals tested was inconsistent.

LBW: Since no appropriate data exist for dimethyl dichlorosilane, LBW values for hydrogen chloride will be used (on ppm-basis) to derive LBW values for dimethyl dichlorsilane. Because two moles of hydrogen chloride are produced for every mole of dimethyl dichlorosilane, a molar adjustment factor of 2 was applied to the hydrogen chloride LBW values.

Derivation of LBW values for HCl

The LBW values were based on a lethality study in rats. The rat study included six exposure durations and various concentrations. Probit analyses using DoseResp was performed and yielded LC_{01} values for the 10 min, 30 min, 1-, 2-,4-, and 8hrs exposure durations of 3370, 1602, 1002, 627, 393 and 246 ppm (5116, 2433, 1522, 952, 596, and 373 mg/m³), respectively, which were used as

point of departure for LBW derivation. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The probit analyses yielded an n-value of 1.48, which was supported by the n-value of 1.59 calculated by Arts *et al.* (2000) from the C*t study. To maintain consistency with other hydrogen halogenides, the 8 hour value was set equal to the 4 hour value, as performed for the most potent hydrogen halogenide HF.

Additional toxicological information (including relevant results of a general literature search, if any)

No data concerning lethality and nonlethal toxicity in humans from dimethyldichlorosilane exposure were located in the available literature.

Chlorosilanes react violently with water to produce hydrogen chloride gas. Data suggest that the acute toxicity of chlorosilanes is due to the hydrogen chloride hydrolysis product; acute toxicity of the chlorosilanes is both qualitatively (based on clinical signs) and quantitatively (based on molar equivalents of hydrogen chloride) similar to that of HCl.

Although toxicity data are limited for individual chlorosilanes, well-conducted 1-hr inhalation toxicity studies in rats are available for a series of chlorosilanes. In general, LC_{50} values for monochlorosilanes were approximately twice the LC_{50} values for dichlorosilanes and three times the LC_{50} values for trichlorosilanes. Clinical signs were consistent with hydrogen chloride exposure and included lacrimation, salivation, dried material around or on the eyes and/or nose, green staining around the nose and mouth, and perineal urine staining. Labored breathing, rales, hypoactivity, closed or partially closed eyes, prostration, corneal opacity or opaqueness, and swollen and/or necrotic paws were also observed. Hemorrhage, congestion and/or consolidation of the lungs, ectasia of the lungs, gaseous distension of the gastrointestinal tract, absence of body fat, obstruction of nostrils, dried and/or firm nares, alopecia around the eyes and discoloration of hair were observed at necropsy

No data concerning developmental/reproductive toxicity for exposure to dimethyldichlorosilane were located in the available literature.

H319: Causes skin irritation. H315: Causes serious eye irritation. H335: May cause respiratory irritation

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived

No data concerning the carcinogenicity of dimethyldichlorosilane in humans or experimental animals were identified in the available literature.

Odour and derivation of the LOA value

Odour: sharp, acrid odour

No LOA was derived.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **4.8**	*AEGL-1* 4.8	*ERPG-1* 11		*IDLH:* not derived
AGW level **90**	*AEGL-2* 59	*ERPG-2* 54		
LBW level **270**	*AEGL-3* 270	*ERPG-3* 400		

Stofdocument deel A

CAS-nr: 624-92-0 **Dimethyldisulfide** CH_3SSCH_3 **VN-nr: 2381**
GEVI: 336

Synoniemen: DMDS, methyldithiomethaan, 2,3-dithiabutaan (Engels: Dimethyl disulfide) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	320	220	180	140	110	73
Levensbedreigende waarden	LBW (mg/m³)	790	550	430	350	270	140

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,255 ppm; 1 ppm = 3,92 mg/m³

Explosiegrens: 1,1 vol% ≈ 43.000 mg/m³

Geur: Walgingwekkend, zwavelachtig, knoflookachtig, rotte vis

LOA: 0,0016 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze tot lichtgele vloeistof
Brand: Zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,06

Molecuulmassa: 94,2 g/mol

Zuurgraad: Niet bekend.
LogKow: 1,9
Wateroplosbaarheid: 0,27 g/100 ml (slecht)
Verzadigde dampdruk: 30 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid.
MAK: niet afgeleid.
TLV-TWA: 2.0 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: irritatie van de luchtwegen, keelpijn, hoesten, branderig gevoel, hoofdpijn, misselijkheid, braken, speekselvloed, loopneus

AGW → LBW: lethargie, zwaktegevoel, moeite met ademhalen

Boven LBW: spiertrekkingen, bewustzijnsverlaging, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt irriterend op de luchtwegen
- De stof kan inwerken op het centrale zenuwstelsel, met als gevolg bewustzijnsverlaging.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, kan in het lichaam worden opgenomen via de huid

Oogcontact: roodheid en pijn, slecht zien.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: spoelen met veel water / kleding verwijderen, spoelen en wassen met water en zeep en arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken en arts raadplegen.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 624-92-0 **Dimethyl disulfide** **CH_3SSCH_3** **UN-nr: 2381**

Basis for the Dutch Intervention Values

VRW: Not recommended, in contrast to ERPG

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017	ERPG, 2015

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	320	220	180	140	110	73	Absence of clinical effects in rats
LBW	790	550	430	350	270	140	Mortality in rats

Derivation of the Dutch Intervention Values

VRW: No suitable and consistent human or animal data were available to derive a VRW..In absence of appropriate data, VRW-values were set at Not Recommended.

AGW: In the absence of suitable acute exposure studies, the AGW-values were derived from subchronic and subacute inhalation studies in rats. Groups of 20 rats (10 male, 10 female) were exposed via whole-body inhalation exposure to 10, 50, 150 or 250 ppm (39, 196, 588, or 980 mg/m³) for 6 hours/day, 5 days/week for a period of 13 weeks. No clinical effects were observed up to a concentration of 980 mg/m³. In another study, rats (4 animals per group) were exposed for 6 hours per day to 100 ppm (392 mg/m³) for 20 days, or 250 ppm (980 mg/m³) for 13 days. At 392 mg/m³ no toxic signs were observed. At 980 mg/m³ lethargy, respiratory difficulty, and reduced weight gain were observed. However, as these effects were not observed in the subchronic study at 980 mg/m³, the exposure to 980 mg/m³ for 6 hours was used as the point of departure for deriving the AGW values. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the default values of n=1 and n=3 when extrapolating to longer and shorter durations, respectively.

LBW: Varying lethality data for dimethyl disulfide are reported in literature with 4-h LC_{50} values ranging from 805 to 1250 ppm (3154 to 4898 mg/m³) in rats, while repeated exposure to 600 ppm (2351 mg/m³) for 5 days, 6 hours per day, did not result in any mortality in rats. Furthermore, one study reported an LC_{50} value of 2520 ppm (9874 mg/m³) in rats after 30 minutes exposure, while in another study rats survived 30 minutes exposure to 3300 ppm (12,931 mg/m³). Although these results are not always consistent, they illustrate a steep concentration-response relationship for DMDS. One key study in rats was selected for calculation of the LBW values: groups of 5 male and 5 female rats were exposed for 4 hours to concentrations of 500, 700, 775, 800, 840, 875, 950, 1100, and 1581 ppm (1959, 2743, 3037, 3135, 3291, 3429, 3722, 4310, and 6195 mg/m³), followed by a 14-day observation period. Mortality incidences were 0/10, 0/10, 3/10, 4/10, 5/10, 9/10, 10/10, 10/10, 10/10, respectively. Using Doseresp, the LC_{01} was calculated as 2737 mg/m³. This point of departure is supported by a study summarized in the REACH dossier, in which 10 rats (5 males and 5 females) were subjected to whole-body inhalation exposure with concentrations of 847, 1188, 1308, or 1650 ppm (3319, 4655, 5125, or 6465 mg/m³) for 4 hours, followed by a 14-day observation period. Mortality incidences for all concentrations were 0/10, 4/10, 4/10 and 9/10, respectively. Using Doseresp, the LC_{01} for that study was calculated as 3319 mg/m³. The LC_{01} of 2737 mg/m³ was used as PoD for the LBW. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the default values of n=1 and n=3 when extrapolating to longer and shorter durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

DMDS is used as an insecticide. In insects, the mechanism of action is dysfunction of the mitochondria. The

mechanism of action in mammals is not known, however, steep dose-response curves were demonstrated in mice and rats.

Inhalation developmental and reproductive toxicity studies in rats and rabbits indicated that DMDS is not reprotoxic.

A study in the REACH dossier was used to support the point of departure for the LBW values. In this study, the acute inhalation toxicity of DMDS was evaluated in a 4-hour, single-exposure study in rats (5 animals per sex per dose). Rats were exposed through whole-body vapor exposure at concentrations of 847, 1188, 1308, or 1650 ppm (3319, 4655, 5125, or 6465 mg/m^3) for 4 hours, followed by a 14-day observation period and clinical observations immediately following each exposure and at 1, 2, 4, 6 and 8 hours post-exposure. Mortality incidences for all concentrations were 0/10, 4/10, 4/10 and 9/10, respectively.

No harmonised H-sentences for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified.

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: Repellent, pungent garlic, decaying fish

OT_{50}: 0.0001 mg/m^3 [Ruth, 1986]
LOA = 11.8 * OT_{50} * 1.33 = 0.0016 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies below VRW-level.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [31]

VRW level **NR**	*AEGL-1* -	*ERPG-1* 0.04		*IDLH:* not derived.
AGW level **180**	*AEGL-2* -	*ERPG-2* 193		
LBW level **430**	*AEGL-3* -	*ERPG-3* 963		

[31] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 68-12-2

Dimethylformamide

C_3H_7NO

VN-nr: 2265

GEVI: 30

Synoniemen: N,N-dimethylmethaanamide, DMF (Engels: N,N-dimethylformamide)

Status: geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	500	350	280	220	170	110
Levensbedreigende waarden	LBW (mg/m³)	9.800*	6.800*	5.400	4.300	2.800	1.400

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,329 ppm; 1 ppm = 3,04 mg/m³

Explosiegrens: LEL = 2,2 vol% ≈ 67.000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

Geur: licht visachtige (amine) geur

LOA: 4.708 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze vloeistof
Brand: Brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,01

Molecuulmassa:	73,1 g/mol
Zuurgraad:	7 – 8
LogKow:	-1,0
Wateroplosbaarheid:	volledig
Verzadigde dampdruk:	3,8 mbar

Overige informatie

Publieke grenswaarde:
15 mg/m³ (8 uur; H)
MAK: 15 mg/m³ (8 uur; H)
TLV-TWA: 30 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW: prikkeling, keelpijn en hoesten, buikpijn, misselijkheid, braken, diarree of verstopping, duizeligheid, verhoogde bloeddruk

AGW→LBW: effecten op de ongeboren vrucht, leverfunctiestoornissen, ontstekingen in het maagdarmkanaal met bloederig braaksel en/of ontlasting,

Boven LBW: leverfalen, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De lever is het belangrijkste doelorgaan van DMF. In de lever vinden enzymatische (o.a. CYP2E1) omzettingen plaats waarbij reactieve metabolieten gevormd worden die mogelijk levertoxiciteit veroorzaken. Metabolieten kunnen binden aan glutathion.
- DMF kan embryotoxiciteit veroorzaken

Effecten bij blootstelling aan vloeistof

Huidcontact: prikkeling, buikpijn, misselijkheid, braken, diarree of verstopping, duizeligheid, verhoogde bloeddruk

Oogcontact: pijn, hoornvliesbeschadiging

Carcinogeniteit

IARC classificatie: 2A
CRP: niet afgeleid wegens onvoldoende gegevens

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust en onmiddellijk arts raadplegen.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en onmiddellijk arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: mond laten spoelen (uitspugen!) en onmiddellijk arts raadplegen.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 68-12-2 **_N,N_-Dimethylformamide** **C_3H_7NO** **UN-nr: 2265**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with the AEGL

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: Same PoD value but different uncertainty factors, 2h value added

Date: 06-10-2016 | AEGL-document Final, 2011

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	No appropriate endpoint was available
AGW	500	350	280	220	170	110	Developmental toxicity in rabbits
LBW	9,800*	6,800*	5,400	4,300	2,800	1,400	Mortality in rats

* value higher than 10% of LEL

Derivation of the Dutch Intervention Values

VRW: A VRW value is not recommended because an appropriate VRW endpoint was not noted in any of the available studies.

AGW: AGW values were derived based on a study in which groups of 15 pregnant Himalayan rabbits were exposed to DMF at 0, 50, 150, or 450 ppm (0, 152, 456, or 1,368 mg/m^3) for 6 h/day on GD 7-19. Developmental toxicity was evident at 1,368 mg/m^3 as increases in external malformations and total malformations (external, soft tissue, and skeletal combined), but no developmental effects were observed at 456 mg/m^3. To protect against irreversible developmental effects, the rabbit NOAEL of 456 mg/m^3 for 6 h was used as the point of departure. An interspecies uncertainty factor of 1 was applied because it appears that primates are not as sensitive as rodents. Monkeys inhaled DMF at 500 ppm (1,520 mg/m^3) for 6 h/day, 5 days/week, for up to 13 weeks with no measurable adverse effects, while subchronic DMF inhalation exposure produced significant hepatic effects in rats at concentrations of 200 -400 ppm (608-1,216 mg/m^3) and in mice at 100 - 200 ppm (304 – 608 mg/m^3). From these data, humans are expected to be less sensitive than rodents. The default intraspecies uncertainty factor of 3 was considered sufficient, resulting in a total uncertainty factor of 3. Application of higher uncertainty factors would result in AGW-values that are inconsistent with available human data: in a single exposure study to assess DMF metabolism, no adverse effects were reported after exposure to 87 ppm (265 mg/m^3) for 4h or 81 ppm (246 mg/m^3) for 2h. Time scaling was performed using $C^n * t = k$, with the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively. In contrast to the 10-minute AEGL-2 value, time scaling was also applied for the 10-minute AGW value.

LBW: LBW values were based on a study in which groups of three male and three female rats were exposed to DMF at 3,700 ppm (11,251 mg/ m^3) for 1 or 3 h; no mortality occurred, but exposure for 7 h to the same exposure concentration resulted in death of two of three males and three of three females. As point of departure a concentration of 3,700 ppm (11,251 mg/m^3) DMF for 3 hours was taken. An interspecies uncertainty factor of 1 was applied because it appears that primates are not as sensitive as rodents (see AGW). The default intraspecies uncertainty factor of 3 was considered sufficient, resulting in a total uncertainty factor of 3. Time scaling was performed using $C^n * t = k$, with the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

DMF may cause liver toxicity due to metabolisation into reactive metabolites. Hepatic cytochrome P450 2E1 (CYP2E1) is an important catalyst in the metabolism of DMF in both rats and humans. Reactive intermediates can be bound to glutathione to form less reactive conjugates.

Rats and mice appeared to be more sensitive to DMF exposure than primates; therefore, humans are expected to be less sensitive than rodents.

DMF has a high potential to be absorbed through the skin. Two case reports of accidental dermal exposure

of DMF workers described symptoms including local erythematous rash, abdominal pain, vomiting, and liver toxicity as indicated by increased serum enzymes and histologically confirmed hepatic damage. The dermal exposure likely had contributed to the systemic effects observed in these cases.

Animal developmental toxicity studies (rats and rabbits) reported reduced maternal body weight and developmental effects including reduced fetal weight, external, skeletal, and visceral malformations, skeletal variations, and increased number and percentage of dead implants. As developmental effects were considered in the setting of the AGW values, no developmental or reproductive effects are expected to occur upon DMF exposure at dosages below AGW levels.

H312: Harmful in contact with skin; H319: Causes serious eye irritation; H332: Harmful if inhaled; H360D: May damage the unborn child.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: 2A (probably carcinogenic to humans) No carcinogenic risk potency (CRP) was derived because a risk level was not available.	Odour: faint amine (fishy) odour In contrast to the AEGL a LOA was derived. ODT: 300 mg/m^3 [Ruth, 1986] LOA = 11.8 * ODT * 1.33 = 4,708 mg/m^3 (The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/ODT) + 0.5. A correction factor of 1.33 is applied to this value) The LOA lies below the 10-min, 30-min and 1-h LBW values.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **NR**	*AEGL-1* NR	*ERPG-1* 6.1		*IDLH:* 1500 mg/m^3 (30 minutes)
AGW level **280**	*AEGL-2* 280	*ERPG-2* 300		
LBW level **5400**	*AEGL-3* 1600	*ERPG-3* 610		

Stofdocument deel A

CAS-nr: 57-14-7 **1,1-Dimethylhydrazine** $(CH_3)_2NNH_2$ **VN-nr: 1163** **GEVI: 663**

Synoniemen: N,N-dimethylhydrazine, asym-dimethylhydrazine, dimazine (Eng.: Dimethyl hydrazine) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	140	45	23	11	5,6	2,8
Levensbedreigende waarden	LBW (mg/m³)	490	160	82	41	20	10

Datum samenstelling: 28-11-2008

Conversiefactor: 1 mg/m³ = 0,4 ppm; 1 ppm = 2,5 mg/m³

Explosiegrens: LEL = 2 vol% ≈ 50 000 mg/m³

Geur: ammoniak-achtige stekende geur

LOA: 96 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze hygroscopische rokende vloeistof, die geel wordt aan de lucht

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,2

Molecuulmassa:	60,1 g/mol
Zuurgraad:	Geen data
LogKow:	-1,2
Wateroplosbaarheid:	Volledig
Verzadigde dampdruk:	145 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV- TWA: 0,025 mg/m³ (proposed)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW:	geen effect tot matige of ernstige irritatie van de luchtwegen, longoedeem, misselijkheid, braken, sufheid, kortademigheid, spiertrillingen
AGW → LBW:	ademnood, pijn op de borst, CZS depressie (ademstilstand, ernstige bloeddrukdaling, bewusteloosheid), convulsies
Boven LBW:	sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- 1,1-Dimethylhydrazine heeft een effect op het centraal zenuwstelsel wat zich uit in spiertrillingen en convulsies
- 1,1-Dimethylhydrazine veroorzaakt contact irritatie aan ademhalingsorganen, huid en ogen
- Sterfte is waarschijnlijk het gevolg van respiratoire stilstand en cardiovasculaire collaps.
- 1,1-Dimethylhydrazine heeft een steile dosis-respons relatie.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn, branderig gevoel.

Oogcontact: bijtend, slecht zien

Carcinogeniteit

IARC classificatie: 2B

CRP: 22 mg/m³ (blootstelling 1 uur)

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: 1,1-dimethylhydrazine wordt door de huid opgenomen. Vanwege brandgevaar verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*:* geen.[3]

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 57-14-7 **1,1- Dimethyl hydrazine** $(CH_3)_2NNH_2$ **UN-nr: 1163**

Basis for the Dutch Intervention Values

VRW: AEGL values are adopted (except 10 min value for which time scaling was applied), 2 hr value added

AGW: Same point of departure as for AEGL values but using different uncertainty factors, 2h value added

LBW: Same point of departure as for AEGL values but using different uncertainty factors, 2h values added

Date: 28-11-2008	Final AEGL document 2000

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	140	45	23	11	5.6	2.8	Neurotoxicity (muscular fasciculation, behavioural changes)
LBW	490	160	82	41	20	10	Threshold for animal lethality

Derivation of the Dutch Intervention Values

VRW: There are no suitable human data to derive a VRW. The experimental data with animals indicate that there is an almost non existent margin between exposures resulting in no response and those causing lethality. Therefore, VRW values for dimethylhydrazine are not recommended.

AGW: The exposure value of 360 ppm (900 mg/m³) for 15 minutes, derived from a study with dogs was chosen as starting point for the derivation of the AGW. This exposure level resulted in behavioral changes and mild muscle fasciculations. A total uncertainty factor of 10 was applied. For interspecies variation a factor of 3 was applied, because the response to inhaled dimethylhydrazine was comparable between different laboratory species, especially for LC_{50} values. They did not vary more than a 3-fold. The dog was found to be the most sensitive species. In deviation to the AEGL document, a factor of 3 was used for intraspecies variation, despite the variability observed in the effects (varying from extreme toxicity to no observable effects at the same dose levels). Regression analyses of exposure response data with dogs and rats, with exposures that varied from 5 to 240 minutes indicated a near linear exposure response of 0.84 for rats and 0.80 for dogs. Therefore, for time scaling, a linear relationship was assumed, and a value of 1. Time scaling using the equation $C^n \times t = k$, with n = 1, was used to derive the time specific AGWs. In contrast to the 10 min AEGL-2 value, time scaling was also applied for the 10 min AGW value.

LBW: The lethality threshold for dogs exposed to 1,1-dimethylhydrazine was estimated from the 1-hr LC_{50} of 981 ppm (2452 mg/m³). Reducing this value 3-fold to 327 ppm (818 mg/m³) results in an exposure concentration 3 times higher than the 1-hr concentration associated with the no-effect level in dogs (96 ppm = 240 mg/m³). A total uncertainty factor of 10 was applied based on the same grounds as for the AGW derivation: a factor 3 for interspecies variation, because only small differences in effects were observed between species. A factor 3 for intraspecies variation was applied in view of the small within species variability among several animal species. Scaling to the LBW time frames was done using the equation $C^1 \times t = k$, as was done for time specific AGW values, including the 10 min LBW.

Additional toxicological information (including relevant results of a general literature search, if any)

The mechanisms of toxicity after acute inhalation exposure are directed to contact irritation (irritation of respiratory tract, pulmonary edema) nausea, vomiting as well as to neurologic effects, including muscle fasciculation, behavioral changes, tremors and convulsions. There is a very steep dose-response relationship indicating a very narrow margin between exposures producing no toxic responses and those resulting in significant toxicity.

No relevant information on reproductive and developmental toxicity with regard to the derivation of AGW values. Only studies parenteral applications were available, showing developmental effects only at maternally toxic doses.

H301: Toxic if swallowed, H314: causes severe skin burns and eye damage, H331: Toxic if inhaled, H350:

May cause cancer

Carcinogenicity and derivation of the CRP value

IARC classification: 2B (Possibly carcinogenic to humans)

Derivation of the carcinogenic risk potency (CRP):

10^{-4} risk level after inhalation: 1 x 10^{-4} mg/m^3 [AEGL]

CRP = (10^{-4} risk level * average life span in hours)/DRCF

= (1 x 10^{-4} * 613.200) /2.8 = 22 mg/m^3

In deviation to the AEGL document, a multistage factor of 2.8 was used in the above calculation, instead of 6. Therefore, the one-hour value in this document is a factor 2 higher than the CRP calculated in the AEGL document.

Odour and derivation of the LOA value

Ammonia-like pungent odour.

OT_{50}: 6.1 mg/m^3 [Guidance for the application of Odor in Chemical Emergency Responses, 2002]

LOA = 11.8 * OT_{50} * 1.33 = 96 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The lower level of the LOA lies under the AGW-10 minute value and the LBW 10 and 30 min value, but above all other AGW values and the 1-8 hour LBW values. Apart from the 10-min LBW, the upper level is higher than all the proposed intervention values.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH: = 37.5 mg/m^3 (30 min)*
AGW level **23**	*AEGL-2* 7.4	*ERPG-2* -		
LBW level **82**	*AEGL-3* 27	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 77-78-1 **Dimethylsulfaat** $(CH_3)_2SO_4$ **VN-nr: 1595** **GEVI: 668**

Synoniemen: methylsulfaat, zwavelzure dimethylester, $DMSO_4$ (Engels: dimethyl sulfate) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,18	0,18	0,18	0,18	0,18	0,18
Alarmeringsgrenswaarden	AGW (mg/m³)	0,88	0,88	0,88	0,88	0,88	0,88
Levensbedreigende waarden	LBW (mg/m³)	44	30	24	12	6,0	3,0

Datum vaststelling: 06-10-2016 Conversiefactor: 1 mg/m³ = 0,190 ppm; 1 ppm = 5,25 mg/m³

Explosiegrens: 3,6 vol% ≈ 188.830 mg/m³

Geur: typerende naar ui ruikende geur

LOA: geen data

Fysisch-chemische eigenschappen

Uiterlijk: heldere kleurloze viskeuze vloeistof
Brand: brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,0

Molecuulmassa: 126,1 g/mol

Zuurgraad: geen data
LogKow: 0,2 (berekend)

Wateroplosbaarheid: 2,8 g/100 ml (matig)
Verzadigde dampdruk: 0,7 mbar

Overige informatie

Publieke grenswaarde:
Niet afgeleid
MAK: niet afgeleid
TLV-TWA: 0,53 mg/m³ (H)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen gegevens
VRW → AGW: oogirritatie, tranenvloed
AGW → LBW: misselijkheid, kortademigheid, hoofdpijn, , braken, slecht zien, N.B.: effecten kunnen pas na enkele uren of zelfs dagen merkbaar worden
Boven LBW: longoedeem, longontsteking, ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof is corrosief voor de ogen, huid en de luchtwegen.
- Bij inhalatie (of ingestie) kunnen zwellingen in de keel (glottis- en larynxoedeem) optreden met als gevolg verstikkingsgevaar.
- Blootstelling aan de stof kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- De stof is sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact!

Effecten bij blootstelling aan vloeistof

Huidcontact: *bijtend*, roodheid en pijn, branderig gevoel, brandwonden, blaren

Oogcontact: *bijtend*, tranenvloed, slecht zien, ernstige brandwonden

Carcinogeniteit

IARC classificatie: 2A
CRP: 10 mg/m³

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: kleding uittrekken (NIET lostrekken), direct spoelen met veel water (minimaal 20 min.), dan pas eventueel aan de huid vastgeplakte kleding verwijderen en verder spoelen, en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken, direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 77—78-1 **Dimethyl sulfate** **$(CH_3)_2SO_4$** **UN-nr: 1595**

Basis for the Dutch Intervention Values

VRW: Same point of departure, different UF, no time-scaling applied, 2h value added

AGW: Same point of departure, different UF, no time-scaling applied, 2h value added

LBW: Same study, but different point of departure, different UFs and different value for n, 2 hr value added

Date: 06-10-2016 AEGL, interim 2006

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.18	0.18	0.18	0.18	0.18	0.18	Altered nasal cell proliferation in rats
AGW	0.88	0.88	0.88	0.88	0.88	0.88	Breathing problems in rats, mice and golden hamsters
LBW	44	30	24	12	6.0	3.0	Threshold for lethality in rats

Derivation of the Dutch Intervention Values

VRW: No human data are available for VRW derivation. The VRW values are based on 14-day repeated exposure study in rats (6h/day, 5d/week). In this study slight altered nasal cell proliferation was observed in the 0.1 ppm (0.53 mg/m³) exposure group, which was repeatedly exposed to dimethyl sulfate for 2 weeks. At 0.7 and 1.5 ppm (3.7 and 7.9 mg/m³, respectively), histopathology revealed dimethyl sulfate-related lesions (erosion, ulceration and atrophy of respiratory and olfactory epithelia). Also, more pronounced effects above the VRW threshold, as breathing difficulties and asthmatic-like breathing, were reported at 0.5 ppm (2.6 mg/m³) after first treatment of 6-hour exposure in a repeated dose study with rats, mice and golden hamsters. Therefore, 0.1 ppm (0.53 mg/m³ /6hr) was selected as point of departure to derive VRW values. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. No interspecies uncertainty factor was applied, given that the rat is the most sensitive species, it concerns a repeated exposure study and the effects observed are considered to be less severe than those defined for the VRW. Time scaling was not applied as irritation is considered a concentration-dependent effect.

AGW: No human data are available for AGW derivation. In a repeated dose inhalation study in which rats, mice and golden hamsters were exposed to 0.5 (rat), 2 (rat), 20 (hamster), 34 (rat), or 48 (mice) ppm (corresponding with 2.63, 10.5, 105, 179, or 252 mg/m³) dimethyl sulfate for 6 hr/day, 2 days/week, every 4th month for 15 months). Breathing problems and asthmatic-like breathing sounds were already observed after the first 6-hour exposure to 0.5 ppm (2.63 mg/m³). Above this value irreversible lesions must be expected. Therefore, the effects seen at 0.5 ppm (2.63 mg/m³) after a 6-hour exposure are used as point of departure for AGW derivation. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. No interspecies uncertainty factor was applied, given that the rat is the most sensitive species, it concerns a repeated exposure study and the effects observed are considered to be less severe than those defined for the AGW. Time scaling was not applied as irritation is considered a concentration-dependent effect.

LBW: The LBW values are based on an acute toxicity study in rats. In this study groups of rats (n=5) were exposed to 10, 49, 64, 71 and 127 ppm (corresponding with 52.5, 267, 336, 373, and 667 mg/m³, respectively) of dimethyl sulfate (whole body) for one hour and a 3 week observation period. The LBWs are based on the 1h LC_{01} of 241 mg/m³ for rats, calculated using Doseresp. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The equation $C^n \times t = k$ was used for time-scaling, using default values of n=1 and n=3 to extrapolate to longer and shorter exposure durations.

Additional toxicological information (including relevant results of a general literature search, if any)

Only the intact dimethyl sulfate -molecule has alkylating properties. This step is nonenzymatic and should already begin within the first minutes after tissue contact, leading to methylation (and deactivation) of proteins, essential amines, nucleobases and other cellular molecules. Exposure to dimethyl sulfate results in local and systemic effects depending on extent and duration of exposure. In evaluating the toxicity of dimethyl sulfate local effects are in the foreground for nonlethal and lethal intoxication and occur at concentrations much lower than those producing systemic effects. It is suggested that toxic effects are caused by the corrosive potential of sulfuric acid and the effects of methanol to the nervous system. Formation of methanol

leads to headache, dizziness, wariness, visual disturbances, seizures, coma, paralysis, and kidney injury. A major cause of effects in inhalation dimethyl sulfate intoxication is respiratory failure as consequence of mucosal inflammation and edema of respiratory tract. Irritation is confined to the bronchi and bronchiole, and dimethyl sulphate -mist does not get far enough to cause irritation of the lung tissue itself, indicated by lacking of congestion or edema of alveolar walls and exudate in alveolar cavity. Usually a latency period of 4 to 12 hours between exposure and onset of effects was reported from human case studies.

Upon inhalation of dimethyl sulfate, no developmental/reproductive toxicity was observed in experimental animals.

H301: Toxic if swallowed, H314: Causes severe skin burns and eye damage, H317: May cause an allergic skin reaction, H330: Fatal if inhaled, H341: Suspected of causing genetic effects, H350: May cause cancer

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: 2A (probably carcinogenic to humans) Derivation of the carcinogenic risk potency (CRP): 10^{-4} risk level after inhalation: 1 x 10^{-4}/2.2 (mg/m^3) = 0.045 µg/m^3 [ECB, 2002 and Schögel, 1972] CRP = (10^{-4} risk level * average life span in hours)/DRCF = (0.045* 613.200) /2.8 = 10 mg/m^3 The derived AGW values are assumed to be appropriate to avoid relevant cell damage in respiratory tract, which may contribute to cell replication and may be viewed as a risk factor for development of malignant effects.	Odor: slight onion-like No LOA was derived.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level 0.18	*AEGL-1* 0.13	*ERPG-1* -		*IDLH: 37 mg/m^3 (30 minutes)*
AGW level 0.88	*AEGL-2* 0.63	*ERPG-2* -		
LBW level 24	*AEGL-3* 8.4	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 75-18-3 **Dimethylsulfide** $CH_3 – S – CH_3$ **VN-nr: 1164**
GEVI: 33

Synoniemen: 2-thiopropaan, methylthiomethaan, thiobismethaan (Engels: dimethyl sulfide) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	6800*	4700	2400	1200	590	290
Levensbedreigende waarden	LBW (mg/m³)	21.000*	15.000*	12.000*	9400*	7400*	3700

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,387 ppm; 1 ppm = 2,58 mg/m³

Explosiegrens: 2,2 vol% ≈ 57.000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

Geur: Onaangenaam, koolachtig

LOA: 0,039 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze tot lichtgele zeer vluchtige vloeistof
Brand: Zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,6

Molecuulmassa: 62,1 g/mol

Zuurgraad: Niet bekend
LogKow: 1,1

Wateroplosbaarheid: 0,2 g/100 ml (slecht)

Verzadigde dampdruk: 527 mbar

Overige informatie

Publieke grenswaarde:
Niet afgeleid.
MAK: niet afgeleid.
TLV-TWA: 26 mg/m³.

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: prikkeling van de ogen, hoofdpijn, duizeligheid, slaperigheid

AGW → LBW: onregelmatige ademhaling, sufheid, zwaktegevoel, spierverlamming, bewustzijnsdaling

Boven LBW: sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Dimethylsulfide kan inwerken op het centraal zenuwstelsel, met als gevolg bewustzijnsverlaging
- Lokaal contact kan irritatie geven

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid

Oogcontact: prikkeling, roodheid

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: spoelen met veel water / kleding verwijderen, spoelen en wassen met water en zeep en arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 75-18-3 **Dimethyl Sulfide** **$CH_3 – S – CH_3$** **UN-nr: 1164**

Basis for the Dutch Intervention Values

VRW: Not recommended, in contrast to ERPG

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017 ERPG 2004

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	6800*	4700	2400	1200	590	290	Tremors in rats
LBW	21,000 *	15,000 *	12,000 *	9400 *	7400 *	3700	Mortality in rats

* value higher than 10% of LEL

Derivation of the Dutch Intervention Values

VRW: No reliable human or animal data were available to derive VRW values. In absence of appropriate data, the VRW was set to Not Recommended.

AGW: AGW-values are based on an acute toxicity study in rats. Groups of 10 rats (5 males and 5 females) were exposed whole-body to a nominal concentration of 47,000 mg/m^3 for 3 hours, 107,000 mg/m^3 for 4 hours, 207,000 mg/m^3 for 70 minutes, and 495,000 mg/m^3 for 18 minutes. Actual concentrations were not determined. At 47,000 mg/m^3 no mortality occurred, but tremors were observed after 30-45 minutes of exposure and unconsciousness after 60-80 minutes. At the higher concentrations, unconsciousness was observed after 20-30 minutes, 10-15 minutes, and 1-5 minutes, respectively. The exposure duration of 30 minutes to a concentration of 47,000 mg/m^3 (onset of tremors) was taken as point of departure for the AGW-values. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the default values of n=1 and n=3 when extrapolating to longer and shorter durations, respectively.

LBW: LBW-values are based on a lethality study in rats. Groups of 5 male and 5 female rats were whole-body exposed for 4 hours to concentrations of 800, 3,000, 6,000, 12,000, 24,000, 36,000, 39,000, 42,000, 45,000 and 48,000 ppm (2,067, 7749, 15,499, 30,997, 61,995, 92,992, 100,742, 108,491, 116,241, and 123,990 mg/m^3), followed by a 14-day observation period. Mortality incidences for all concentrations tested were: 0/10, 0/10, 0/10, 0/10, 0/10, 2/10, 5/10, 5/10, 8/10, and 9/10, respectively. Using Doseresp, the 4-hour LC_{01} and LC_{50} were calculated as 74,440 mg/m^3 and 104,100 mg/m^3, respectively The 4-hour LC_{01} value of 74,440 mg/m^3 was used as point of departure for deriving the LBW-values. The point of departure for the LBW-values is supported by a another study in which 10 rats (5 males and 5 females) were exposed whole-body to a nominal concentration of 47,000 mg/m^3 for 180 minutes, 107,000 mg/m^3 for 240 minutes, 207,000 mg/m^3 for 70 minutes or 495,000 mg/m^3 for 18 minutes. Mortality incidences for these exposures were 0/10, 4/10, 10/10 and 10/10, respectively.
The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the default values of n=1 and n=3 when extrapolating to longer and shorter durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Dimethyl sulfide irritates the mucous membranes and induces CNS-depression.

Information on the toxicokinetics of dimethyl sulfide is very limited. No reliable animal data are available. A human case report, where two fatalities occurred in a storage tank of a paper manufacturing plant, reported that dimethyl sulfide was widely distributed in the tissues of one of the victims.

No data were found on reproductive toxicity by inhalation of dimethyl sulfide.

No harmonised H-sentences for human health.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified. No carcinogenic risk potency (CRP) was derived.	Odour: Unpleasant, cabbage-like OT: 0.0025 mg/m^3 [Ruth, 1986] LOA = 11.8 * OT * 1.33 = 0.039 mg/m^3 (The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value) The LOA lies far below the AGW values.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)*** [32]

VRW level **NR**	*AEGL-1* -	*ERPG-1* 1.27		*IDLH:* not derived
AGW level **2400**	*AEGL-2* -	*ERPG-2* 2540		
LBW level **12,000**	*AEGL-3* -	*ERPG-3* 12,700		

[32] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 123-91-1 **1,4-Dioxaan** **$C_4H_8O_2$, cyclisch** **VN-nr: 1165** **GEVI: 33**

Synoniemen: diethyleendioxide, diethyleenether, p-dioxaan (Engels: 1,4-dioxane) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	180	180	180	180	180	180
Alarmeringsgrenswaarden	AGW (mg/m³)	2100	1500	1200	920	730	370
Levensbedreigende waarden	LBW (mg/m³)	5000	3500	2800	2200	1700	870

Datum vaststelling: 28-11-2008

Conversiefactor: 1 mg/m³ = 0,273 ppm; 1 ppm = 3,67 mg/m³

Explosiegrens: LEL = 1,9 vol% ≈ 70.000 mg/m³

Geur: sterke etherachtige geur

LOA: 6,3 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,08

Molecuulmassa:	88,1 g/mol
Zuurgraad:	geen data
LogKow:	-0,4
Wateroplosbaarheid:	volledig
Verzadigde dampdruk:	41 mbar

Overige informatie

Publieke grenswaarde: 20 mg/m³ (8 uur)
MAK: 73 mg/m³
TLV-TWA: 92 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW	geen effecten
VRW → AGW:	oog-, keel- en neusirritatie, tranenvloed
AGW → LBW:	bewustzijnsdaling, benauwdheid, longschade, nierschade, leverschade
Boven LBW:	coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt irriterend op de huid, ogen en luchtwegen
- 1,4-Dioxaan kan het centrale zenuwstelsel onderdrukken.
- Nierschade en leverschade kunnen optreden na blootstelling aan 1,4-dioxaan.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, ruwe huid

Oogcontact: roodheid, pijn

Carcinogeniteit

IARC classificatie: 2B
CRP: 31.000 mg/m³

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust en arts raadplegen

Ontsmetting vloeistof

huid:	verontreinigde kleding uittrekken, afspoelen met water
ogen:	spoelen met water (evt. contactlenzen verwijderen)
inslikken:	mond laten spoelen (uitspugen!), GEEN braken opwekken en direct arts raadplegen

Specifieke behandeling en materialen: geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 123-91-1 **1,4-Dioxane** **$C_4H_8O_2$, cyclic** **UN-nr: 1165**

Basis for the Dutch Intervention Values

VRW: Same point of departure as for AEGL-1, using different uncertainty factors, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted except for the 10-min value, 2h value added

Date: 28-11-2008 | AEGL document: Interim, 2005

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	180	180	180	180	180	180	Threshold of notable discomfort
AGW	2100	1500	1200	920	730	370	Threshold of irreversible liver toxicity
LBW	5000	3500	2800	2200	1700	870	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: For the derivation of VRW values, eye irritation in human volunteers at 50 ppm (183 mg/m³) throughout a 6-hour exposure period was used as point of departure. The severity level of the eye irritation was not defined but was considered to be below the notable discomfort level as described in the VRW definition. To derive VRW values the same exposure concentration was used for all time points. In contrast to AEGL-1, no uncertainty factor was applied to derive the VRW, as the point of departure is below the definition of VRW.
The derived VRW-values are supported by data from two different studies with human volunteers. Volunteers exposed for 15 minutes at 300 ppm (1100 mg/m³) complained of irritation to eyes, nose and throat. At a similar concentration of 280 ppm (1026 mg/m³), another study reported slight mucous membrane irritation in humans.

AGW: Exposure at 2000 ppm (7330 mg/m³) for 4 hours was considered a threshold for irreversible liver toxicity in rats and was used as the basis for AGW derivation. A total uncertainty factor of 10 was used. An interspecies uncertainty factor of 3 and an intraspecies factor of 10 were applied. Time scaling using the equation $C^n \times t = k$ was carried out to derive exposure duration-specific values with the default values of n=3 and n=1 for extrapolation to shorter and longer exposure durations, respectively. Time extrapolation was continued to the 10-minute period because even at higher concentrations of 1600 ppm (5900 mg/m³) for 10 minutes or 1400 ppm (5130 mg/m³) for 5 minutes exposed subjects did not experience more severe effects than moderate eye, nose and throat irritation.

LBW: No acute inhalation toxicity study that followed today's standards and guidelines was available for dioxane. The derivation of the LBW values was based on a 4-hour LC_{50} of 14,300 ppm (52,400 mg/m³) in rats. The LC_{50} reported in the key study is supported by other studies in rats. For extrapolation from the LC_{50} value to the threshold for lethality, a factor of 3 was used. This factor was considered adequate because available data indicate a very steep dose-response curve for lethality after inhalation exposure. A total uncertainty factor of 10 was used. An interspecies uncertainty factor of 3 and an intraspecies factor of 10 were applied. Time scaling using the equation $C^n \times t = k$ was carried out using the default values of n=3 and n=1 for extrapolation to shorter and longer exposure durations, respectively. Time extrapolation was continued to the 10-minute period because even at higher concentrations of 1600 ppm (5860 mg/m³) for 10 minutes or 1400 ppm (5130 mg/m³) for 5 minutes exposed subjects did not experience more severe effects than moderate eye, nose and throat irritation.

Additional toxicological information (including relevant results of a general literature search, if any)

Fatalities after repeated inhalation exposure to unknown concentrations of dioxane at the workplace are described. Exposure probably also comprised dermal contact. The men experienced nausea and vomiting, described as "stomach trouble", followed after 2-3 days by oliguria and anuria. About 3-7 days after the first symptoms, coma developed, followed by death. Microscopic examinations revealed centrilobular liver necrosis, almost symmetrical necrosis of the outer renal cortex and haemorrhages around the glomeruli.

Volunteers exposed for 15 minutes at 300 ppm (1100 mg/m³) complained of irritation to eyes, nose and throat. At a similar concentration of 280 ppm (1026 mg/m³), another study reported slight mucous membrane irritation in humans. More distinct irritation was observed at 1400-1600 ppm (5130-5860 mg/m³) and severe irritation occurred

at 2800-5500 ppm (10,260-20,160 mg/m^3). Three of the subjects exposed to 5500 ppm (20,160 mg/m^3) noticed a slight vertigo which disappeared quickly after leaving the exposure. The shallow increase of irritative effects with concentration also supports the interpretation that the effects found at 50 ppm (183 mg/m^3) can be considered as mild.

Acute toxic effects in animals are mainly central nervous system depression, kidney and liver damage, peripheral nervous system effects as well as irritative effects. At lethal concentrations, narcosis has been observed in rats and guinea pigs.

No relevant studies documenting developmental or reproductive effects of 1,4-dioxane in humans were identified.

H319: Causes serious eye irritation; H335: May cause respiratory irritation; H351: Suspected of causing cancer.

Carcinogenicity and derivation of the CRP value

IARC classification: 2B, possibly carcinogenic to humans

Derivation of the carcinogenic risk potency (CRP):

10^{-4} risk level after inhalation: 0.14 mg/m^3 [AEGL]

CRP = (10^{-4} risk level * average life span in hours)/DRCF

= (0.14 * 613,200) /2.8 = 31,000 mg/m^3

When administered orally, dioxane produced malignant tumours of the nasal cavity and liver in rats, liver tumours in mice, and tumours of the liver and gallbladder in guinea pigs. A lifetime bioassay exposing rats at 111 ppm (410 mg/m^3) for 7 hours/day, 5 days/week found no evidence for carcinogenic effects. Two epidemiological studies in humans found no higher incidence of cancer deaths in workers exposed to 1,4-dioxane.

Odour and derivation of the LOA value

Odour: strong ethereal odour that diminishes rapidly during exposure

OT_{50}: 0.11 ppm (0.40 mg/m^3) [AEGL (2005)]
LOA = 11.8 * OT_{50} * 1.33 = 6.3 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is far below the VRW values

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **180**	*AEGL-1* 62	*ERPG-1* not derived	*IDLH:* 7330 *(30 minutes)*
AGW level **1200**	*AEGL-2* 1200	*AEGL-2* not derived	
LBW level **2800**	*AEGL-3* 2800	*AEGL-3* not derived	

Stofdocument deel A

CAS-nr: 106-89-8 **Epichloorhydrine** C_3H_5ClO **VN-nr: 2023**

GEVI: 63

Synoniemen: 1-chloor-2,3-epoxypropaan, (2-chloormethyl)oxiraan, γ-chloorpropyleenoxide (Engels:epichlorohydrin)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	22	22	22	22	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	67	46	37	29	23	17
Levensbedreigende waarden	LBW (mg/m³)	170	120	95	76	60	30

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,260 ppm; 1 ppm = 3,85 mg/m³

Explosiegrens: LEL= 2,3 vol% ≈ 89.000 mg/m³

Geur: zoet, scherp en chloroform-achtig

LOA: 240 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,05

Molecuulmassa:	92,5 g/mol
Zuurgraad:	Geen data
LogKow:	0,45
Wateroplosbaarheid:	6 g/100 ml (matig) (10°C)
Verzadigde dampdruk:	17 mbar

Overige informatie

Publieke grenswaarde:

0,19 mg/m³ (8 uur)

MAK: 8 mg/m³

TLV-TWA: 2 mg/m³ (huid)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: irritatie van slijmvliezen (met name ogen en neus), roodheid huid

AGW → LBW: effect op de ongeboren vrucht, matige tot ernstige irritatie van luchtwegen, speekselvloed, keelpijn, hoesten, benauwdheid, branderig gevoel op de borst, misselijkheid, hoofdpijn, lever- en nierfunctiestoornissen

Boven LBW: ademstilstand, longoedeem, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Epichloorhydrine is een alkylerend epoxide verbinding en bevat een uiterst reactieve oxiraanring.
- Blootstellingen kunnen primair resulteren in irritatie van de slijmvliezen (ogen, neus, keel) en de huid. Deze klachten kunnen zich pas enkele uren na blootstelling openbaren en enkele dagen aanhouden.
- De stof kan mogelijk ontwikkelingstoxiciteit en abortus veroorzaken, alsmede depressie van het CZS.
- Blootstelling aan epichloorhydrine kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Herhaaldelijke of langdurige blootstelling kan huidsensibilisatie veroorzaken met als gevolg allergische contactdermatitis.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, irritatie, roodheid, pijn, brandwonden, blaren, zwelling
Oogcontact: bijtend, irritatie, roodheid, pijn, slecht zicht, brandwonden, permanent verlies gezichtsvermogen

Carcinogeniteit

IARC classificatie: 2A
CRP: 18.250 mg/m³

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.
Specifieke behandeling en materialen*: geen.*
Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 106-89-8 **Epichlorohydrin** **C_3H_5ClO** **UN-nr: 2023**

Basis for the Dutch Intervention Values

VRW: Same point of departure than AEGL but using different uncertainty factors 2h value added;

AGW: Different point of departure and different value for n than AEGL values, 2 h value added;

LBW: Different point of departure and different value for n than AEGL values, 2 h value added.

Date: November 2015 | AEGL document: Final, 2014

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	22	22	22	22	NA	NA	Threshold for irritation in humans
AGW	67	46	37	29	23	17	NOAEL for developmental toxicity in rats
LBW	170	120	95	76	60	30	Threshold for lethality (LC_{01}) in rats

Derivation of the Dutch Intervention Values

VRW: Irritation is the most sensitive effect experienced by humans exposed to low concentrations of epichlorohydrin, and this endpoint will therefore be used to derive VRW values. Four human subjects were exposed to epichlorohydrin at concentrations of 17, 68, and 136 ppm (65, 262, 524 mg/m³) for 2 minutes. Three subjects exposed to 68 ppm (262 mg/m³) of epichlorohydrin reported no irritating effect, and one reported irritation to the pharynx. Two subjects exposed to 136 ppm (524 mg/m³) reported a cooling sensation in the eyes and mouth and two reported irritation to the eyes or pharynx. The point-of-departure is 17 ppm (65 mg/m³) for a 2 minute exposure; this concentration and time is a no-effect level for irritation. The default uncertainty factor of 3 for intraspecies variability is applied. Time-scaling is not performed because the irritative effects are not expected to become more severe with increasing exposure duration at this concentration. The 4-h and 8-h VRW values are set to NA (not applicable), due to conflict with AGW-values.

AGW: Groups of five or six presumed pregnant female rats were exposed to epichlorohydrin vapour concentrations of 0, 25, 50 or 100 ppm (0, 96, 193 or 385 mg/m³) epichlorohydrin for 7 hours/day on gestation days 6-15 and killed on day 16. Maternal toxicity consisting of decreased weight gain, decreased intra-abdominal adipose tissue, decreased thymus size, and an increased incidence of pale liver was observed in the 50 and 100 ppm (193 and 385 mg/m³) exposure groups. Three out of six rats exposed to 100 ppm (385 mg/m³) had 100% resorptions, one had normal foetuses and two rats had no evidence of being pregnant (no implantation sites). These effects were not reported at the 50 ppm (193 mg/m³) exposure concentration or below. Since resorptions can be induced by a single exposure and therefore are considered as an appropriate endpoint for an AGW, the 7-hour 50 ppm (193 mg/m³) exposure level as a NOAEL for developmental toxicity in rats is chosen as point of departure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was performed using the equation $C^n xt=k$, using the default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. The approach deviates from the AEGL-2 derivation where the AEGL-2 levels were calculated by dividing the AEGL-3 levels by 3.

LBW: LBW values were based on a rat lethality study. In this study, groups of 20 male Wistar rats were exposed under dynamic conditions to atomized (aerosolized) epichlorohydrin in a mixture of alcohol and lutrol (1:1) at epichlorohydrin concentrations of 296, 638, 1038, or 1440 mg/m³, respectively for 4 hours and observed for 2 weeks. The concentrations of epichlorohydrin in the chamber atmospheres were determined spectrophotometrically on air samples reacted with hydroxylamine. The number of deaths and time to death were concentration related. Using DoseResp the 4h LC_{01} value was calculated which was used as point of departure for deriving the LBW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was performed using the equation $C^n xt=k$, using the default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. The LC_{01} values were 1731, 1200, 952, 756, 600 and 300 mg/m³ for 10 min, 30 min, 1h, 2h, 4h and 8h exposure duration respectively. This approach deviates from the AEGL-3 derivation. AEGL-3 levels were based on two rat studies. A 1h study was used to derive the 10 min, 30 min and 1h AEGL-3 values. A 6h study was used to derive the 4h and 8h AEGL-3 value. Time-scaling was done by applying an n-value of 0.87 which was based on rat LC_{50} values for 1-, 4-, 6-, and 8-hour exposure derived from other studies.

Additional toxicological information (including relevant results of a general literature search, if any)

The mechanism by which epichlorohydrin exerts its toxic effects is not known. Epichlorohydrin is a direct alkylating agent, which may account for some of its irritant properties.

Occupational exposure to epichlorohydrin did not reveal developmental or reproductive effects in human males as determined by sperm count and various hormone levels. A range finding study in rats using a concentration of 0, 25, 50 or 100 ppm (0, 96, 192 or 385 mg/m^3) epichlorohydrin for 7 hours/day on gestation days 6-15, revealed maternal toxicity and effects of epichlorohydrin on resorptions (3/6 rats had 100% resorptions). These effects were used as POD for AGW.

H350: May cause cancer. H301/311/331: Toxic by inhalation, in contact with skin and if swallowed. H314: Causes burns. H317: May cause sensitisation by skin contact.

Carcinogenicity and derivation of the CRP value

IARC classification: 2A (probably carcinogenic to humans)

Derivation of the carcinogenic risk potency (CRP):

10^{-4} risk level after inhalation: 8.33 * 10^{-2} mg/m^3

CRP = (10^{-4} risk level * average life span in hours)/DRCF = 8.33 * 10^{-2} mg/m^3 * 613.200) /2.8 = 18,243 mg/m^3

A cohort study of workers in the USA showed slight excesses of lung cancer. Another cohort in Europe was inconclusive. Carcinogenicity studies in rats showed that 30, 6-hour exposures (5 days/week) to 100 ppm of epichlorohydrin vapour followed by lifetime observation was very effective in inducing squamous cell carcinomas in the nasal cavity of rats. Whereas lifetime exposure to 30 ppm (6 hours/day, 5 days/week) was almost ineffective. This study demonstrated that short-term high level exposures are more effective than long-term low-level exposures for nasal tumour induction.

Odour and derivation of the LOA value

Odour: sweet, pungent or chloroform-like

OT_{50}: 15 mg/m^3 [Shell Oil 1992 & Van Doorn 2002] adjusted by [Ruijten et al., 2009]

LOA = 11.8 * OT_{50} * 1.33 = 240 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies above the VRW and AGW at all time points. It is lower than the LBW levels at the 10, 30, 60 and 120 minutes time points and higher than the other LBW time points.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **22**	*AEGL-1* 6.5	*ERPG-1* 19		*IDLH:* 290 mg/m^3 (30 minutes)
AGW level **37**	*AEGL-2* 92	*ERPG-2* 77		
LBW level **95**	*AEGL-3* 280	*ERPG-3* 390		

Stofdocument deel A

CAS-nr: 64-17-5 **Ethanol** **CH_3CH_2OH** **VN-nr: 1170**

GEVI: 33

Synoniemen: ethylalcohol, alcohol (Engels: ethanol) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	640	640	640	640	640	640
Alarmeringsgrenswaarden	AGW (mg/m³)	6.700*	6.700*	6.700*	6.700*	6.700*	6.700*
Levensbedreigende waarden	LBW (mg/m³)	NA	NA	NA	NA	NA	NA

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,521 ppm; 1 ppm = 1,918 mg/m³

Explosiegrens: 3,1 vol% ≈ 59.000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

Geur: zoete, typerende geur

LOA: 15,6 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,03

Molecuulmassa: 46,1 g/mol

Zuurgraad: -

LogKow: -0,3

Wateroplosbaarheid: volledig

Verzadigde dampdruk: 59 mbar

Overige informatie

Publieke grenswaarde: 260 mg/m³

MAK: 960 mg/m³

TLV-TWA: 1918 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: prikkeling, hoesten

VRW → AGW: hoofdpijn, opwinding, warmtegevoel

*Boven **AGW***: coördinatiestoornissen, bewustzijnsdaling, branderig gevoel achter het borstbeen, onderkoeling, ernstige bloeddrukdaling, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof kan irritatie van de luchtwegen veroorzaken.
- De stof kan inwerken op het centrale zenuwstelsel.
- Na inademen van hoge concentraties kan de stof aanleiding geven tot o.a. ontremming en opwinding gevolgd door bewustzijnsverlaging.

Effecten bij blootstelling aan vloeistof

Huidcontact: droge huid.

Oogcontact: prikkeling, roodheid, branderig gevoel, pijn.

Carcinogeniteit

IARC classificatie: 1

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, en arts raadplegen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, afspoelen met water.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 64-17-5 **Ethanol** **CH_3CH_2OH** **UN-nr: 1170**

Basis for the Dutch Intervention Values

VRW: Based on additional information to that described in ERPG-document, different values are derived, other time-points added

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added

LBW: Not recommended, in accordance with the ERPG.

Date: 31-10-2017 | ERPG 2010

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	640	640	640	640	640	640	Respiratory irritation in humans
AGW	6,700*	6,700*	6,700*	6,700*	6,700*	6,700*	Lacrimation and marked coughing in humans
LBW	NR	NR	NR	NR	NR	NR	Not recommended

* value higher than 10% of LEL

Derivation of the Dutch Intervention Values

VRW: VRW levels were based on results from a human volunteer study (see below under "additional toxicological information") in which 8 female and male volunteers were exposed in an inhalation chamber for 4 hour to up to 1000 ppm (1918 mg/m^3). No adverse systemic or local effects were observed, whereas repeatedly changing the concentration from 1900 to 100 ppm (3643 and 192 mg/m^3) (one hour for each exposure level, for 4 hours in total) in a second experiment caused temporary irritation. Symptoms included tickling in the throat; irritation of the eyes, nose, throat, skin; blurred vision; unpleasant taste and discomfort. These data are supported by a human volunteer study in which healthy subjects inhaled an aerosol of 25% ethanol in water for 30 min via a micronebulizer with ethanol air concentrations in inspired air varying from 0.18 to 0.20% (corresponding to 3452-3835 mg/m^3). All subjects had initial coughing which subsided, and a dry throat. Three of the six complained of chest tightness at the end of the 30-min period. There was no change in FEV_1. Subjects had a statistically significant decrease in flow rates on partial expiratory flow volume curves that lasted up to 90 minutes following inhalation.
A 4-hour exposure to 1918 mg/m^3 was selected as point of departure for deriving the VRW. These data were considered more reliable with respect to the applied exposure. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Timescaling was not applied. This approach was considered appropriate because mild irritation effects are considered concentration-dependent rather than concentration x time dependent.

AGW: Data from a inhalation study in human volunteers (number, gender and exposure duration not stated) indicate that concentrations greater than 40,000 mg/m^3 are intolerably irritating while at concentrations between 10,000 and 20,000 mg/m^3 some coughing and smarting of the eyes and nose occurred (which disappeared in 5 to 10 minutes, suggesting adaptation), and at 30,000 mg/m^3 continuous lacrimation and marked coughing occurred. The exposure to 20,000 mg/m^3 was selected as point of departure for AGW-values. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. In the second part of the study volunteers were exposed for 3 or 6 hours to 15000 mg/m^3 ethanol to determine a.o. blood concentration levels. Though this part of the study was not designed to establish clinical effects it does demonstrate that this concentration is tolerable for 3 to 6 hours. Since no increase of the effect is expected by extension of the exposure duration time-scaling was not applied.

LBW: Appropriate data for deriving LBW-values are not available. Results of acute inhalation studies show that the lowest lethal concentration reported is 12,700 ppm (24,353 mg/m^3) during a 22 hour exposure of rats, while rats exposed for 3.75 hours survived 45,000 ppm (86,291 mg/m^3). A rat LC_{50} was reported to be 20,000 ppm (38,352 mg/m^3) for 10 hours. The lowest reported lethal exposure in mice is 29,000 ppm (55,610 mg/m^3) after 7 hours of exposure, whereas the LC_{50}-value was 21,000 ppm (40,269 mg/m^3) after 4 hours. It is noted that the outcome of the acute animal studies are derived from secondary literature sources (i.e. other than ERPG-document). Details on study

methods are therefore not available. Moreover, selecting these animal data as point of departure would result in LBW-values that are in conflict with human data. Human exposure data (see AGW) show that one hour exposures to 30,000 mg/m^3 and 40,000 mg/m^3 cause marked eye and respiratory irritation, but did not result in systemic effects such as central nervous system depression. In absence of appropriate data, LBW-values were set at Not Recommended.

Additional toxicological information (including relevant results of a general literature search, if any)

Ethanol has an effect on the central nervous system and is irritating to the mucous membranes. Upon inhalation in humans, the irritating effects are more pronounced.

There are no data available on the effects on human reproduction after inhalation of ethanol. No clear effects of ethanol were observed in animal inhalation studies on reproduction (effects on fertility or on development).

Additional human data were derived from a report of the Health Council of the Netherlands (2006)[33]. In a human volunteer study (Seeber et al., 1997)[34], healthy volunteers were exposed in an exposure laboratory to ethanol by inhalation; this included two experiments. The first experiment focused on neurobehavioural effects and included exposure of 12 male and female subjects to 80, 400 and 800 ppm (153, 767, 1534 mg/m^3) ethanol for 4 hours. The second experiment included exposure of 8 male and female subjects to 1000 ppm (1918 mg/m^3) for 4 hours under three exposure conditions: 1918 mg/m^3 as a constant level and 1918 mg/m^3 as the average exposure with hourly changes of 100/1900/100/1900 ppm (192/3643/192/3643 mg/m^3) or 1900/100/1900/100 ppm (3643/192/3643/192 mg/m^3). No adverse effects on well-being (rated on a 7 points scale comprising tension, tiredness, complaints, and annoyance) were (self)reported. Increasing the concentration directly from 0 or 192 to 3,643 mg/m^3 caused temporary irritation. The female subjects gave a stronger response than the males. Symptoms included tickling in the throat; irritation of the eyes, nose, throat, skin; blurred vision; unpleasant taste and discomfort.

No harmonised H-sentences for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: 1 (carcinogenic to human)

No carcinogenic risk potency (CRP) was derived. Reliable inhalation data were not available.

Odour and derivation of the LOA value

Odour: sweet

Odour threshold: 0.997 mg/m^3 [Nagata, 2003]
LOA = 11.8 * OT * 1.33 = 15.6 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is below the VRW.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated) [35]

VRW level **640**	*AEGL-1* -	*ERPG-1* 3384		*IDLH:* 6329 mg/m^3 (30 minutes)
AGW level **6,700**	*AEGL-2* -	*ERPG-2* 6204		
LBW level **NR**	*AEGL-3* -	*ERPG-3* NR		

[33] Health Council of the Netherlands. Ethanol (ethyl alcohol); Evaluation of the health effects from occupational exposure. The Hague: Health Council of the Netherlands, 2006; publication no. 2006/06OSH
[34] Seeber A, Blaszkewicz M, Golka K, Kiesswetter E. Solvent exposure and ratings of well-being: dose-effect relationships and consistency of data. Environ Res 1997; 73(1-2): 81-91
[35] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 140-88-5 **Ethylacrylaat** **$CH_2=CHCOOC_2H_5$** **VN-nr: 1917**
GEVI: 339

Synoniemen: acrylzuur ethylester, ethyl-2-propenoaat (Engels: Ethyl acrylate) ***Status***: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	320	140	81	47	28	16
Alarmeringsgrenswaarden	AGW (mg/m³)	960	410	240	140	84	49
Levensbedreigende waarden	LBW (mg/m³)	3900	1700	990	500	290	170

Datum vaststelling: 13-05-2009 Conversiefactor: 1 mg/m³ = 0,240 ppm; 1 ppm = 4,16 mg/m³

Explosiegrens: LEL = 1,7 vol% ≈ 71.000 mg/m³

Geur: Aardachtige, bijtende, plastic-achtige geur
LOA: 0,16 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,1

Molecuulmassa:	100,1 g/mol
Zuurgraad:	Geen data
LogKow:	1,4
Wateroplosbaarheid:	2 g/100 ml (matig)
Verzadigde dampdruk:	39 mbar

Overige informatie

Publieke grenswaarde: 21 mg/m³ (8 uur)
MAK: 21 mg/m³
TLV-TWA: 21 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: mogelijk lichte irritatie

VRW → AGW: oog-, neus- en huidirritatie.

AGW → LBW: luchtwegirritatie, benauwdheid, longoedeem, duizeligheid, verminderde reflexen, lever- en nierschade

Boven LBW: ademnood, convulsies, cardiovasculaire collaps, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Ethylmethacrylaat werkt irriterend op de ogen, huid en bovenste en onderste luchtwegen.
- Ethylmethacrylaat heeft effecten op het centrale zenuwstelse.
- Ethylmethacrylaat kan bij hoge concentraties schade veroorzaken aan lever en nieren.
- De stof is sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact! Kruisgevoeligheid met andere monoacrylaten is mogelijk!

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren

Oogcontact: bijtend, roodheid en pijn, slecht zien

Carcinogeniteit

IARC classificatie: 2B (orale blootstelling)
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 140-88-5 **Ethyl acrylate** **CH_2=CHCOOC_2H_5** **UN-nr:1917**

Basis for the Dutch Intervention Values

VRW: Same point of departure as for AEGL values but difference in time scaling , 2-hr value added

AGW: Same point of departure as for AEGL values but difference in time scaling, 2-hr value added

LBW: AEGL values were adopted, 2-hr value added

Date: 13-05-2009 | AEGL document: Interim, 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	320	140	81	47	28	16	Reversible lesions in the olfactory epithelium in rats
AGW	960	410	240	140	84	49	Reversible lesions in the olfactory epithelium in monkeys
LBW	3900	1700	990	500	290	170	$BCML_{05}$ for lethality in the rat

Derivation of the Dutch Intervention Values

VRW: Limited data were available upon which to base VRW values. A concentration of 25 ppm (104 mg/m³) resulted in reversible lesions of the olfactory epithelium in rats after 3 hours. This same concentration did not result in any effects in monkeys following repeated exposures, but slight irritation was reported for dogs at this concentration. Therefore, 25 ppm (104 mg/m³) was chosen as a probable threshold for VRW effects. A total uncertainty factor of 3 was used including a 1 for interspecies extrapolation and 3 for intraspecies extrapolation. Use of greater uncertainty factors was not necessary because the lesion is reversible, the mechanism of irritation is not expected to differ between individuals, and similar lesions were found in monkeys, guinea pigs, rabbits, and rats. Data were scaled across time using $C^n \times t = k$, using n=1.3 (see derivation LBW values). In contrast, AEGL values were not scaled across time, however the data indicate that the severity of the effect increased with exposure time, hence time scaling was considered appropriate.

AGW: Data in humans relevant to derivation of AGW values were not found. No serious, long lasting health effects were reported. Prolonged exposure (not defined) to 50-75 ppm (210-310 mg/m³) has been reported to produce drowsiness, headache, and nausea; no further details could be found. Exposure of monkeys to 75 ppm (310 mg/m³) for 3 hours, which resulted in damage to 15% of the olfactory epithelium, was used to derive AGW values. A total uncertainty factor of 3 was used including a factor 1 for interspecies extrapolation and a factor 3 for intraspecies extrapolation. Use of greater uncertainty factors was not necessary because the lesion is reversible, the mechanism of irritation is not expected to differ between individuals, and similar lesions were found in monkeys, guinea pigs, rabbits, and rats. Data were scaled across time using $C^n \times t = k$. In contrast to the AEGL values where default values for n were used, the substance specific n-value of 1.3 was used for time scaling (see derivation LBW values).The AGW values are less than those reported to produce drowsiness, headache, and nausea in humans.

LBW: Animal data relevant to derivation of LBW values are limited to 1- and 4-hour LC_{50} studies in rats. These were well conducted studies with analytically determined exposure concentrations. Clinical signs of irritation were observed in animals during exposure and death was attributed to cardiopulmonary collapse. Calculated LC_{50} values were 6493 ppm (27035 mg/m³) for 1 hour and 2180 ppm (9077mg/m³) for 4 hours. From these data, 1- and 4- hour $BMCL_{05}$ values were calculated by a log-probit analysis using US EPA Benchmark Dose Software version. The resulting 1-hour $BMCL_{05}$ of 2387 ppm (9939 mg/m³) was used to derive the 10- minute, 30-minute, and 1-hour LBW values. The resulting 4-hour $BMCL_{05}$ of 706 ppm (2940 mg/m³) was used to derive the 2-, 4-, and 8-hour LBW values. The 4-hour was used to derive the 2-hour value because it results in the lowest value. Time scaling was performed using the equation $C^n \times t = k$, with n=1.3 (calculated by combining the 1- and 4- hour LC_{50} data sets in 3-dimensional probit analysis). A total uncertainty factor of 10 was used including a factor 3 for interspecies extrapolation and a factor 3 for intraspecies extrapolation. Use of greater uncertainty factors was not necessary because the mechanism of irritation is not expected to differ between individuals and similar lesions were found in

monkeys, guinea pigs, rabbits, and rats.

Additional toxicological information (including relevant results of a general literature search, if any)

Irritant to the mucus membranes. The target within the respiratory tract was shown to be the olfactory epithelium lining the dorsal meatus in both monkeys and rats. Both the severity and extent of the lesions were concentration and time dependent. Metabolism and subsequent removal of the chemical by carboxylesterase in the upper respiratory tract reduces the toxicity by reducing systemic uptake and by preventing the chemical from getting to the lower respiratory tract. At lethal concentrations, death was attributed to cardiopulmonary collapse, and was accompanied by cloudy swelling and/or congestion of other visceral organs.

No reports of developmental or reproductive toxicity in humans were found. Developmental toxicity in rat studies show that the fetus may be affected at maternally toxic concentrations.

H302: Harmful if swallowed; H312: Harmful in contact with skin; H315: Causes skin irritation; H317: May cause an allergic skin reaction; H319: Causes serious eye irritation; H332: Harmful if inhaled; H335: May cause respiratory irritation.

Carcinogenicity and derivation of the CRP value

IARC classification: 2B (possibly carcinogenic to humans)

No carcinogenic risk potency (CRP) was derived

Route specific tumors have been found in the forestomach following oral administration, but none were found following inhalation exposure.

Odour and derivation of the LOA value

Odour: pungent, disagreeable, acid

Odour thresholds of 0.00024 ppm (0.0010 mg/m^3) for detection and 0.00037 ppm (0.00154 mg/m^3) for recognition were reported [AEGL (2007); U.S. EPA (1992)].

LOA = 11.8 * OT_{50} * 1.33 = 0.16 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is far below the VRW values

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level 81	*AEGL-1* 35	*ERPG-1* 0.04		*IDLH*: 1250 (30 minutes)
AGW level 240	*AEGL-2* 150	*ERPG-2* 120		
LBW level 990	*AEGL-3* 1000	*ERPG-3* 1200		

Stofdocument deel A

CAS-nr: 75-04-7 **Ethylamine** **CH_3-CH_2-NH_2** **VN-nr: 2270** **GEVI: 338**

Synoniemen: 1-aminoethaan, ethaanamine, MEA (Engels: ethylamine) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	28	28	28	28	28	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	280	140	92	60	41	26
Levensbedreigende waarden	LBW (mg/m³)	1500	790	510	330	230	140

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,533 ppm; 1 ppm = 1,88 mg/m³

Explosiegrens: LEL = 2,3 vol% ≈ 43.000 mg/m³

Geur: Scherpe ammoniak-achtige geur

LOA: 1,35 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot gele oplossing

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,3

Molecuulmassa:	45,1 g/mol
Zuurgraad:	pK_a 10,71 bij 25°C
LogKow:	-0,1
Wateroplosbaarheid:	volledig
Verzadigde dampdruk:	460 mbar

Overige informatie

Publieke grenswaarde: 9 mg/m³ (8 uur)
MAK: 9,4 mg/m³
TLV-TWA: 9,4 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	mogelijk blauw en/of wazig zicht en het zien van halo's rond lichtbronnen
VRW → AGW:	oog-, huid- en bovenste luchtwegirritatie, hoesten, niezen, tranenvloed
AGW → LBW:	onderste luchtwegirritatie, benauwdheid, longoedeem, verlies van gezichtsvermogen, verminderde coördinatie, apathie
Boven LBW:	convulsies, ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Ethylamine werkt irriterend tot bijtend op de ogen, de huid en de luchtwegen, waarschijnlijk door het sterk alkalische karakter van de stof.
- Depressie van het centraal zenuwstelsel kan ontstaan.
- Inademing kan, uitsluitend na verschijnselen van bijtende effecten op de slijmvliezen van de ogen en/of hogere luchtwegen, longontsteking en/of longoedeem veroorzaken. Dit kan pas na enkele uren optreden en versterkt worden door lichamelijke inspanning.
- Expositie van de ogen aan het gas kan verlies van cornea-epitheel en cornea oedeem veroorzaken.
- In ernstige gevallen bestaat kans op verstikking door zwellingen in de keel.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, branderig gevoel, ernstige brandwonden, mogelijk ernstige bevriezings-verschijnselen zoals pijn, blaren, wonden.
Stof kan door de huid worden opgenomen.

Oogcontact: wazig en blauw zicht, bijtend, tranenvloed, slecht zien, ernstige brandwonden, permanent verlies van gezichtsvermogen

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen:	frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
ogen:	kort uitspoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen (zie opmerking hieronder).

Ontsmetting vloeistof

huid:	aan de huid vastgevroren kleding NIET lostrekken, spoelen met veel water / kleding uittrekken en onmiddellijk arts raadplegen.
ogen:	minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken:	n.v.t. (gas).

Specifieke behandeling en materialen:
Neem contact op met het NVIC (Tel: +31 (0)30 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 75-04-7 **Ethylamine** **CH_3-CH_2-NH_2** **UN-nr: 2270**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 16-12-2010 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	28	28	28	28	28	NR	Analogy with methylamine; mild (nasal) irritation in rats
AGW	280	140	92	60	41	26	Same ratio between LBW and AGW as for methylamine
LBW	1500	790	510	330	230	140	Threshold for lethality in rats

Derivation of the Dutch Intervention Values

VRW:

In the absence of data that address VRW level effects of ethylamine, the data on other alkylamines were considered. Because ethylamine and methylamine are both primary amines with similar toxicity values, the VRW for ethylamine was based on the VRW for methylamine on a ppm basis.

The VRW for methylamine was based on a rat study. Point of departure was a single 6-hour exposure to 75 ppm. Exposures were actually repeated for two-weeks (10 exposures) and resulted in mild irritation of the nasal turbinates. Repeat exposure to higher concentrations (250 ppm and/or 750 ppm) caused more severe nasal lesions and /or systemic toxicity and mortality. A single 6-hour exposure to 75 ppm is expected to cause no more than mild irritation. A total uncertainty factor of 10 was applied to the point of departure, including 3 for interspecies uncertainty and 3 for human variability, because mild nasal irritation from an alkaline irritant gas is a direct surface-contact effect not involving metabolism, and is not likely to vary greatly between species or among humans. A modifying factor of 0.5 was used since the point of departure was a repeated exposure. Application of these uncertainty and modifying factors to point of departure yields a VRW value for methylamine of 15 ppm. The resulting VRW value of 15 ppm was adopted for 10 minutes to 8 hours because mild sensory irritation is not expected to vary greatly over time.

The VRW is supported by human data for the structurally related compounds diethylamine and dimethylethylamine, which caused eye and nasal irritation and/or vision disturbances in healthy adults at approximately 10 ppm diethylamine and dimethylethylamine.

AGW:

In the absence of empirical data for ethylamine that fall within the scope of the AGW, the AGW values for ethylamine were based on analogy with methylamine. Ethyl- and methylamines are both primary amines and have similar toxicity.

The LBW and AGW values for methylamine were based on the threshold for lethality and severe irritation, respectively. The ratio between 1 hour LBW and AGW values for methylamine was used to modify the LBW values for ethylamine in order to derive AGW values. The ratio between the 1-hour LBW and AGW values for methylamine was 5.5. Thus a modifying factor of 5.5 was applied to the LBW values for ethylamine to derive the AGW values.

LBW:

The LBW was based on lethality data from a study in which rats (5/sex/dose; 48-76 days old) were exposed to concentrations of 14,000-24,000 ppm (26,000-45,000 mg/m³) for 6 minutes, 8200-12,900 ppm (15,000-24,200 mg/m³) for 20 minutes, or 4100-7050 ppm (7700-13,200 mg/m³) for 60 minutes. The probit-analysis based dose-response program of ten Berge was used to calculate the LC_{01} at each LBW exposure duration. The program incorporated all of the data at the 6-, 20-, and 60-minute time points. The data indicated a time-scaling value of n=1.6. A total uncertainty factor of 10 was applied, including 3 for interspecies uncertainty and 3 for human variability, because lethality from an alkaline irritant gas is a direct surface-contact effect not involving metabolism, and is not likely to vary greatly between species or among humans. Time scaling was applied to derive a 2-hour LBW,

using the equation $C^n \times t = k$.

Additional toxicological information (including relevant results of a general literature search, if any)

Ethylamine is a potent eye and respiratory irritant, which in humans has caused vision disturbances ("halo vision" due to corneal edema). Animal studies consistently found eye and respiratory irritation, corneal erosions, edema, and opacity, labored breathing, rales, peribronchitis, pneumonitis, and lung lesions. The mechanism of ethylamine toxicity has not been elucidated, although its irritant properties are likely related to its high alkalinity and corrosiveness to exposed tissues such as skin, eyes, and the respiratory mucosa.

Ethylamine of undefined concentration was stated to cause "blue haze – a thin blue film on the cornea" in occupationally exposed workers. Other aliphatic amines (e.g. diethylamine, triethylamine, dimethylamine, dimethylethylamine) have also been reported to cause similar visual effects after exposure for several hours (hazy vision, blurred objects, blue halo's). These effects were due to edema of the corneal epithelium. A group of amines has been reported to cause vision disturbances in workers exposed for several hours to concentrations too low to cause discomfort or disability.

No data were found on developmental or reproductive toxicity of ethylamine.

H319: Causes serious eye irritation; H335: May cause respiratory irritation.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

No carcinogenicity studies of ethylamine were located. A short-term test designed to predict the carcinogenic potential of compounds by their ability to inhibit DNA replication in mouse testes yielded negative results.

Odour and derivation of the LOA value

Odour: pungent ammonia-like odour

OT_{50}: 0.046 ppm (0.086 mg/m^3) [AEGL (2008); Ruijten (2005)]

LOA = 11.8 * OT_{50} * 1.33 = 1.35 mg/m^3

(The concentration Level leading to distinct Odour Awareness (l=3) is calculated using the formula: $l = 2.33 * \log (C/OT_{50}) + 0.5$. A correction factor of 1.33 is applied to this value)

The LOA is below the VRW; therefore subjects can be aware of the odour below the level where health effects may be expected.

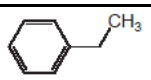
Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **28**	*AEGL-1* 14	*ERPG-1* not derived		*IDLH*: 1130 (30 minutes)
AGW level **92**	*AEGL-2* 92	*ERPG-2* not derived		
LBW level **510**	*AEGL-3* 507	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 100-41-4
C_8H_{10}

Ethylbenzeen



VN-nr: 1175
GEVI: 33

Synoniemen: ethylbenzol, fenylethaan, α-methyltolueen (Engels: ethylbenzene)

Status: geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	150	150	150	150	150	150
Alarmeringsgrenswaarden	AGW (mg/m³)	13.000*	7.100*	4.900	3.500	2.900	2.600
Levensbedreigende waarden	LBW (mg/m³)	21.000*	11.000*	8.000*	5.900*	4.400	4.000

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,226 ppm; 1 ppm = 4,42 mg/m³

Explosiegrens: LEL= 1,2 vol% ≈ 53.000 mg/m³
* berekende interventiewaarde hoger dan 10% LEL

Geur: aromatisch, typerend
LOA: 11,8 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,00

Molecuulmassa: 106,2 g/mol

Zuurgraad: geen data
LogKow: 3,6

Wateroplosbaarheid: zeer slecht oplosbaar

Verzadigde dampdruk: 9,5 mbar

Overige informatie

Publieke grenswaarde:
215 mg/m³ (H)
MAK: 88 mg/m³ (H)
TLV-TWA: 88 mg/m³ (H)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen klachten

VRW → AGW: irritatie van luchtwegen en ogen, hoofdpijn, opwinding, onrust, slaperigheid, lichte duizeligheid

AGW → LBW: ernstige irritatie van de luchtwegen en ogen, duizeligheid, sufheid, bewustzijnsdaling

Boven LBW: coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Ethylbenzeen werkt irriterend op de slijmvliezen van de luchtwegen
- Blootstelling aan hoge concentraties ethylbenzeen kan leiden tot kortdurende CZS excitatie gevolgd door depressie van het CZS.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, droge huid, pijn

Oogcontact: roodheid en pijn, tranenvloed

Carcinogeniteit

IARC classificatie: 2B
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, en onmiddellijk arts raadplegen.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), bij aanhoudende irritatieklachten (oog)arts raadplegen.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

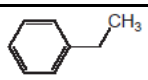
***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 100-41-4
C_8H_{10}

Ethylbenzene



UN-nr: 1175

Basis for the Dutch Intervention Values

VRW: AEGL value adopted, 2h value added

AGW: AEGL value adopted, 2h value added

LBW: AEGL value adopted, 2h value added

Date: 16-10-2018 | AEGL 2009 (interim)

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	150	150	150	150	150	150	Eye and respiratory tract irritation in humans
AGW	13,000 *	7,100*	4,900*	3,500	2,900	2,600	CNS effects: narcosis in rats
LBW	21,000 *	11,000 *	8,000*	5,900*	4,400	4,000	Lethality in rats

* value higher than 10% of LEL

Derivation of the Dutch Intervention Values

VRW: VRW values were based on human exposure data. Nine human volunteers were exposed to a concentration of 100 ppm (442 mg/m^3) ethylbenzene for 8 hours in an exposure chamber. No clinical signs were observed. In another study, 11 human volunteers were exposed to 180 ppm (795 mg/m^3) for 8 hours which resulted in reported symptoms of irritation of the upper respiratory tract and eye, headache, sleepiness and transient feelings of drunkenness towards the end of the exposure. Exposure to 442 mg/m^3 was used as a NOEL for irritation. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was not applied as mild irritation is considered to be concentration-dependent rather than concentration x time-dependent.

AGW: AGW values were derived from animal data. Male CFY rats (n=8/concentration) were exposed for 4 hours in whole-body inhalation chambers to concentrations of 400 – 2180 ppm (1767 – 9631 mg/m^3) and monitored for motor activity. Up to a concentration of 1500 ppm (6626 mg/m^3), increased activity was observed while at higher concentrations decreased activity was observed. Exposure to 9631 mg/m^3 was listed as a minimum narcotic concentration. Therefore, a 4-hour exposure to 6626 mg/m^3 was taken as a point of departure as the highest non-narcotic concentration. As the central nervous system response following exposure to ethyl benzene is assumed to be directly related to the venous blood concentration, the internal dose was modelled using a rat PBPK model (see AEGL technical support document for figure). The default intraspecies uncertainty factor of 3 was considered sufficient. An interspecies UF of 1 was considered sufficient because of the use of PBPK modeling (which accounted for some of the kinetic differences) and similarity of effects in rats and humans. The total UF of 3 was applied within a human PBPK model, which was then used to calculate equivalent exposure concentrations for each time point. The 2-hour AGW value was obtained by interpolation from the curve of modelled AGW-values.

LBW: LBW values were derived from an animal study in which male rats (n=6/concentration level) were whole body exposed to 2000 ppm (8835 mg/m^3) for 6 hours on 3 consecutive days. No mortality occurred. This point of departure is supported by another study where rats were exposed to 2000 ppm (8835 mg/m^3), 4000 ppm (17,670 mg/m^3) or 8000 ppm (35,340 mg/m^3) for four hours. Mortality was 6/6 at the highest concentration, 3/6 at the middle concentration and 0/6 at the lowest concentration. The highest non-lethal exposure to 8835 mg/m^3 for 6 hours in rats was used to derive the LBW values. As for the AGW, because the central nervous system response following exposure to ethyl benzene is assumed to be directly related to the venous blood concentration, the internal dose was modeled using a rat PBPK model. The default intraspecies uncertainty factor of 3 was considered sufficient. An interspecies UF of 1 was considered sufficient because of the use of PBPK modeling (which accounted for some of the kinetic differences) and similarity of effects in rats and humans. The total UF of 3 was applied within a human PBPK model, which was then used to

calculate equivalent exposure concentrations for each time point. The 2-hour LBW value was obtained by interpolation from the curve of modelled LBW-values.

Additional toxicological information (including relevant results of a general literature search, if any)

Ethylbenzene is rapidly absorbed and excreted. Excretion occurs mainly as mandelic and phenylglyoxylic acids via urine. The two primary effects of ethylbenzene are irritation of the mucous membranes and central nervous system effects. Ethylbenzene is able to cross the blood-brain barrier and rapidly causes CNS effects, which is likely due to direct interaction of the substance with molecular receptors in the CNS. The cochlear duct in the inner ear may also be a target organ, however, no data were found on ototoxicity after single exposure.

Developmental toxicity studies in rats and rabbits did not indicate an increased sensitivity of the developing fetus. However, reproductive toxicity studies in rats indicate that weanling rats are more sensitive than adults, probably because of lower body weight.

H332: Harmful if inhaled; H304: May be fatal if swallowed and enters airways; H373: Specific organ toxicity (hearing organs)

Carcinogenicity and derivation of the CRP value

IARC classification: 2B (possibly carcinogenic to humans)

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: aromatic odour.

In contrast to the AEGL a LOA was derived.

OT: 0.75 mg/m^3 [Nagata 2003]
LOA = 11.8 * 0.75 * 1.33 = 11.8 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies well below all intervention values.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [36]

VRW level **150**	*AEGL-1* 144	*ERPG-1* -		*IDLH:* 800 ppm (3500 mg/m^3) (30 minutes)
AGW level **4900**	*AEGL-2* 4800	*ERPG-2* -		
LBW level **8000**	*AEGL-3* 7800	*ERPG-3* -		

[36] Note that the AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL.

Stofdocument deel A

CAS-nr: 541-41-3 **Ethylchloorformiaat** **ClCOO-C_2H_5** **VN-nr: 1182**

GEVI: 663

Synoniemen: chloormierenzuur ethylester, ethylchloorcarbonaat, ethylchloormethanaat (Engels: Ethyl chloroformate)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	17	12	9,4	4,7	2,4	1,2
Levensbedreigende waarden	LBW (mg/m³)	51	36	28	14	7	3,5

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,222 ppm; 1 ppm = 4,51 mg/m³

Explosiegrens: LEL = 3,2 vol% ≈ 144.000 mg/m³

Geur: scherp

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot gele vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,2

Molecuulmassa: 108,5 g/mol
Zuurgraad: Geen data
LogKow: 0,6
Wateroplosbaarheid: reactie
Verzadigde dampdruk: 55 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: irritatie van de ogen en luchtwegen

AGW → LBW: ernstige irritatie van de ogen en luchtwegen, tranenvloed, keelpijn, hoesten, speekselvloed, druk op de borst, piepende ademhaling, benauwdheid, longoedeem

Boven LBW: ademnood, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Ethylchloorformiaat werkt bijtend op ogen en luchtwegen.
- Ethylchloorformiaat kan longoedeem veroorzaken, waarbij de verschijnselen pas na enkele uren kunnen optreden en versterkt kunnen worden door lichamelijke inspanning.
- Ethylchloorformiaat ontleedt in aanwezigheid van water of vochtige lucht in chloorwaterstof, CO_2, ethanol.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, brandwonden

Oogcontact: bijtend, tranenvloed, roodheid en pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen, zo nodig arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen:.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 541-41-3 **Ethyl chloroformate** **ClCOO-C_2H_5** **UN-nr: 1182**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: Same rationale as for AEGL (one-third of LBW), 2h value added

LBW: Different point of departure as for AEGL, 2h value added

Date: November 2015 | AEGL document: Interim, 2008

Proposal for the Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Insufficient data
AGW	17	12	9.4	4.7	2.4	1.2	3-fold reduction of LBW values
LBW	51	36	28	14	7	3.5	Estimated lethality threshold in the rat

Derivation of the Dutch Intervention Values

VRW: VRW values for ethyl chloroformate are not recommended due to insufficient data. Absence of VRW values does not imply that exposure below the AGW value is without adverse effects.

AGW: No acute inhalation data consistent with the definition of AGW with both exposure concentration and duration parameters were available. Therefore, the AGW values for ethyl chloroformate are based upon a 3-fold reduction of the LBW values; this is considered an estimate of a threshold for irreversible effects. This approach is justified based on the steep concentration curve with regard to lethality (1-hour rat LC_{50}: 189-200 ppm (853-903 mg/m³); rats exposed to 47 ppm (212 mg/m³) for 1-hour were clinically normal and showed no mortality).

LBW: In contrast to AEGL, the LBW-values were based on a different rat lethality study (Fischer et al (1981)). This alternative study was selected to be in line with the Dutch Probit for ethyl chloroformate. A 1-h LC_{50} value of 848 mg/m³ was derived (sexes combined). One-third of this value (283 mg/m³) was used as the point-of-departure for the derivation of ethyl chloroformate LBW values. This concentration is considered a threshold for lethality. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n \times t = k$, with default values of n=1 and n=3 when extrapolating to longer and shorter exposure durations, respectively. The resulting LBW-values are supported by read-across using data of methyl chloroformate.

Additional toxicological information (including relevant results of a general literature search, if any)

Data concerning human exposure to ethyl chloroformate are limited to one occupational case report lacking exposure concentration and duration information. This report suggests that ethyl chloroformate is a respiratory tract irritant and is capable of inducing delayed pulmonary edema.

Chloroformates hydrolyze in water or moist air to produce the parent hydroxy compound, hydrogen chloride, carbon dioxide, and a carbonate. They are direct-acting contact irritants, and are corrosive to the eyes, skin, gastrointestinal and respiratory tracts. Inhalation may result in coughing, labored breathing, sore throat, unconsciousness, convulsions, and death. Lung edema frequently occurs, and symptoms of this may not manifest for several hours after exposure and may be aggravated by physical exertion. Ingestion may result in a burning sensation of the digestive tract, nausea, vomiting, and abdominal pain.

No reports regarding developmental/reproductive toxicity of ethyl chlorofomate were found

H302: Harmful if swallowed. H314: Causes severe skin burns and eye damage. H330: Fatal if inhaled

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Carcinogenicity data in Swiss mice suggest that ethyl chloroformate may be a tumor promoter by the dermal

Odour and derivation of the LOA value

Odour: sharp

No LOA was derived due to lack of information.

route.	

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* ID		*IDLH:* not derived
AGW level **9.4**	*AEGL-2* 7.2	*ERPG-2* 23		
LBW level **28**	*AEGL-3* 22	*ERPG-3* 45		

ID: Insufficient data

Stofdocument deel A

CAS-nr: 107-15-3

Ethyleendiamine

$H_2NCH_2CH_2NH_2$

VN-nr: 1604

GEVI: 83

Synoniemen: 1,2-diaminoethaan, 1,2-ethaandiamine, dimethyleendiamine (Engels: Ethylenediamine)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	150	100	81	64	51	40
Levensbedreigende waarden	LBW (mg/m³)	450	320	250	200	160	130

Datum vaststelling: 13-05-2009

Conversiefactor: 1 mg/m³ = 0,400 ppm; 1 ppm = 2,50 mg/m³

Explosiegrens: LEL = 2,5 vol% ≈ 62500 mg/m³

Geur: ammoniak-achtige, muffe geur

LOA: 5,2 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot lichtgele hygroscopische vloeistof, aan vochtige lucht rokend
Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,02

Molecuulmassa:	60,1 g/mol
Zuurgraad:	pKa1 = 10.7 pKa2 = 7.6
LogKow:	-2
Wateroplosbaarheid:	volledig
Verzadigde dampdruk:	15 mbar

Overige informatie

Publieke grenswaarde:

niet afgeleid

MAK: niet afgeleid

TLV-TWA: 25 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: mogelijke lichte irritatie van slijmvliezen van ogen en bovenste luchtwegen

AGW → LBW: irritatie slijmvliezen ogen en luchtwegen, longoedeem

Boven LBW: sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Ethyleendiamine veroorzaakt sterke irritatie van ogen, slijmvliezen en luchtwegen.
- Ethyeeldiamine kan longoedeem veroorzaken, echter uitsluitend na verschijnselen van irriterende effecten op de slijmvliezen van ogen en/of hogere luchtwegen.
- De stof is sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact!

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn, branderig gevoel. De stof kan via de huid worden opgenomen.

Oogcontact: *bijtend*, roodheid en pijn, tranenvloed, slecht zien.

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en arts raadplegen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), actieve kool (carbomix) toedienen, GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 107-15-3 **Ethylenediamine** **$H_2NCH_2CH_2NH_2$** **UN-nr: 1604**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with the AEGL

AGW: Same point of departure as for AEGL, different uncertainty factors, 2-hr value added

LBW: Same point of departure as for AEGL, different uncertainty factors, 2-hr value added

Date: 13-05-2009 AEGL document: Final, 2005

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	150	100	81	64	51	40	Bronchiolar edema and kidney swelling in animals
LBW	450	320	250	200	160	130	Threshold of lethality in rats

Derivation of the Dutch Intervention Values

VRW: VRW values were not recommended due to insufficient data.

AGW: AGW values were based on a study in which rats and guinea pigs (6/group) were exposed to approximately 484 ppm (1210 mg/m³) for 30 minutes to 8 hours. Both species exposed for 8 hours had bronchiolar edema of unspecified severity and “light cloudy swelling of the kidney”. An uncertainty factor of 3 was used for interspecies variability because a similar response was seen in two species, and a modifying factor of 3 was used because the key study did not specify the severity of the bronchiolar edema. An intraspecies uncertainty factor of 3 was applied. Timescaling was performed using the equation $C^n \times t = k$ and n=3 (default). In contrast to the 10 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: LBW values were derived from a range-finding test in which 0/6 rats died from exposure for 8 hours to 1000 ppm (2500 mg/m³) but 6/6 died from 8-hour exposure to 2000 ppm (5000 mg/m³). Toxic effects (other than death) were not described, and 1000 ppm (2500 mg/m³) was considered to be the lethality threshold. This was the only single-exposure study adequate for LBW derivation. A total uncertainty factor of 20 was applied: 3 for interspecies variability and 3 for intraspecies variability and a modifying factor of 2 for the uncertainties in the used data (a.o. concentrations). Data were not available to determine the concentration-time relationship, and scaling across time was performed using the equation $C^n \times t = k$ and n=3 (default). In contrast to the 10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Ethylenediamine is an eye, mucous membrane, and respiratory irritant and a known respiratory and skin sensitizer. Sensitized individuals may experience more severe and/or different effects at a given exposure concentration or duration than non-sensitized people respiratory irritation and asthma-like symptoms were described in individuals exposed to concentrations ranging from < 1 ppm (2,5 mg/m³) during a workday to 30 ppm (75 mg/m³) for 15 minutes.

No relevant information on reproductive and developmental toxicity with regard to the derivation of the AGW values.

H302: Harmful if swallowed; H312: Harmful in contact with skin; H314: Causes severe skin burns and eye damage; H317: May cause an allergic skin reaction; H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled.

Carcinogenicity and derivation of the CRP value
IARC classification: not classified No carcinogenic risk potency (CRP) was derived. No inhalation carcinogenicity studies were located and animal dietary and skin painting studies yielded negative results.

Odour and derivation of the LOA value
Odour: ammonia like OT_{50}: 0.133 ppm (0.33 mg/m^3) [AEGL (2007); Hellman and Small (1974)] LOA = 11.8 * OT_{50} * 1.33 = 5.2 mg/m^3 (The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value) The LOA is below the AGW, therefore subjects will be aware of the odour below the level where health effects may be expected.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)				
VRW level NR	*AEGL-1* NR	*ERPG-1* not derived		*IDLH:* 2500 (30 minutes)
AGW level 81	*AEGL-2* 24	*ERPG-2* not derived		
LBW level 250	*AEGL-3* 50	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 106-93-4 **Ethyleendibromide** **$BrCH_2CH_2Br$** **VN-nr: 1605**

GEVI: 66

Synoniemen: 1,2-dibroomethaan, EDB (Engels: ethylene dibromide) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	65	65	65	65	65	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	970	430	260	150	93	56
Levensbedreigende waarden	LBW (mg/m³)	2900	1300	770	460	280	170

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,128 ppm; 1 ppm = 7,82 mg/m³

Explosiegrens: geen data

Geur: scherp, zoete, chloroformachtige geur

LOA: 1.200 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,08

Molecuulmassa:	187,9 g/mol
Zuurgraad:	geen data
LogKow:	1,9
Wateroplosbaarheid:	0,4 g/100 ml (slecht)
Verzadigde dampdruk:	15 mbar

Overige informatie

Publieke grenswaarde: 0,002 mg/m³
MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW: lichte irritatie van ogen en neus

AGW → LBW: irritatie van de luchtwegen, misselijkheid, braken, duizeligheid, diarree, ademhalingsdepressie, sufheid

Boven LBW: longontsteking en –oedeem, lever- en nierschade, coma en sterfte

LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt irriterend op de ogen, de huid en de luchtwegen.
- Blootstelling aan (zeer hoge concentraties) ethyleendibromide kan longoedeem en chemische pneumonitis veroorzaken.
- De stof kan inwerken op de lever, de nieren en het centrale zenuwstelsel met als gevolg functiestoornissen en orgaanschade.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn. De stof wordt door de huid opgenomen!

Oogcontact: roodheid en pijn, (reversibele) hoornvliesbeschadiging

Carcinogeniteit

IARC classificatie: 2A
CRP: 37 mg/m³

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en onmiddellijk arts raadplegen

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen.

ogen: zie hierboven.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 106-93-4 **Ethylene dibromide** **$BrCH_2CH_2Br$** **UN-nr: 1605**

Basis for the Dutch Intervention Values

VRW: Different point of departure as AEGL, different uncertainty factors, 2h value added

AGW: Different point of departure as AEGL, 2h value added

LBW: Different point of departure as AEGL, different uncertainty factors, 2h value added

Date: 06-10-2016 | AEGL document: interim, 2008

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	65	65	65	65	65	NR	Neurotoxicity in monkeys
AGW	970	430	260	150	93	56	LBW-values divided by three
LBW	2900	1300	770	460	280	170	Threshold for lethality in rats

Derivation of the Dutch Intervention Values

VRW: VRW levels were based on repeated exposure of monkeys to 50 ppm (391 mg/m^3), 7 hours/day for 49 exposures in 70 days. Effects indicative of neurotoxicity was observed throughout the study where monkeys exposed similarly to 25 ppm (196 mg/m^3) showed no effects. It is noted that the neurotoxic effects were already observed at the first day of exposure. A total uncertainty factor or 3 (see LBW rationale) was applied. The VRW was set equal for all time points because CNS-effects are generally concentration-dependent but not time-dependent. The 8h VRW was not recommended due to conflict with the AGW level.

AGW: Due to lack of suitable data consistent with AGW-level effects, the LBW values were divided by 3

LBW: The derivation of the LBW values was based on an acute inhalation study in rats in which rats were exposed to ethylene dibromide in concentrations ranging from 100 to 10000 ppm (782 – 78200 mg/m^3) for exposure durations up to 16h. These data were analysed using Doseresp and the resulting LC_{01} values were 8707, 3872, 2322, 1393, 835 and 501 mg/m^3 for 10 min, 30 min, 1 hour, 2 hour, 4 hour and 8 hour with an n-value of 1.4. An uncertainty factor of 1 is used for the interspecies sensitivity, because similar effects and mode of actions were shown for various species (rodents, non-human primates and humans). Furthermore, PBPK modeling indicates that rats exposed to ethylene dibromide take up about three times more of the substance than humans and rats produce about five times more active metabolites from the P450 pathway when exposed to the substance than humans do. Rats also were predicted to produce about 80 times more GST metabolites than humans. The toxic effects of inhaling 1,2-dibromoethane are similar in humans and rats indicating similar pharmacodynamics. The difference in metabolite production would overwhelm any difference in pharmacodynamics, therefore an uncertainty factor of 1 is justified for interspecies variability. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. This default intraspecies factor of 3 will cover a variability in the human population of a factor 10. Therefore, there is no reason to deviate from the default intraspecies uncertainty factor of 3.

Additional toxicological information (including relevant results of a general literature search, if any)

When ethylene dibromide is metabolized, two reactive metabolites are produced. The metabolites of the P450 pathway bind to protein and the metabolites of the GST-pathway bind to DNA. The DNA reactive metabolites are considered to be related to the genetic toxicity and carcinogenicity of ethylene dibromide. The protein reactive metabolites are considered to be related to the cytotoxicity. The formation of bromine during metabolism is considered to contribute to the acute toxicity of ethylene dibromide.

A study on reproductive toxicity shows that after exposure of male rats to a concentration of 89 ppm (696 mg/m^3) of ethylene dibromide for 7h/day, 5 days/week for 10 weeks, moderate to severe atrophy of the testes, epididymis, prostate and seminal vesicles was observed. None of the males exposed to 89 ppm impregnated even one female rat. A total of 10/50 females died after exposure to 80 ppm for 7h/day, 5 days/week for 3 weeks and none had normal estrous cycles until 3-4 days postexposure. Only 8/20 females exposed to 80 ppm mated, and all that mated became pregnant. Rats were not exposed after mating. The number of viable implants/dam in females exposed to 80 ppm was reduced by 30% compared with that of controls. The

presence of general toxicity made it difficult to relate the observed reproductive effects to the ethylene dibromide exposure. In a developmental toxicity study in rats exposed to 80 ppm (626 mg/m^3) 23 h/day during GD6-15 half of the pregnant dams died. The other half of the dams experienced early resorptions and fetal deaths.

H350: May cause cancer, H331: Toxic if inhaled, H311: Toxic in contact with skin, H301: Toxic if swallowed, H319: Causes serious eye irritation, H315: Causes skin irritation, H335: May cause respiratory irritation

Carcinogenicity and derivation of the CRP value

IARC classification:

2A (probably carcinogenic to humans)

Derivation of the carcinogenic risk potency (CRP):

10^{-4} risk level after inhalation: 10^{-4}/0.6 mg/m^3 = 1.67 x 10^{-4} mg/m^3 [EPA, 2004]

CRP = (10^{-4} risk level * average life span in hours)/DRCF

= (1.67 x 10^{-4} mg/m^3* 613,200) /2.8 =37 mg/m^3

Odour and derivation of the LOA value

Odour: pungent, sweetish, chloroform like odour

Odour threshold: 78.2 mg/m^3 [Ruth, 1986]

LOA = 11.8 * ODT * 1.33 = 1,227 mg/m^3

(The concentration Level leading to distinct Odour Awareness (l=3) is calculated using the formula: l = 2.33 * log (C/ODT + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies above all intervention values except for the 10 min AGW value, and 10 min and 30 min LBW value.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **65**	*AEGL-1* 130	*ERPG-1* -		*IDLH: 782 (30 minutes)*
AGW level **260**	*AEGL-2* 190	*ERPG-2* -		
LBW level **770**	*AEGL-3* 360	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 75-21-8 **Ethyleenoxide** **$CH_2(-O-)CH_2$** **VN-nr: 1040** **GEVI: 263**

Synoniemen: 1,2-epoxyethaan, T-gas, oxiraan (Engels: Ethylene oxide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	360	150	81	46	26	14
Levensbedreigende waarden	LBW (mg/m³)	5400	2200	1200	680	380	210

Datum vaststelling: November 2015 | Conversiefactor: 1 mg/m³ = 0,545 ppm; 1 ppm = 1,83 mg/m³

Explosiegrens: LEL = 2,6 vol% ≈ 48.000 mg/m³

Geur: Zoete, ether-achtige geur

LOA: 3000 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos onder druk tot vloeistof verdicht gas.

Brand: zeer brandgevaarlijk, bij vele reacties kans op brand en explosie.

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,5

Molecuulmassa: 44,1 g/mol
Zuurgraad: Geen data
LogKow: - 0,3
Wateroplosbaarheid: Volledig
Verzadigde dampdruk: 1500 mbar

Overige informatie

Publieke grenswaarde: 0,84 mg/m³ (8 uur)
MAK: niet afgeleid
TLV-TWA: 1,83 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: irritatie van oog, keel, neus en luchtwegen, kortademigheid, hoofdpijn, duizeligheid, zwakte.

AGW → LBW: benauwdheid, moeilijkheden met praten, verlies van coördinatie, bewusteloosheid, effecten op de ongeboren vrucht.

Boven LBW: verlamming van de ademhaling, longoedeem, lever- en nierfunctiestoornissen, sterfte.

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Ethyleenoxide is een krachtig alkylerend agens dat irreversibel bindt aan eiwitten en nucleïnezuren.
- Acute expositie veroorzaakt ernstige irritatie van ogen, longen en luchtwegen, en depressie van het centrale zenuwstelsel. Verlamming van de ademhalingsspieren, lever- en nierbeschadiging kunnen optreden.
- Blootstelling aan ethyleenoxide kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- De stof veroorzaakt mogelijke reprotoxische effecten.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, ernstige bevriezings-verschijnselen zoals pijn, blaren, wonden.

Oogcontact: bijtend, roodheid en pijn, slecht zien.

Carcinogeniteit

IARC classificatie: 1
CRP: 2475 mg/m³

Beknopte medische informatie

Ontsmetting damp

algemeen: IN ALLE GEVALLEN ARTS RAADPLEGEN, frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: *bij bevriezingsletsel:* aan de huid vastgevroren kleding NIET lostrekken, spoelen met veel water / kleding verwijderen en direct spoedeisende medische hulp inzetten.

ogen: *bij damp en bevriezingsletsel:* minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas).

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 75-21-8 **Ethylene oxide** $CH_2(-O-)CH_2$ **UN-nr: 1040**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL values adopted (except 10 min value for which time scaling was applied), 2hr value added

LBW: Same point of departure than AEGL, using different uncertainty factors, 2hr value added

Date: November 2015 | AEGL document: Final, 2010

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended.
AGW	360	150	81	46	26	14	NOAEL for developmental toxicity and neurotoxicity in rats.
LBW	5400	2200	1200	680	380	210	LC_{01} for lethality in rats.

Derivation of the Dutch Intervention Values

VRW: Values for VRW were not derived because concentrations causing mild sensory irritation are ≥ 260 ppm (480 mg/m³), which is above the AGW levels and would not serve as a warning of potential exposure. Therefore, VRW values are not recommended.

AGW: The AGW values were based on an acute neurotoxicity study in rats exposed to 0, 100, 300, or 500 ppm (0, 180, 550, 920 mg/m³) for 6 hours and a developmental toxicity study utilizing pregnant rats exposed to 10, 33, or 100 ppm (18, 60, 180 mg/m³) ethylene oxide, 6 h/day during organogenesis. The point of departure is 100 ppm (180 mg/m³), the no-observed-adverse effect level (NOAEL) for neurotoxicity (droopy/half-closed eyelids, impaired locomotion, low arousal, and no response to approach) and developmental toxicity (decrease in fetal body weight and increase in litter incidence of delayed ossification of the vertebrae). The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. For time-scaling $C^n \times t = k$ was used, where n = 1.2, based on analysis of rat lethality data. In contrast to the 10 minute AEGL-2, time scaling was also applied for the 10 minute AGW value.

LBW: LBW values were derived from a lethality study utilizing rats. An LC_{01} value (628 ppm; 1152 mg/m³), which is considered an approximation of the lethality threshold, was derived from a 4-hour acute inhalation study with rats. An uncertainty factor of 1 for interspecies differences and the default uncertainty factor of 3 for intraspecies variability (total uncertainty factor of 3) were applied to the LC_{01}. Selecting the default interspecies uncertainty factor of 3 would result in LBW-values conflicting with available human data; a study performed under workers showed that exposure to concentrations up to 785 mg/m³ (8h TWA) did not lead to immediate health effects. It is noted that the exposure concentrations are calculated from biomonitoring data. Time-scaling was performed using $C^n \times t = k$, where n = 1.2. In contrast to the 10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Ethylene oxide is a direct-acting alkylating agent; it alkylates DNA and proteins. Ethylene oxide is also a mild primary irritant and a central nervous system depressant. Pharmacokinetic data show that ethylene oxide is readily absorbed from the respiratory tract of both humans and animals. In humans, ethylene oxide vapors affect the eyes, respiratory tract, central and peripheral nervous systems, gastrointestinal tract (probably secondary effects to nervous system toxicity), haematopoietic system, and possibly the reproductive system and fetus. Acute exposure to ethylene oxide at the odour detection level (≥ 260 ppm (480 mg/m³)) causes eye and upper respiratory tract irritation and signs and symptoms of effects on the central and peripheral nervous system (headache, speech difficulty, recent memory loss, weakness, dizziness, incoordination, numbness in fingers, unconsciousness).

Two epidemiologic studies presented suggestive evidence that exposure to ethylene oxide is associated with adverse reproductive outcomes: spontaneous abortions, preterm births, and postterm births.

H315: Causes skin irritation; H319: Causes serious eye irritation; H331: Toxic if inhaled; H335: May cause respiratory irritation; H340: May cause genetic defects; H350: May cause cancer.

Carcinogenicity and derivation of the CRP value

IARC classification: 1 (carcinogenic to human)

Derivation of the carcinogenic risk potency (CRP):

10^{-4} risk level after inhalation: 1,13* 10^{-2} mg/m^3 [AEGL]

CRP = (10^{-4} risk level * average life span in hours)/DRCF

= 1,13 * 10^{-2} mg/m^3 * 613.200) /2.8 = 2475 mg/m^3

Ethylene oxide is carcinogenic in mice and rats. Positive results have been obtained using the mouse lung tumor bioassay (70 ppm; 130 mg/m^3) and the standard 2-year bioassays in mice and rats at concentrations ≥ 100 ppm (180 mg/m^3). The evidence of carcinogenicity based on human studies is limited.

Odour and derivation of the LOA value

Odour: pleasantly to sickeningly sweet, fruity, alcoholic, or acetone- or ether like

OT_{50}: 191 mg/m^3 [AEGL]

LOA = 11.8 * OT_{50} * 1.33 = 3000 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies above the AGW and LBW levels at all time points.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **NR**	*AEGL-1* NR	*ERPG-1* NA		*IDLH:* 1470 (30 min)
AGW level **81**	*AEGL-2* 83	*ERPG-2* 92		
LBW level **1200**	*AEGL-3* 370	*ERPG-3* 920		

Stofdocument deel A

CAS-nr: 16219-75-3 **5-Ethylideen-2-norborneen** **C_9H_{12}** **VN-nr: 1993 n.o.s.** **GEVI: 30**

Synoniemen: ENB, 5-ethylideenbicyclo[2.2.1]-hept-2-een (Engels: 5-ethylidene-2-norbornene)

Status: geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	9,3	9,3	9,3	9,3	9,3	9,3
Alarmeringsgrenswaarden	AGW (mg/m³)	590	410	330	260	210	130
Levensbedreigende waarden	LBW (mg/m³)	2400	1600	1300	1000	820	410

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,200 ppm; 1 ppm = 5,00 mg/m³

Explosiegrens: 0,8 vol% ≈ 40000 mg/m³

Geur: zoet, aromatisch, terpentijn-achtig

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,02

Molecuulmassa:	120,2 g/mol
Zuurgraad:	-
LogKow:	3,8
Wateroplosbaarheid:	0,01 g/100 ml (zeer slecht)
Verzadigde dampdruk:	5,6 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-ceiling: 25 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: prikkeling, lichte oogirritatie

VRW → AGW: irritatie van ogen en neus, keelpijn en hoesten, tranen

AGW → LBW: hoofdpijn, misselijkheid, ataxie, tremoren

Boven LBW: convulsies, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof veroorzaakt irritatie van ogen, neus en luchtwegen.
- De stof heeft effecten op het CZS.

Effecten bij blootstelling aan vloeistof

Huidcontact: prikkeling, roodheid en pijn.

Oogcontact: prikkeling, roodheid en pijn, tranenvloed

Carcinogeniteit

IARC classificatie: geen
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, en onmiddellijk arts raadplegen.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en onmiddellijk arts raadplegen.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 16219-75-3 **5-ethylidene-2-norbornene** **C_9H_{12}** **UN-nr: 1993 n.o.s.**

Basis for the Dutch Intervention Values

VRW: Based on information as described in ERPG-document, different values are derived, other time-points added

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017 | ERPG 2016

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	9.3	9.3	9.3	9.3	9.3	9.3	Nasal, eye and respiratory irritation in humans
AGW	590	410	330	260	210	130	No effect level in a subacute rat study
LBW	2400	1600	1300	1000	820	410	Acute lethality in rats

Derivation of the Dutch Intervention Values

VRW: The VRW levels were based on a human volunteer study in which four and two subjects inhaled 5.6 ppm (28 mg/m³) or 11.2 ppm (56 mg/m³) 5-ethylidene-2-norbornene, respectively, for 30 minutes. Transient ocular and respiratory irritation were reported at exposure levels of 11.2 ppm (56 mg/m³) or 5.6 ppm (28 mg/m³). At 56 mg/m³, one subject reported transient eye and nasal irritation after 21 minutes. One subject had slight throat irritation post exposure. At 28 mg/m³, three subjects had transient eye irritation. The 30-min exposure to 28 mg/m³ was selected as point of departure for deriving VRW-levels. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Timescaling was not applied. This approach was considered appropriate because mild irritant effects generally do not vary greatly over time.

AGW: The AGW values were based on a subacute repeated dose study in rats. Rats (10/sex/conc) were exposed to 0, 52, 148 or 359 ppm (0, 260, 740, 1795 mg/m³ for 6h/d, for 9 days. At the highest concentration, a slight decrease of body weight gain and relative kidney weights was observed. An increase of absolute and relative thyroid gland weights was observed at the mid and high concentration. Further, vacuolar depletion of thyroid colloid was observed in all male and female groups. All effects observed are considered the result of repeated exposure and are therefore not considered suitable to serve as point of departure for derivation of AGWs. In the absence of more suitable data, the highest concentration level of 1795 mg/m³ for 6 hours was selected as point of departure for the AGW. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$ with the default n = 1 and n= 3, to extrapolate to longer and shorter durations, respectively.

LBW: LBW-levels were based on results of a rat 4-hour acute inhalation study. Rats (5/sex/conc) were exposed for 4 hours to 2206, 2813, 3431 ppm (corresponding to 11030, 14065 and 17155 mg/m³) resulting in the following lethality: 1/5, 2/5 and 5/5 for males and 1/5, 1/5 and 4/5 for females. These data were analysed with Doseresp and the following LC_{01} values were obtained: 8967 mg/m³ for males and 8096 mg/m³ for females. LC_{50} values were 13470 mg/m³ for males and 14860 mg/m³ for females. Results of a second acute inhalation study reported the following 4-hour LC_{50}-vales for multiple species: rat (male): 1246 ppm (6230 mg/m³), rat (female): 2249 ppm (11245 mg/m³), mouse (male): 1110 ppm (5550 mg/m³), mouse (female): 732 ppm (3660 mg/m³), rabbit (male): 3104 ppm (15520 mg/m³), guinea pig (male): 2896 ppm (14480 mg/m³). Due to lack of individual lethality data this second study could not be used for calculating LC_{01} values. Rat data were used as these were considered the most relevant and reasonable data. The 4-hour LC_{01} value of 8152 mg/m³ (sexes combined) was used as point of departure for deriving the LBW-values. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time

scaling was performed using the equation $C^n \times t = k$ with the default n = 1 and n= 3, to extrapolate to longer and shorter durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

5-Ethylidene-2-norbornene is irritating to the skin, eye and respiratory tract.

In an oral reproductive/developmental toxicity screening test, some reproductive effects were observed: reduced implantation and delivery indices, reduced number of births and number of live offspring (day 4 of lactation). An inhalation developmental toxicity study revealed no developmental effects that could serve as point of departure for AGW conform van Raaij et al. (2003).

No harmonized H-sentences for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: sweet, aromatic, turpentine-like

Odour threshold appears to be between 0.035 and 0.07 mg/m^3 [ERPG, 2016]

Using the lowest threshold of 0.035 mg/m^3 leads to:]
LOA = 11.8 * OT * 1.33 = 0.55 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is below the VRW.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [37]

VRW level **9.3**	*AEGL-1* -	*ERPG-1* 0.98		*IDLH:* -
AGW level **330**	*AEGL-2* -	*ERPG-2* 490		
LBW level **1300**	*AEGL-3* -	*ERPG-3* 2450		

[37] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 109-90-0 **Ethylisocyanaat** CH_3CH_2NCO **VN-nr: 2481**

GEVI: 663

Synoniemen: isocyanaatethaan, ethaanisocyanaat (Engels: ethyl isocyanate) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	3,6	1,2	0,59	0,30	0,15	0,074
Levensbedreigende waarden	LBW (mg/m³)	24	8,2	4,1	2,0	1,0	0,51

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,338 ppm; 1 ppm = 2,96 mg/m³

Explosiegrens: geen data

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk, damp met lucht vormt een explosief mengsel

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,3

Molecuulmassa:	71,1 g/mol
Zuurgraad:	geen data
LogKow:	1,3
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	215 mbar

Overige informatie

Publieke grenswaarde:
niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: irritatie ogen, neus en keel

AGW → LBW: effecten op de ongeboren vrucht, matige tot ernstige irritatie van de luchtwegen, tranenvloed, keelpijn, hoesten, benauwdheid, longoedeem

Boven LBW: ernstige longschade, sterfte

LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Primaire effecten zijn irritatie van de slijmvliezen van ogen, neus en keel.
- Blootstelling aan ethylisocyanaat kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Ethylisocyanaat veroorzaakt vergelijkbare toxische effecten als methylisocyanaat.
- Ethylisocyanaat kan mogelijk embryotoxiciteit veroorzaken
- Ethylisocyanaat is mogelijk sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact!

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, irritatie, roodheid, pijn, blaren, brandwonden. De stof wordt door de huid opgenomen!
Oogcontact: bijtend, roodheid, pijn en brandwonden.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer..

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 109-90-0 **Ethyl isocyanate** **CH_3CH_2NCO** **UN-nr: 2481**

Basis for the Dutch Intervention Values

VRW: Not recommended (in accordance with AEGL)

AGW: Same rationale as for AEGL (analogy with methyl isocyanate; note: AGW for MIC deviates from AEGL-2). No additional modifying factor applied.

LBW: Same rationale as for AEGL (analogy with methyl isocyanate; note: LBW for MIC deviates from AEGL-3). No additional modifying factor applied.

Date: 06-10-2016 | AEGL Document: Final, 2013

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	3.6	1.2	0.59	0.30	0.15	0.074	Based on AGW values for methyl isocyanate (decreased fetal body weight, cardiac arrhythmias, fetal death).
LBW	24	8.2	4.1	2.0	1.0	0.51	Based on LBW values for methyl isocyanate (threshold of animal lethality).

Derivation of the Dutch Intervention Values

VRW: VRW values were not derived for ethyl isocyanate due to a lack of relevant human and animal data. The available data, however, shows that ethyl isocyanate exerts toxic effects that are similar to methyl isocyanate (respiratory irritation and delayed lethality). VRW values are not derived for methyl isocyanate due to poor warning properties. On the basis of similarities between ethyl isocyanate and methyl isocyanate, VRW values for ethyl isocyanate were not derived. Absence of VRW values does not imply that concentrations below the AGW values are without any effect.

AGW: No appropriate data for derivation of AGW values are found for ethyl isocyanate. AGW values were based on the AGW values as established for the related compound methyl isocyanate. The AGW-values for methyl isocyanate were based on 3 animal studies. Mice (n=12-24) were exposed to 0, 2, 6, 9, 15 ppm (0, 4.8, 14, 21, 36 mg/m^3) methyl isocyanate for 3 hours on day 8 of gestation. The LOEL for lower fetal body weights in the absence of maternal toxicity was an exposure of mice at 2 ppm (4.8 mg/m^3) for 3 hours on day 8 of gestation. In the second animal study rats were exposed to 3, 10, 30 ppm (7.1, 24, 71 mg/m^3) methyl isocyanate for 2 hours. The exposure of rats at 3 ppm (7.1 mg/m^3) for 2 h was a LOEL for cardiac arrhythmias evaluated 4 months post-exposure. In contrast to the AEGL, the AGW-level was also based on an additional point of departure. In the third animal study (neonatal survival study with mice) pregnant mice were exposed to 0, 1, 3 ppm (0, 2.4, 7.1 mg/m^3) methyl isocyanate for 6h/d on day 14-17 of gestation. Although the exposures were repeated on 4 consecutive days, the exposure to the fetus is considered similar to a single exposure because the stage of development and potential susceptibility changes daily throughout gestation and is different on each of the exposure days. In addition, the lower pup survival seen experimentally following repeated maternal exposure is the same end point as fetal and infant death in humans observed following accidental exposure. A significant increase in the total number of dead fetuses at birth was observed in both exposure groups (controls: 0.4%; 1 ppm (2.4 mg/m^3): 3.3%; 3 ppm (7.1 mg/m^3): 6.4%). The 6-h exposure at 1 ppm was used as point of departure to derive AGW for methyl isocyanate. Analogously, a 6-h exposure to 1 ppm is also used as point of departure for ethyl isocyanate (*i.e.,* 2.96 mg/m^3 for ethyl isocyanate). These three exposure concentration and duration scenarios yield identical AGW values when used for derivation. As for methyl isocyanate, the experimental concentrations were reduced by a modifying factor of 3 to estimate a threshold for the observed effects. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$, using n=1 (derived from rat LC_{50} values).

LBW: No appropriate data for derivation of LBW values are found for ethyl isocyanate. LBW values were determined by using the LBW values established for the related compound methyl isocyanate. The

LBW-values for methyl isocyanate were based on mortality data from a rat study. Rats were exposed by inhalation to various concentrations methyl isocyanate (17.5-541 ppm; 41.7-1,285 mg/m^3) for 7.5-240 minutes. Point of departure was the 1-hour LC_{50}-value of 41.3 ppm. Based on the rat LC_{50} data in this study a n-value of 1 was calculated. Analogously, for the derivation of LBW values for ethyl isocyanate a 1-hour value of 41.3 ppm (122 mg/m^3) was used as point of departure. This concentration was divided by 3 to obtain an estimate of the threshold for lethality. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was performed using $C^n \times t = k$, with the chemical-specific n-value of 1.

Additional toxicological information (including relevant results of a general literature search, if any)

No studies are available that address the mechanism(s) of toxicity of ethyl isocyanate. It is thought that ethyl isocyanate exhibits comparable toxic effects (respiratory irritation and delayed lethality) to methyl isocyanate. The exact mechanism of action for the systemic effects is unknown. High concentrations may cause lung edema.

There is no information available on developmental or reproductive toxicity and genotoxicity of ethyl isocyanate.

No harmonized H-sentences for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: pungent, penetrating odour

No LOA was derived (due to lack of data)

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH:* not established
AGW level **0.59**	*AEGL-2* 0.10	*ERPG-2* -		
LBW level **4.1**	*AEGL-3* 0.30	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 75-08-1 **Ethylmercaptaan** CH_3CH_2SH **VN-nr: 2363** **GEVI: 33**

Synoniemen: Ethaanthiol, thioethanol, ethylsulfhydraat (Engels: ethyl mercaptan) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	2,6	2,6	2,6	2,6	2,6	2,6
Alarmeringsgrenswaarden	AGW (mg/m³)	560	390	310	240	190	97
Levensbedreigende waarden	LBW (mg/m³)	1.700	1.200	920	730	580	290

Datum vaststelling: 24-09-2009 — 1 mg/m³ = 0,387 ppm; 1 ppm = 2,58 mg/m³

Explosiegrens: LEL = 2,8 vol% ≈ 72.000 mg/m³

Geur: typerende knoflookachtige geur (walgingwekkend), rotte kool

LOA: 3,5 x 10^{-4} mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,09

Molecuulmassa:	62,1 g/mol
Zuurgraad:	Geen data
LogKow:	2,4 (berekend)
Wateroplosbaarheid:	0,7 g/100 ml (slecht)
Verzadigde dampdruk:	590 mbar

Overige informatie

Publieke grenswaarde:
niet afgeleid
MAK: 1,3 mg/m³
TLV-TWA: 1,3 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: mogelijk lichte oogirritatie en hoofdpijn, misselijkheid

VRW → AGW: oogirritatie, tranenvloed, rode ogen, lichte irritatie van de luchtwegen

AGW → LBW: benauwdheid, longoedeem, ophoesten van bloed, hyperventilatie, hoornvliesbeschadiging, fotofobie, misselijkheid en braken, hoofdpijn, duizeligheid, verwarring/opwinding, pijn op borst, bewustzijnsdaling

Boven LBW: ademstilstand, coma, convulsies, collaps, stefte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Ethylmercaptaan blokkeert de ademhalingsketen in de cel. Hierdoor wordt de energiehuishouding verstoord en kan lactaatacidose ontstaan.
- Primaire doelorganen zijn het centrale zenuwstelsel en het cardiovasculaire systeem.
- Ethylmercaptaan werkt in lage concentraties irriterend op de ogen en luchtwegen.
- De stof kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Verlamming van de geurzenuw kan optreden bij hoge concentraties, waardoor de geurwaarneming en het daarmee gepaard gaande waarschuwingssignaal achterwege kan blijven.
- Door de snelle activering van sulfide in het lichaam wordt de toxiciteit van ethylmercaptaan met name bepaald door de concentraties en minder door de blootstellingsduur.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, pijn
Oogcontact: roodheid en pijn

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, 100% zuurstof, halfzittende houding, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!) en arts raadplegen.

Specifieke behandeling en materialen: Bij vergiftiging door deze stof is specifieke eerste hulp noodzakelijk; specifieke antidota (o.a. 100% zuurstof) moeten met gebruiksaanwijzing ter plekke beschikbaar zijn.. Voor aanwijzingen over verdere behandeling zo nodig het NVIC (+31(0)30-274 88 88) bellen. .

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 75-08-1 **Ethyl mercaptan** CH_3CH_2SH **UN-nr: 2363**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added; time scaling was also applied for the 10 minute AGW value

LBW: AEGL value is adopted, 2h value added; time scaling was also applied for the 10 minute LBW value

Date: 24-09-2009 | AEGL document: Final, 2013

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	2.6	2.6	2.6	2.6	2.6	2.6	Threshold for respiratory irritation in animals
AGW	560	390	310	240	190	97	1/3 LBW
LBW	1,700	1,200	920	730	580	290	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: The VRW values are based on a NOAEL for respiratory irritation in rabbits exposed to 10 ppm (26 mg/m³) for 20 minutes. At 100 ppm (260 mg/m³) and higher the respiratory rate, and respiratory volume decreased and the tidal volume increased. A total uncertainty factor of 10 (3 for interspecies and 3 for intraspecies differences) was applied. The use of higher factors would yield VRW values that are inconsistent with the available human data (0.4 ppm (1.0 mg/m³) for 3 hrs/day for 5 or 10 days did not produce mucosal irritation in humans). The VRW values were held constant across time, because mild irritancy generally does not vary greatly over time and because it is not expected that prolonged exposure will result in an enhanced effect.

AGW: In the absence of inhalation data, with concentration and duration parameters within the definition of the AGW, the AGW are based on a 3-fold reduction of the LBW values. This is considered a threshold for irreversible effects and is considered appropriate given the steep concentration-response curve (a 4 hour exposure to 2600 ppm (6,700 mg/m³) caused 40% lethality in mice, the 4-hr mouse LC_{50} was 2,770 ppm (7,200 mg/m³), and after a 4 hour exposure to 3,573 ppm (9,200 mg/m³) 100% of the mice died; the 4-hr rat LC_{01} and LC_{50} were 3808 (9,800 mg/m³) and 4,740 ppm (12,000 mg/m³), respectively. In contrast to the 10 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: The LC_{01} of 2,250 ppm (5,800 mg/m³) in mice exposed to ethyl mercaptan for 4 hours was used as starting point to derive the LBW values. The mice data, rather than the rat data, were selected for derivation of the LBW-values, because more mice were tested and yielded less uncertainty and a better concentration-response curve. An intraspecies factor of 3 was applied and considered sufficient in view of the steepness of the lethal response curve. The available data indicate that the mouse is the most sensitive species and therefore an interspecies factor 3 is considered sufficient. The similarities in toxicity profile and the robust database of hydrogen sulfide further substantiates the interspecies factor of 3. Time scaling was performed using the equation $C^n \times t = k$, with the default values n=1 to extrapolate to longer and n=3 to extrapolate to shorter time points. In contrast to the 10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Ethylmercaptan, methylmercaptan and hydrogen sulfide have a comparable mechanism of toxicity, but differ in toxic potency in the following order: hydrogen sulfide > methylmercaptan > ethylmercaptan. Hydrogen sulfide and ethyl and methylmercaptan are both irritants and asphyxiants. In humans at relatively low concentrations (<10 ppm; 26 mg/m³), minor ocular and respiratory irritation occur, while at higher concentrations (hundreds to thousands of ppm), the central nervous system is affected and paralysis of the respiratory center may lead to rapid death. Liver and kidney damage is also mentioned in literature, but is considered to be secondary to asphyxiation.

No data on developmental and/or reproductive toxicity was located.

H332: Harmful if inhaled.

Carcinogenicity and derivation of the CRP value
IARC classification: not classified No carcinogenic risk potency (CRP) was derived. The limited genotoxicity data are equivocal. No chronic or carcinogenicity studies were available.

Odour and derivation of the LOA value
Odour: typical (nauseating) odour of decaying cabbage OT_{50}: 8.7 x 10^{-6} ppm (2.2 x 10^{-5} mg/m^3) [AEGL, (2013); Nagata (2003)] LOA = 11.8 * OT_{50} * 1.33 = 3.5 x 10^{-4} mg/m^3 (The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value) The LOA is lower than the VRW values.

Other standards and guidelines *(1h values in mg/m^3, unless otherwise indicated)*				
VRW level **2.6**	*AEGL-1* 2.5	*ERPG-1* Not derived		*IDLH:* 1290 (30 minutes)
AGW level **310**	*AEGL-2* 310	*ERPG-2* Not derived		
LBW level **920**	*AEGL-3* 930	*ERPG-3* Not derived		

Stofdocument deel A

CAS-nr: 115-21-9 **Ethyltrichloorsilaan** $C_2H_5Cl_3Si$ **VN-nr: 1196**

GEVI: X338

Synoniemen: silaan, ethyltrichloor, trichloorethylsilaan (Engels: ethyl trichlorosilane) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	4,1	4,1	4,1	4,1	4,1	4,1
Alarmeringsgrenswaarden	AGW (mg/m³)	250	120	76	47	30	30
Levensbedreigende waarden	LBW (mg/m³)	760	360	230	140	89	89

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,147 ppm; 1 ppm = 6,80 mg/m³

Explosiegrens: LEL = 2,7 vol% ≈ 184.000 mg/m³

Geur: scherpe stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze rokende vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,3

Molecuulmassa:	163,5 g/mol
Zuurgraad:	geen data
LogKow:	geen data
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	56 mbar

Overige informatie

Publiek grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW	geen informatie
VRW → AGW:	oog- en luchtwegirritatie, tranenvloed, hoesten, lichte benauwdheid
AGW → LBW:	ernstige oog- en luchtwegirritatie, pijn op de borst, benauwdheid, longontsteking, longoedeem
Boven LBW:	ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Chloorsilanen reageren zeer snel met water onder vorming van chloorwaterstof (HCl). De acute toxiciteit van ethyltrichloorsilaan wordt veroorzaakt door chloorwaterstof.
- Inhalatie van chloorwaterstof veroorzaakt een type I inhalatie intoxicatie.
- Chloorwaterstof veroorzaakt irritatie van de slijmvliezen van ogen en luchtwegen.
- Chloorwaterstof kan bij inhalatie longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, brandwonden.

Oogcontact: bijtend, roodheid en pijn, hoornvliesbeschadiging, ernstige brandwonden.

Carcinogeniteit

IARC classificatie: niet geclassificeerd.

CRP: niet afgeleid.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust; in geval van rode ogen halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken (voorzichtig i.v.m mogelijk reeds beschadigde huid), minimaal 20 min. spoelen met veel water of douchen, en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen:.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 115-21-9 **Ethyl trichlorosilane** **$C_2H_5Cl_3Si$** **UN-nr: 1196**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same rationale as AEGL (analogy with HCl), 2h value added

LBW: Same rationale as AEGL (analogy with HCl), 2h value added

Date: November 2015 | AEGL document: Final, 2012

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	4.1	4.1	4.1	4.1	4.1	4.1	Based on HCl (Threshold for irritation in humans)
AGW	250	120	76	47	30	30	Based on HCl (one-third of LBW)
LBW	760	360	230	140	89	89	Based on HCl (Calculated threshold for lethality in animals)

Derivation of the Dutch Intervention Values

VRW: Since no appropriate data exist for ethyl trichlorosilane, VRW values for hydrogen chloride will be used (on ppm-basis) to derive VRW values for ethyl trichlorosilane. The use of hydrogen chloride as a surrogate for ethyl trichlorosilane was deemed appropriate since it is believed that the hydrolysis product, HCl, is responsible for the adverse effects. Because three moles of hydrogen chloride are produced for every mole of ethyl trichlorosilane, a molar adjustment factor of 3 was applied to the hydrogen chloride VRW values.

Derivation of VRW values for HCl

The hydrogen chloride VRW values were based on a no-adverse-effect-level of 1.8 ppm (2.73 mg/m³) in exercising asthmatics with an exposure duration of 45 min. Because the test subjects were considered a sensitive subpopulation and the endpoint was essentially a no-effect level, no uncertainty factor was applied to account for sensitive human subpopulations. The VRW values were held constant for all specified exposure periods since mild irritant effects represent threshold effects and generally do not vary over time.

AGW: Since no appropriate data exist for ethyl trichlorosilane, AGW values for hydrogen chloride will be used (on ppm-basis) to derive AGW values for ethyl trichlorosilane. Because three moles of hydrogen chloride are produced for every mole of ethyl trichlorosilane, a molar adjustment factor of 3 was applied to the hydrogen chloride AGW values.

Derivation of AGW values for HCl

The AGW values of HCl for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data. The only study of HCl that addressed effects that meet the definition of an AGW, severe nasal lesions, was a study on hydrogen halides by Stavert et al. (1991). Nevertheless, this study was not considered a suitable basis for derivation of AGW values because 6% of the animals died after exposure to HCl at 1300 ppm (1974 mg/m³), only one concentration was tested and the number of animals tested was inconsistent.

LBW: Since no appropriate data exist for ethyl trichlorosilane, LBW values for hydrogen chloride will be used (on ppm-basis) to derive LBW values for ethyl trichlorosilane. Because three moles of hydrogen chloride are produced for every mole of ethyl trichlorosilane, a molar adjustment factor of 3 was applied to the hydrogen chloride LBW values.

Derivation of LBW values for HCl

The LBW values were based on a lethality study in rats. The rat study included six exposure durations and various concentrations. Probit analyses using DoseResp was performed and yielded LC_{01} values for the 10 min, 30 min, 1-, 2-,4-, and 8hrs exposure durations of 3370, 1602, 1002, 627, 393 and 246 ppm (5116, 2433, 1522, 952, 596, and 373 mg/m³), respectively, which were used as

point of departure for LBW derivation. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The probit analyses yielded an n-value of 1.48, which was supported by the n-value of 1.59 calculated by Arts *et al.* (2000) from the C*t study. To maintain consistency with other hydrogen halogenides, the 8 hour value was set equal to the 4 hour value, as performed for the most potent hydrogen halogenide HF.
.

Additional toxicological information (including relevant results of a general literature search, if any)

No data concerning lethality or nonlethal toxicity in humans from ethyl tichlorosilane were located in the available literature.

Chlorosilanes react violently with water to produce hydrogen chloride gas. Data suggest that the acute toxicity of chlorosilanes is due to the hydrogen chloride hydrolysis product; acute toxicity of the chlorosilanes is both qualitatively (based on clinical signs) and quantitatively (based on molar equivalents of hydrogen chloride) similar to that of HCl.

Although toxicity data are limited for individual chlorosilanes, well-conducted 1-hr inhalation toxicity studies in rats are available for a series of chlorosilanes. In general, LC_{50} values for monochlorosilanes were approximately twice the LC_{50} values for dichlorosilanes and three times the LC_{50} values for trichlorosilanes. Clinical signs were consistent with hydrogen chloride exposure and included lacrimation, salivation, dried material around or on the eyes and/or nose, green staining around the nose and mouth, and perineal urine staining. Labored breathing, rales, hypoactivity, closed or partially closed eyes, prostration, corneal opacity or opaqueness, and swollen and/or necrotic paws were also observed. Hemorrhage, congestion and/or consolidation of the lungs, ectasia of the lungs, gaseous distension of the gastrointestinal tract, absence of body fat, obstruction of nostrils, dried and/or firm nares, alopecia around the eyes and discoloration of hair were observed at necropsy.

No data concerning developmental/reproductive toxicity for exposure to ethyl trichlorosilane were located in the available literature.

No harmonized H-sentences for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified.

No carcinogenic risk potency (CRP) was derived

No data concerning carcinogenicity for exposure to ethyl trichlorosilane were located in the available literature.

Odour and derivation of the LOA value

Odour: pungent odour

No LOA was derived due to lack of data.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **4.1**	*AEGL-1* 4.1	*ERPG-1* not derived		*IDLH:* not derived
AGW level **76**	*AEGL-2* 50	*ERPG-2* not derived		
LBW level **230**	*AEGL-3* 220	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 108-95-2 **Fenol** C_6H_5-OH **VN-nr: 2312**

GEVI: 60

Synoniemen: carbolzuur, hydroxybenzeen, fenylalcohol (Engels: Phenol) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	25	25	25	25	25	25
Alarmeringsgrenswaarden	AGW (mg/m³)	160	110	90	71	57	45
Levensbedreigende waarden	LBW (mg/m³)	NA	NA	NA	NA	NA	NA

Datum vaststelling: 13-05-2009

Conversiefactor: 1 mg/m³ = 0,255 ppm; 1 ppm = 3,91 mg/m³

Explosiegrens: LEL = 1,3 vol% ≈ 50.000 mg/m³

Geur: Medicinale, zoete geur

LOA: 0,99 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze hygroscopische kristallen, kleurt roze aan de lucht.
Brand: brandbaar.

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,0

Molecuulmassa:	94,1 g/mol
Zuurgraad:	Geen data
LogKow:	1,5
Wateroplosbaarheid:	8 g/100 ml (matig)
Verzadigde dampdruk:	0,3 mbar

Overige informatie

Publieke grenswaarde: 8 mg/m³
MAK: niet afgeleid
TLV-TWA: 19,6 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: irritatie ogen en luchtwegen, tranenvloed, hoesten, duizeligheid, hoofdpijn

AGW → LBW: ernstige irritatie ogen, neus en luchtwegen, benauwdheid, coördinatieproblemen, zwakte,

Boven LBW: longoedeem, ademnood, cyanose ataxie, sedatie, bewustzijnsdaling, coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder AGW zonder effecten is

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Fenol werkt bijtend op ogen, huid en luchtwegen.
- Inademing van de damp kan longoedeem veroorzaken.
- Acute irritatie door fenol wordt mogelijk veroorzaakt door verstoring van eiwit, enzym en membraanfunctie.
- Zowel de damp als de vloeistof worden door de huid opgenomen.
- Fenol werkt op het centrale zenuwstelsel, de lever en de nieren, met als mogelijke gevolgen: anorexia, gewichtsverlies, zwakte, spierpijn, cyanose, bevingen, convulsies, plotselinge instorting, bewusteloosheid en orgaanafwijkingen.
- De systemische effecten van fenol zijn mogelijk gerelateerd aan remming van natriumkanalen in het hart en beïnvloeding van de acetylcholine afgifte.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, pijn, ernstige brandwonden.
Stof wordt door de huid opgenomen!
Oogcontact: bijtend, roodheid, pijn, slecht zien.

Carcinogeniteit

IARC classificatie: 3
CRP: niet afgeleid.

Beknopte medische informatie

Ontsmetting damp

algemeen: ALTIJD SPOED! IN ALLE GEVALLEN ARTS RAADPLEGEN! frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof / vaste stof

huid: bij *onbedekte huid* onmiddelijk deppen met een mengsel van polyethyleenglycol en alcohol (70:30) en direct spoedeisende medische hulp inzetten; bij *bedekte huid*: aan de huid vastgeplakte kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken en handelen als bij onbedekte huid..

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**:* Bij vergiftiging door deze stof is specifieke eerste hulp noodzakelijk. Een mengsel van polyethyleenglycol en alcohol (70:30) dient bij voorkeur ter plekke voorhanden te zijn.

Neem contact op met het NVIC (tel: +31 (0)30-274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 108-95-2 **Phenol** **C_6H_5-OH** **UN-nr: 2312**

Basis for the Dutch Intervention Values

VRW: Values based on other toxicological information than used as point of departure for the AEGL values

AGW: AEGL values are adopted (except 10 min value for which time scaling was applied), 2 hr value added

LBW: Not recommended, in accordance with AEGL

Date: 13-05-2009 | AEGL: Final, 2006

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	25	25	25	25	25	25	No effects in humans
AGW	160	110	90	71	57	45	Irritation and CNS depression in rats
LBW	NR	NR	NR	NR	NR	NR	Not recommended

Derivation of the Dutch Intervention Values

VRW: The VRW was based on a study in 8 human volunteers exposed by face mask to phenol at 5-25 mg/m³ (1.3-6.4 ppm) for 8 hours, with two breaks of 0.5 hours each after 2.5 and 5.5 hours. The author did neither report any complaints or adverse effects of phenol exposure nor did the report explicitly state the absence of any effects. The highest concentration causing no adverse effects (25 mg/m³) was used as a point of departure for the VRW values. No uncertainty factors were applied because it concerns a study in humans and the effect level was below that defined for VRW. No time scaling was applied because the point of departure is considered to be a threshold for irritation.

AGW: Inhalation data relevant for the derivation of AGW values are lacking. Therefore, a combination of studies was used as the basis for derivation of AGW values. Exposure of 6 female Harlan-Wistar rats for 8 hours at a nominal phenol aerosol at 900 mg phenol/m³ caused no deaths, but resulted in ocular and nasal irritation as well as in slight loss of coordination with spasms of the muscle groups within 4 hours and tremors and prostration (in 1/6 rats) within 8 hours. Another study reported a decreased white blood cell count after rats were exposed to 211 ppm (826 mg/m³) or 156 ppm (611 mg/m³) phenol for 4 hours. Although both studies had shortcomings, i.e., aerosol exposures, nominal concentrations, and no description of toxic signs in one study, taken together, they had consistent results. The derivation of AGW values was based on an exposure concentration of 900 mg/m³ for 8 hours. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Based on the small data base and study shortcomings, a modifying factor of 2 was applied. The equation $C^n \times t = k$ was used to derive exposure duration-specific values, using default values of n=1 and n=3 for extrapolation to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: Although phenol is a high-production-volume chemical, no acute inhalation studies of adequate quality were available for the derivation of the LBW value. Therefore, due to insufficient data and the uncertainties of a route-to-route extrapolation, LBW values were not recommended. It is noted that no lethality was observed in various single dose inhalation studies using different species up to air concentrations of 900 mg/m³ (aerosols, rats). One repeated dose inhalation study (7h/d, 5d/wk, for 4 wks) in guinea pigs is described in which animals died at day 28. However, this study was not used due to the uncertainties in the exposure concentration and because deaths were observed only after repeated exposure. Also, this study lacked control animals.

Additional toxicological information (including relevant results of a general literature search, if any)

Phenol causes local tissue damage at the sites of contact. The mechanism of acute irritation of skin and mucous membranes is not known. With regard to systemic exposure it has been reported that phenol results in hypotension and arrhythmias in humans.
Once absorbed, phenol is rapidly distributed in the organism. In experiments on rodents the phenol concentration in the blood reached its maximum immediately after the end of exposure and then decreased rapidly (half life after p.o. 150 mg/kg bw: 15 min). The elimination of phenol and its metabolites is nearly

completed within 24 hours. Since phenol is rapidly metabolized, systemic toxicity may be due to the combined actions of the parent compound and its metabolites.

Phenol is also a normal product of protein catabolism and it is taken up directly from cigarette smoke and food (especially smoked products).

No studies evaluating developmental or reproductive effects of phenol in humans were found.

H301: Toxic if swallowed; H311: Toxic in contact with skin; H314: Causes severe skin burns and eye damage; H331: Toxic if inhaled; H341: Suspected of causing genetic defects; H373: May cause damage to organs.

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to carcinogenicity to humans).

No carcinogenic risk potency (CRP) was derived.

Two epidemiological studies evaluating carcinogenic effects in phenol-exposed workers did not show a clear correlation between phenol exposure and increased tumor incidences, but a very weak carcinogenic effect cannot be excluded on basis of the available data. No valid inhalation studies evaluating the potential carcinogenic activity were located.

Odour and derivation of the LOA value

Odour: characteristic, sweet, tarry odour

OT_{50}: 0,063 mg/m^3 [AEGL, Don (1986)]
LOA = 11.8 * OT_{50} * 1.33 = 0,99 mg/m^3

(The concentration Level leading to distinct Odour Awareness (l=3) is calculated using the formula: l = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is below the VRW, therefore subjects will be aware of the odour below the level where health effects may be expected.

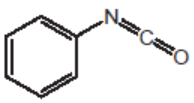
Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **25**	*AEGL-1* 59	*ERPG-1* 39		*IDLH: 980* (30 minutes)
AGW level **90**	*AEGL-2* 90	*ERPG-2* 200		
LBW level **NR**	*AEGL-3* NR	*ERPG-3* 780		

Stofdocument deel A

CAS-nr: 103-71-9
C_7H_5NO

Fenylisocyanaat



VN-nr: 2487
GEVI: 663

Synoniemen: fenylcarbimide, fenylcarbonimide, isocyanatobenzeen, PIC (Engels: phenyl isocyanate)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,11	0,11	0,11	0,11	0,11	0,11
Alarmeringsgrenswaarden	AGW (mg/m³)	14	4,8	2,4	1,2	0,59	0,30
Levensbedreigende waarden	LBW (mg/m³)	25	8,4	4,2	2,1	1,0	0,52

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,202 ppm; 1 ppm = 4,96 mg/m³

Explosiegrens: LEL = 1,2 vol% ≈ 60.000 mg/m³

Geur: stekend

LOA: niet afgeleid.

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: brandgevaarlijk, bij vele reacties kans op brand en explosie

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,01

Molecuulmassa:	119,1 g/mol
Zuurgraad:	geen data
LogKow:	2,6
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	2,6 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: irritatie ogen, neus en keel

AGW → LBW: matige tot ernstige irritatie van de luchtwegen, tranenvloed, keelpijn, hoesten, benauwdheid, longoedeem, mogelijk effecten op de ongeboren vrucht

Boven LBW: ernstige longschade, sterfte

LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Primaire effecten zijn irritatie van de slijmvliezen van ogen, neus en keel.
- Blootstelling aan fenylisocyanaat kan een astmatische reactie veroorzaken
- Blootstelling aan hoge concentraties fenylisocyanaat kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Fenylisocyanaat veroorzaakt vergelijkbare toxische effecten als methylisocyanaat.
- In analogie met methylisocyanaat kan niet worden uitgesloten dat fenylisocyanaat embryotoxiciteit kan veroorzaken
- Fenylisocyanaat is sensibiliserend voor de huid en mogelijk ook voor de luchtwegen.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn, bijtend, blaren, brandwonden
Oogcontact: bijtend, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende hulp inzetten.

Ontsmetting vloeistof
huid: overmaat stof opdeppen, verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en direct spoedeisende hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), (oog)arts raadplegen, blijven spoelen of druppelen tijdens vervoer.

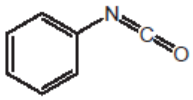
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende hulp inzetten.

***Specifieke behandeling en materialen**: geen.*
Neem contact op met het NVIC (Tel: 030 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 103-71-9
C_7H_5NO

Phenyl isocyanate



UN-nr: 2487

Basis for the Dutch Intervention Values

VRW: Different rationale than for AEGL, values are derived, 2h value added

AGW: Different point of departure as for AEGL values, different n-value is used, 2h value added

LBW: Different point of departure as for AEGL values, different uncertainty factors and n-value are used, 2h value added

Date: 16-10-2018 | AEGL document: final 2013

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.11	0.11	0.11	0.11	0.11	0.11	Sensory irritation in rats
AGW	14	4.8	2.4	1.2	0.59	0.30	Respiratory tract injury in rats
LBW	25	8.4	4.2	2.1	1.0	0.52	Lethality in rats

Derivation of the Dutch Intervention Values

VRW: VRW values were based on animal data. Rats (n=4/group) were exposed nose-only to analytically determined phenyl isocyanate concentrations of 0, 1.9, 5.14 or 12.92 mg/m^3 for 45 minutes. This resulted in a concentration-related decrease in respiratory rate (approximately 20-50% decrease relative to controls). On the basis of data presented graphically, the highest exposure (12.92 mg/m^3) resulted in a decrease in respiratory rate of about 50%, suggesting that the RD_{50} for phenyl isocyanate in rats is about 13 mg/m^3. The investigators reported an estimated threshold exposure for upper respiratory tract sensory irritation of 1.1 mg/m^3. This was used as point of departure for the VRW. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was not applied as sensory irritation is considered to be concentration-dependent rather than concentration × time-dependent.

AGW: AGW values were based on animal data. Groups of 20 male Wistar rats were exposed to concentrations of 0, 1, 4, 7, or 10 mg/m^3 phenyl isocyanate for 2 weeks (6 hr/day, 5 days/week), followed by a 2-month observation period. In the 7 and 10 mg/m^3 groups, delayed mortality was observed, which appeared to be associated with respiratory acidosis and hypoxemia. In the 4 mg/m^3 concentration group, goblet cell hyperplasia was found but no clinical signs were observed. The concentration of 4 mg/m^3 was used as point of departure for deriving the AGW values. This PoD is supported by another study in rats, in which groups of 10 male and 10 female Wistar rats were exposed to concentrations of 0, 0.12, 0.57 or 3.14 mg/m^3 for 6 hours/day for 5 days, followed by a 3-week observation period. No significant clinical signs were observed up to 0.57 mg/m^3. At the concentration of 3.14 mg/m^3, rats exhibited serous nasal discharge but no significant treatment-related effects were observed 2-3 days post-exposure. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences.Time scaling was performed using $C^n \times t = k$, with the substance-specific value for n of 1 (based on analogy with methyl isocyanate) for extrapolation to longer and shorter exposure durations.

LBW: LBW values were derived from a lethality study in rats. Groups of five male and five female young-adult Wistar rats (70 animals in total) were exposed to concentrations of 0.14, 1.1, 2.4, 3.1, 5.7, 9.7 or 18 ppm (0.694, 5.45, 11.9, 15.4, 28.2, 48.1 or 89.2 mg/m^3) for 4 hours, followed by an observation period of at least 30 days. No mortality occurred in the lowest two concentration groups and in the 15.4 mg/m^3 groups. At 11.9 mg/m^3, one male rat died. In the 28.2 mg/m^3 group, 3/5 female and 4/5 males died. In the two highest concentration groups (48.1 and 89.2 mg/m^3) all rats died. Most of the deaths occurred within 9 days post-exposure. Doseresp was applied and the calculated 4-hour LC_{50} and LC_{01} values were 23.42 and 10.48 mg/m^3, respectively. The 4-hour LC_{01} value of 10.48 mg/m^3 was used as point of departure for deriving the LBW values. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n \times t = k$, with the substance-specific value for n of 1 (based on analogy with methyl isocyanate) for extrapolation to longer and shorter exposure durations.

Additional toxicological information (including relevant results of a general literature search, if any)
No studies were located that address the mechanism(s) of toxicity of phenyl isocyanate. Because the toxic effects of phenyl isocyanate and other monoisocyanates (respiratory irritation and delayed lethality) are clinically similar to those of the structurally related compound methyl isocyanate, these compounds may share a similar mode of action. No information was found on developmental or reproductive toxicity and genotoxicity of phenyl isocyanate. However, the structurally related compound methyl isocyanate is a developmental toxicant. Phenyl isocyanate has been found to be a potent dermal sensitizer. Information on its potency for respiratory sensitization is limited. Allergenic airway effects were however identified in an exploratory study with guinea pigs. No harmonised H-statements for human health

Carcinogenicity and derivation of the CRP value
IARC classification: not evaluated No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value
Odour: pungent No LOA was derived (due to lack of data).

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)*** [38]

VRW level **0.11**	*AEGL-1* NR	*ERPG-1* 0.50		*IDLH:* not derived
AGW level **2.4**	*AEGL-2* 0.047	*ERPG-2* 2.0		
LBW level **4.2**	*AEGL-3* 0.14	*ERPG-3* 5.9		

[38] Note that the AEGL and ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL and ERPG, respectively.

Stofdocument deel A

CAS-nr: 7782-41-4 **Fluor** F_2 **VN-nr: 1045**

GEVI: geen

Synoniemen: difluor (Engels: fluorine) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	2,7	2,7	2,7	2,7	2,7	2,7
Alarmeringsgrenswaarden	AGW (mg/m³)	66	35	16	11	7,2	4,9
Levensbedreigende waarden	LBW (mg/m³)	110	58	40	27	18	12

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,633 ppm; 1 ppm = 1,58 mg/m³

Explosiegrens: geen data

Geur: Stekende geur

LOA: 2,51 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: licht groengeel gas

Brand: niet brandbaar, bevordert brand van andere stoffen

Relatieve dichtheid gas (lucht=1): 1,3

Molecuulmassa: 38,0 g/mol
Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: reactie
Verzadigde dampdruk: 100.000 mbar

Overige informatie

Publieke grenswaarde: 0,5 mg/m³ (15 min)
MAK: 0,16 mg/m³
TLV-TWA: 1,6 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte irritatie bovenste luchtwegen en ogen

VRW → AGW: lichte tot matige irritatie bovenste luchtwegen en ogen

AGW → LBW: matige tot ernstige irritatie van de luchtwegen huid en ogen, benauwdheid, keelpijn, pijn op de borst, longoedeem, ophoesten van bloed, hartritmestoornissen, koorts

Boven LBW: ernstige longschade, ernstige bloeddrukdaling, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt zeer bijtend op de ogen, de huid en de luchtwegen.
- Blootstelling aan fluor kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Bij blootstelling (o.a. in contact met vocht) kan HF worden gevormd.
- De stof kan bij hoge concentraties inwerken op de nieren en lever met als gevolg functiestoornissen en nier- en leverschade.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, huidletsel

Oogcontact: bijtend, roodheid en pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust, halfzittende houding, vernevelde 4% calciumgluconaatoplossing laten inhaleren en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer (alternatief: druppelen met 1% calciumgluconaat).

huid: spoelen met veel water / kleding uittrekken , daarna zo snel mogelijk 10% calciumglucontaatgel herhaaldelijk dik aanbrengen en inmasseren en direct spoedeisende hulp inzetten.

inslikken: n.v.t. (gas).

Specifieke behandeling en materialen: Bij vergiftiging door deze stof is specifieke eerste hulp noodzakelijk; calciumgluconaatoplossingen en -gel moeten met gebruiksaanwijzing beschikbaar zijn.

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7782-41-4 **Fluorine** F_2 **UN-nr: 1045**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same point of departure and rationale as for AEGL values but using different uncertainty factors, time scaling to 8h value, no time scaling to 10 min, 2h value added

LBW: Same point of departure and rationale as for AEGL values but using different uncertainty factors, time scaling applied to 8 value, 2h value added

Date: 06-10-2016 AEGL document: final, 2010

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	2.7	2.7	2.7	2.7	2.7	2.7	No irritant effects in humans
AGW	66	35	16	11	7.2	4.9	Very mild lung congestion in mice
LBW	110	58	40	27	18	12	Threshold for mortality

Derivation or the Dutch Intervention Values

VRW: In a study with five human volunteers, the subjects were exposed to concentrations of 10 ppm (16 mg/m³) for 15 minutes, 25 ppm (40 mg/m³) for 5 minutes, 50 ppm (79 mg/m³) for 3 minutes, 67 ppm (106 mg/m³) for 1 minute, 78 ppm (123 mg/m³) for 1 minute and 100 ppm (158 mg/m³) for 1 minute. At 25 ppm (40 mg/m3) and higher concentrations increasing irritation to the eyes and nose was observed. In addition, slight irritation to the eyes and skin was reported at exposure to 16 mg/m³ for 3 to 5 minutes every 15 minutes over a 2- to 3-hour period. An exposure to a concentration of 10 ppm (16 mg/m³) for 15 min was selected as the point of departure for derivation of the VRW values.
The default uncertainty factor of 3 is considered sufficient to account for intraspecies differences. A modifying factor of 2 was applied to address the limited data that is available for longer exposure durations. At mildly irritating concentrations there is accommodation to irritating gases. This is also supported by limited workplace monitoring data (i.e. workers exposed to fluorine at average yearly concentrations up to 1.2 ppm (range 0.0 – 17 ppm) over a four-year period reported fewer incidences of respiratory complaints or diseases than a similar group of non-exposed workers). Therefore, the resulting value of 1.7 ppm (2.7 mg/m³) was applied to all time points.

AGW: For the derivation of the AGW values, mild lung congestion was chosen as the threshold for irreversible or serious long lasting effects. In a study with five species (dogs, rats, mice, guinea pigs and rabbits), results were similar between species but mice revealed the lowest threshold concentration. LC_{50} values for 5, 15, 30 and 60 minutes were determined after which animals were exposed to concentrations equal to approximately 50%, 25%, 12.5% and 6% of the LC_{50} values for the respective exposure times to study the occurrence of sublethal effects. The threshold for very mild lung congestion in mice for an exposure of 30 min (67 ppm (106 mg/m³)) was used as point of departure for derivation of the AGW values for shorter exposure durations and the threshold for very mild lung congestion in mice for an exposure of 60 min (30 ppm (47 mg/m³)) was used as point of departure for derivation of the AGW values for longer exposure durations.
An interspecies uncertainty factor of 1 is considered sufficient considering the limited variability between species and the mechanism of action, which is direct chemical (corrosive) destruction of lung tissue. The default uncertainty factor of 3 is considered sufficient to account for intraspecies differences. The total uncertainty factor is therefore 3. Time-scaling was performed using $C^n \times t = k$, with the chemical-specific n-value of 1.77.

LBW: The same study as for AGW was chosen for the derivation of the LBW values. No mortality was observed in any of the five tested species when exposed to a concentration equal to 50% of of the determined LC_{50} for 5, 15 30 or 60 minutes. The 1-hour exposure to 75 ppm (119 mg/m³) in mice was chosen as point of departure for derivation of the LBW values. Mice revealed the lowest concentration for threshold of mortality, although no clear differences were observed between the species.
An interspecies uncertainty factor of 1 is considered sufficient considering the limited variability

between species and the mechanism of action, which is direct chemical (corrosive) destruction of lung tissue. The default uncertainty factor of is considered sufficient to account for intraspecies differences. The total uncertainty factor is therefore 3. Time-scaling was performed using $C^n \times t = k$, with the chemical-specific n-value of 1.77 (based on regression analysis of the mouse LC_{50} data).

Additional toxicological information (including relevant results or a general literature search, if any)

Fluorine causes severe irritation to the skin, eyes and respiratory tract. Penetration into the lungs results in pulmonary haemorrhage and edema and may result in death. Serious systemic effects are unlikely to occur at a level below that would cause serious respiratory effects.

Fluorine is rapidly absorbed following oral ingestion, crosses the placenta in limited amounts, and is found in placental and fetal tissue. Studies on the incidence of reproductive or developmental effects in areas using fluoridated water have found no correlation between fluoridation levels and birth defects. Two studies suggest that fluorine might influence the neurons of the cerebral cortex in the developing brain of a fetus (Du et al. 2008, He et al. 2008). The studies, however, are based on oral exposures and provide equivocal results.

H330: Fatal if inhaled; H314: Causes severe skin burns and eye damage

Carcinogenicity and derivation or the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation or the LOA value

Odour: pungent odour

Odour threshold: 0.16 mg/m^3 [Amoore, 1983]
LOA = 11.8 * ODT * 1.33 =2.51 mg/m^3

(The concentration Level leading to distinct Odour Awareness (l=3) is calculated using the formula: $l = 2.33 * \log (C/OT_{50}) + 0.5$. A correction factor or 1.33 is applied to this value)

The LOA lies below all intervention values.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level 2.7	*AEGL-1* 2.7	*ERPG-1* 0.79		*IDLH:40 mg/m^3 (30 min)*
AGW level 16	*AEGL-2* 7.9	*ERPG-2* 7.9		
LBW level 40	*AEGL-3* 21	*ERPG-3* 32		

Stofdocument deel A

CAS-nr: 7664-39-3 **Fluorwaterstof** HF **VN-nr: 1052**
GEVI: 886

Synoniemen: waterstoffluoride (Eng.: Hydrogen fluoride) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,83	0,83	0,83	0,83	0,83	0,83
Alarmeringsgrenswaarden	AGW (mg/m³)	79	29	20	14	10	10
Levensbedreigende waarden	LBW (mg/m³)	150	51	36	26	18	18

Datum vaststelling: November 2015 — Conversiefactor: 1 mg/m³ = 1,20 ppm; 1 ppm = 0,83

Explosiegrens: geen data

Geur: stekende geur
LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas of hygroscopische vloeistof
Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,5

Molecuulmassa:	20 g/mol
Zuurgraad:	geen data
LogKow:	-0,9
Wateroplosbaarheid:	Volledig
Verzadigde dampdruk:	1000 mbar

Overige informatie

Publieke grenswaarde: 1 mg/m³ (15 min TGG)
MAK: 0,83 mg/m³
TLV-TWA: 2,50 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire bloostelling:

Onder VRW: mogelijk lichte irritatie bovenste luchtwegen en ogen

VRW → AGW: lichte tot milde irritatie bovenste luchtwegen en ogen

AGW → LBW: matige tot ernstige oogirritatie en irritatie van de bovenste (ogen, neus en keel) en onderste luchtwegen (druk op de borst, hoesten, speekselvloed en piepende ademhaling), huidirritatie, kortademigheid, tranende ogen, longoedeem, blijvende longschade.

Boven LBW: longoedeem, pulmonaire bloedingen, , sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling:

- Fluorwaterstof is een sterk irriterende tot bijtende stof en werkt in op de luchtwegen, huid en ogen.
- Afhankelijk van de concentratie kan fluorwaterstof, vanwege de goede wateroplosbaarheid, afgevangen worden in de bovenste luchtwegen (neus). Bij hogere concentraties vindt penetratie in de longen plaats.
- Bij inhalatie kan fluorwaterstof leiden tot een type I inhalatoire intoxicatie.
- Hartritmestoringen zijn ook waargenomen bij accidentele dermale en inhalatoire blootstelling bij mensen. Het is echter nog onduidelijk of inhalatoire blootstelling alleen dit effect ook kan bewerkstelligen.
- Fluorwaterstof kan mogelijk bij inhalatie longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, pijn, ernstige brandwonden
Oogcontact: roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: n.v.t.

Beknopte medische informatie

Algemene informatie bij inademen/inslikken:

Inademing/inslikken van fluorwaterstof kan leiden tot larynx- en glottisoedeem, met risico op verstikking (asfyxie) door zwellingen in de keel. Intubatie eventueel gevolgd door beademing moeten in ernstige gevallen z.s.m. worden uitgevoerd (door specialisten).

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding calciumgluconaatoplossing 4% als vernevelde oplossing laten inhaleren en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken (vastgevroren kleding niet lostrekken), afspoelen met water, daarna zo snel mogelijk calciumgluconaatgel 10% op de besmette huid aanbrengen[1)] en blijven inwrijven en direct spoedeisende medische hulp inzetten.

ogen: *uit*spoelen met water (evt. contactlenzen verwijderen), daarna zo snel mogelijk calciumgluconaatoplossing 4% in de ogen druppelen[2)], dan naar oogarts brengen. Blijven druppelen tijdens vervoer.

inslikken: n.v.t. (gas); maar in geval van inslikken van een oplossing: mond laten spoelen (uitspugen!), 200 ml calciumgluconaat 4% laten drinken[3)], GEEN braken opwekken en direct spoedeisende medische hulp inzetten[1].

Specifieke behandeling en materialen*: calciumgluconaatoplossing 4% (inademen, ogen[39)] en inslikken[40)]); calciumgluconaatgel 10% (huid[41)])*.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

[39] bij het ontbreken van de 4% calciumgluconaatoplossing ogen minimaal 15 min. spoelen met water.
[40] bij het ontbreken van de 4% calciumgluconaatoplossing maximaal 200 ml water of melk laten drinken.
[41] bij het ontbreken van de 10% calciumgluconaatgel de huid met veel water spoelen of douchen.

Stofdocument deel B

CAS-nr: 7664-39-3 **Hydrogen fluoride** **HF** **UN-nr: 1052**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2 h value added

AGW: AEGL value is adopted, 2 h value added

LBW: AEGL value is adopted, 2 h value added

Date: November 2015 | AEGL document: Final 2004

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.83	0.83	0.83	0.83	0.83	0.83	Threshold for slight irritation (respiratory tract) in humans
AGW	79	29	20	14	10	10	Slight irritation (nose, throat, eyes) in animals
LBW	150	51	36	26	18	18	Lethality animals

Derivation of the Dutch Intervention Values

VRW: As starting point for the derivation of the VRW values, the results of a human volunteer study were used. A concentration of 3 ppm (2.49 mg/m³) for 1 hour was considered a sub threshold for lung inflammation in healthy exercising adults of which 2 had increased immune parameters. At this level there were no increases in markers of lung inflammation, which include neutrophils, eosinophils, protein, and methyl histamine. There were no changes in lung functions and no to minor symptoms of irritation. The default intraspecies factor of 3 was used. The same value was applied across all VRW time points, because mild irritancy generally does not vary greatly over time, and it is not expected that prolonged exposure will result in an enhanced effect. Longer exposure duration studies corroborate these findings.

AGW: For the 10-min AGW the 10-minute data from a rat inhalation study by cannulation were used. Mortality occurred at 1764 ppm (1464 mg/m³). The next lower level of 950 ppm (789 mg/m³) was used as starting point, although no serious effects were observed at that level.

For the other AGW values, the 1-hour exposure of dogs at 243 ppm (202 mg/m³) was chosen as basis. The animals displayed signs of irritation and discomfort including blinking, sneezing, and coughing. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences for both point of departures. The values were scaled across time using $C^n \times t = k$, with n=2, derived from time scaling data with the rat. The calculated 8-hr value of 8.6 ppm (7.1 mg/m³) is inconsistent with the human data in which humans inhaling 8.1 ppm (6.7 mg/m³) intermittently for 6 hours suffered no greater effects than slight irritation. Therefore, the 8 hour value was set equal to the 4 hour value. The resulting AGW-values are supported by human data: human subjects exposed intermittently at 8 ppm (6.64 mg/m³) for 6 h over a 10-50 day period experienced only slight irritation.

LBW: The concentration causing death in one of 20 trachea-cannulated rats, exposed for 10 minutes to 1,764 ppm (1464 mg/m³), was chosen as the lethal threshold for the 10-min LBW. Although 1/20 is higher than the usual threshold for the LBW, the trachea-cannulation model is conservative compared with normal nose-breathing, because it bypasses nasal scrubbing and maximizes the pulmonary dose. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences for the 10-min AGW. The 10 min LBW is clearly below levels that cause death in tests in monkeys, rats, dogs, mice, guinea pigs, and rabbits. Furthermore, the use of monkey data (690 ppm (573 mg/m³, 1 hour, no deaths) as starting point for the derivation of the 10 min LBW would lead to a comparable value.

For the other LBW-values, the 60 min value of 263 ppm (218 mg/m³), which was the highest nonlethal concentration for the mouse reported, was used as starting point. The mouse was found to be approximately 3 times more susceptible to the effects of HF than the rat. Therefore, an interspecies factor of 1, instead of the default of 3, was considered acceptable. The default

intraspecies factor of 3 was applied to account for differences in susceptibility between individuals. In addition, a modifying factor of 2 was applied, because the highest non-lethal value of 263 ppm (218 mg/m^3) was close to the 60-min LC_{50} of 342 ppm (284 mg/m^3). The 30-min, 1-, 2-, and 4- hour values were calculated based on the C^n x t = k relationship, with n=2, derived from time-scaling data with the rat. Because the time-scaled 8 hr value of 15 ppm (12.5 mg/m^3) is inconsistent with the animal data (e.g. 18.5 ppm (15.4 mg/m^3) for 50 days in monkeys resulted only in kidney lesions), the 8-hour value was set equal to the 4-hour value. A total uncertainty factor of 6 is considered sufficient. If a total factor of 20 (3x3x2) were used, the predicted 6-h LBW would be 5.4 ppm (4.5 mg/m^3), whereas humans exposed intermittently at 8 ppm (6.64 mg/m^3) for 6 hours over a 25-50 days period experienced only slight irritation. Even a susceptible person should not experience a life-threatening effect at that concentration. In addition, the use of a total factor of 20 would drive the LBW values below the AGW values. The database of HF is very extensive and many other studies with laboratory animals support the LBW values.

Additional toxicological information (including relevant results of a general literature search, if any)

Hydrogen fluoride causes severe irritation to the skin, eyes, and respirator tract, particularly the anterior nasal passage, it appears to be scrubbed from the inhaled air. Penetration into the lungs results in pulmonary hemorrhage and edema and may result in death. Cardiac arrhythmias have been seen in humans following accidental dermal and inhalation exposure. It is unknown whether inhalation exposure alone would also cause this effect. Although renal and hepatic changes have been observed in animal studies, serious systemic effects are unlikely to occur at a level below what would cause serious respiratory effects.

Hydrogen fluoride is not expected to induce reproductive toxicological effects or developmental effects after single high inhalation exposure. The available studies are based on fluoride salts via oral exposure and provide equivocal results.

H300: Fatal if swallowed; H310: Fatal in contact with skin; H314: Causes severe skin burns and eye damage; H330: Fatal if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified.

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: Pungent odour

An unreliable odour threshold of 0.04 ppm (0.03 mg/m^3) was reported in literature (AIHA, 1989)

No LOA was derived due to lack of reliable data.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **0.83**	*AEGL-1* 0.8	*ERPG-1* 1.7		*IDLH:* 25 mg/m^3 (30 min)
AGW level **20**	*AEGL-2* 20	*ERPG-2* 17		
LBW level **36**	*AEGL-3* 36	*ERPG-3* 42		

Stofdocument deel A

CAS-nr: 50-00-0 **Formaldehyde** H_2CO **VN-nr: 2209**

GEVI: 80

Synoniemen: methanal, methylaldehyde, methyleenoxidel (Engels: formaldehyde) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	1,3	1,3	1,3	1,3	1,3	1,3
Alarmeringsgrenswaarden	AGW (mg/m³)	17	17	17	17	17	17
Levensbedreigende	LBW (mg/m³)	130	88	69	55	44	44

Datum vaststelling: 13-05-2009

Conversiefactor: 1 mg/m³ = 0,801 ppm; 1 ppm = 1,25 mg/m³

Explosiegrens: LEL= 7 vol% ≈ 87.000 mg/m³ (methanolvrij formaldehyde)

Geur: stekende, verstikkende geur

LOA: 2,8 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas
Brand: brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,07

Molecuulmassa: 30,0 g/mol
Zuurgraad: Geen data
LogKow: 0,4
Wateroplosbaarheid: 40 g/ 100 ml
Verzadigde dampdruk: 5200 mbar

Overige informatie

Publieke grenswaarde: 0,15 mg/m³ (8 uur)
MAK: 0,37 mg/m³
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte oogirritatie

VRW → AGW: oog- en luchtwegirritatie, keelpijn, hoesten

AGW → LBW: ernstige oog- en luchtwegirritatie, tranenvloed, hoofdpijn, sufheid, benauwdheid, longoedeem

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Formaldehyde werkt sterk irriterend op de luchtwegen.
- Formaldehyde kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- De stof is mogelijk sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, pijn, jeuk, blaren

Oogcontact: roodheid, pijn, tranenvloed, slecht zien

Carcinogeniteit

IARC classificatie: 1
CRP: 1752 mg/m³

Beknopte medische informatie

Ontsmetting gas
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: niet van toepassing.
ogen: niet van toepassing.
inslikken: niet van toepassing.

Specifieke behandeling en materialen*: geen*.

Neem contact op met het NVIC (tel: +31(0)30–274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 50-00-0 **Formaldehyde** **H_2CO** **UN-nr: 2209**

Basis for the Dutch Intervention Values

VRW: Different point of departure as for AEGL-values

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 13-05-2009 | AEGL document: Interim, 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	1.3	1.3	1.3	1.3	1.3	1.3	Slight eye irritation in humans
AGW	17	17	17	17	17	17	Mild lacrimation with adaptation humans
LBW	130	88	69	55	44	44	Highest non-lethal value rats

Derivation of the Dutch Intervention Values

VRW: The VRW values were based on results of a controlled human exposure study with formaldehyde. Healthy subjects (11 males, 10 females) were exposed to various concentrations formaldehyde for 4h/day 5 days/week for 2 consecutive weeks. Exposures were conducted in a double-blind fashion. Minimal objective eye irritation was observed at short-term peak exposures of 1.0 ppm (1.25 mg/m³) that occurred at a baseline exposure of 0.5 ppm (0.63 mg/m³) formaldehyde.
Exposure of 1 ppm (1.25 mg/m³) formaldehyde was used as point of departure. No interspecies uncertainty factor was applied as exposure was conducted in human subjects. No intraspecies uncertainty factor was applied as in additional studies no additional sensitive populations were identified [there were no significant decrements in pulmonary function parameters in exercising asthmatic subjects at 2 or 3 ppm (2.5 – 3.7 mg/m³), and asthmatic subjects reported <moderate eye irritation, the same as healthy subjects, at these concentrations].
Because several studies show there is adaptation to irritation at this low concentration, the 1.0 ppm (1.25 mg/m³) concentration was applied across all exposure durations. The 1.0 ppm (1.25 mg/m³) value is supported by the fact that studies in rat and mice show there is no damage to the respiratory epithelium during single exposure to 2, 3 or 4 ppm (2.5, 3.7 or 5.0 mg/m³) or repeated exposures to 1 or 2 ppm (1.2 or 2.5 mg/m³). Rodents have higher respiratory rates than humans, which increases the dose delivered to the target tissues.

AGW: The AGW was based on a study with twelve healthy male human subjects that inhaled 13.8 ppm (17.2 mg/m³) for 30 minutes. Initially, the exposure caused considerable nose and eye irritation. Mild lacrimation continued for some period of time. The eye irritation was not considered severe, and adaptation occurred in about 10 minutes. Mild lacrimation at 13.8 ppm (17.2 mg/m³) with adaptation was considered the threshold concentration for the inability to escape. The lacrimation experienced by two healthy investigators at 20 ppm (25 mg/m³) during short exposures might impair the ability to escape. The 13.8 ppm (17.2 mg/m³) concentration may also be close to the threshold for an increase in airways resistance, as observed at 8 and 13 ppm (10 and 16 mg/m³) during short exposures by 100% mouth breathing in humans. No intraspecies uncertainty factor was applied to the 13.8 ppm (17.2 mg/m³) concentration because application of an uncertainty factor of 3 would lower the value close to a no-effect concentration in several studies with exercising asthmatics. Because the endpoint is eye and nose irritation to which adaptation occurs, the same value was used across all exposure durations.

LBW: The LBW values were based on the highest non-lethal value for the rat (350 ppm = 440 mg/m³) during a 4-hour exposure. The value was adjusted by interspecies and intraspecies uncertainty factors of 3 each for a total of 10. These uncertainty factors, applied to irritants, are protective of sensitive populations. Furthermore, application of larger uncertainty factors, e.g., a total of 30, would reduce the value to the level of the AGW. No data on time-scaling were found. Therefore, time-scaling was performed using the equation $C^n \times t = k$, and the default value of n = 3 when scaling to shorter exposure periods. The 8-hour value was set equal to the 4-hour value because formaldehyde is well scrubbed in the nasal passages. Furthermore, application of the default of n = 1 when scaling to longer time periods would result in an 8-hour value of 18 ppm (22 mg/m³), comparable to the 8-hour AGW. The 8-hour value is supported by sublethal concentrations in additional animal studies. A concentration of 35 ppm (44 mg/m³) for 18 hours was reported as sublethal for the rat. In chronic studies, mice survived 5 hour/day exposures to 15 ppm

(19 mg/m^3).

Additional toxicological information (including relevant results of a general literature search, if any)

The VRW values were based on a study of Lang *et al.* (Reg Tox Pharm 2008; 50, 23-26). In this study, humans were exposed to various concentrations formaldehyde in a double-blinded fashion. Objective effects

Formaldehyde is a highly cytotoxic respiratory tract irritant. The exact mechanism of formaldehyde's irritant, corrosive, and cytotoxic effects is unknown. Studies with several species of animals confirm that the upper respiratory tract is a critical target for inhaled formaldehyde. Inhaled formaldehyde damages epithelial tissue in specific regions of the upper respiratory tract in rats, mice, and monkeys. Lesions consist of hyperplasia and squamous cell metaplasia. Lung damage occurs at higher concentrations than those affecting only the upper respiratory tract. Since formaldehyde is highly water soluble, it is rapidly and almost completely absorbed from the respiratory tract and extensively 'scrubbed' in the anterior nasal passages. Nose and throat irritation can become more severe during physical exertion. Dermal contact may cause sensitization.

As a result of occupational exposure, formaldehyde asthma may develop

Several studies show there is adaptation to irritation of eye and nose at low concentrations. Except for humans specifically sensitive to formaldehyde exposure, no additional sensitive populations were identified.

There is no indication of reproduction toxicity of formaldehyde.

H301:Toxic if swallowed; H311: Toxic in contact with skin; H314: Causes severe skin burns and eye damage; H317: May cause an allergic skin reaction; H331: Toxic if inhaled; H341: Suspected of causing genetic defects; H350: May cause cancer.

Carcinogenicity and derivation of the CRP value

IARC classification: 1 (carcinogenic to humans)

Derivation of the carcinogenic risk potency (CRP):

10^{-4} risk level after inhalation: 8 µg/m^3 [IRIS]

CRP = (10^{-4} risk level * average life span in hours)/DRCF

= (8 * 10^{-3} mg/m^3 * 613,200) /2.8 = 1752 mg/m^3

Calculations are based on one study in which neoplastic lesions – squamous cell carcinomas, squamous cell papillomas, or polyploid adenomas - were observed in rats exposed to 5.6 ppm (7.0 mg/m^3) and in mice exposed to 14.3 ppm (17.8 mg/m^3) for 6 hours/day, 5 days/week for 24 months.

Odour and derivation of the LOA value

Odour: pungent, suffocating odour.

OT_{50}: 0.145 ppm (0.181 mg/m^3) [Berglund et al., 1987]

LOA = 11.8 * OT_{50} * 1.33 = 2.8 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies above the VRW, but is lower than the AGW and LBW levels at all time points.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **1.3**	*AEGL-1* 1.1	*ERPG-1* 1.2		*IDLH:*25 (30 minutes)
AGW level **17**	*AEGL-2* 17	*ERPG-2* 12		
LBW level **69**	*AEGL-3* 70	*ERPG-3* 50		

Stofdocument deel A

CAS-nr: 7803-51-2 **Fosfine** PH_3 **VN-nr: 2199**

GEVI: 263

Synoniemen: fosforwaterstof (Engels: phosphine) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	17	5,6	2,8	1,4	0,71	0,35
Levensbedreigende waarden	LBW (mg/m³)	30	10	5,1	2,5	1,3	0,64

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,707 ppm; 1 ppm = 1,41 mg/m³

Explosiegrens: LEL = 1,8 vol% ≈ 25.000 mg/m³

Geur: Ui-, vis- of knoflook geur, puur: geurloos

LOA: niet afgeleid.

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloos gas

Brand: zeer brandgevaarlijk, kan met lucht explosief zijn

Relatieve dichtheid: geen data

Molecuulmassa: 34,0 g/mol

Zuurgraad: geen data

LogKow: geen data

Wateroplosbaarheid: 26 g/100 ml (goed)

Verzadigde dampdruk: 41900 mbar

Overige informatie

Publieke grenswaarde: 0,14 mg/m³ (8 uur)

MAK: 0,14 mg/m³

TLV-TWA: 0,42 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling aan damp

*Onder **AGW***: irritatie aan ogen, huid, neus en luchtwegen, hoofdpijn, misselijkheid, braken, zwakte, paresthesie, duizeligheid, tremor

AGW → LBW: benauwdheid, longoedeem, bewustzijnsdaling, hartritmestoornissen, nier- en leverfunctiestoornissen

Boven LBW: convulsies, cardiovasculaire collaps, myocardinfarct, ademnood, coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Fosfine verstoort door effecten op de celademhaling de zuurstofopname en energievoorziening van de cel.
- Fosfine werkt irriterend op de ogen, huid en luchtwegen.
- Hoge blootstelling kan tot longoedeem leiden. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Kinderen zijn mogelijk gevoeliger voor toxiciteit door fosfine.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid

Oogcontact: roodheid, pijn

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: spoelen met water (evt. contactlenzen verwijderen).

Ontsmetting vloeistof

huid: aan de huid vastgevroren kleding NIET lostrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.

ogen: *bij bevriezing*: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: niet van toepassing (gas).

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7803-51-2 **Phosphine** **PH_3** **UN-nr: 2199**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 24-09-2009 | AEGL document: Final, 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	(insufficient data)
AGW	17	5.6	2.8	1.4	0.71	0.35	Irritation nasal mucosa rats
LBW	30	10	5.1	2.5	1.3	0.64	Lethality in rats

Derivation of the Dutch Intervention Values

VRW: No appropriate human or animal data are available for derivation of VRW for phosphine. Therefore VRW values are not recommended. This does not imply that exposure below AGW is without adverse effects.

AGW: AGW values were based on red mucoid nasal discharge in rats exposed to 10 ppm (14 mg/m³) phosphine for 6 hours. Since this endpoint is less severe than effects defined by AGW, the resulting values should be protective. An uncertainty factor of 3 was applied to account for interspecies variability since time to death lethality data from 45 minutes to 30 hours for rats, mice, rabbits, and guinea pigs suggest little species variability. An uncertainty factor of 10 was applied to account for intraspecies variability since the human data suggest that children may be more sensitive than adults when exposed to presumably similar phosphine concentrations. For example, in two reports, exposed children died, but exposed adults survived. For AEGL-values, time scaling was performed using the equation $C^n \times t = k$, and a n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine). It was noted that the derivation of the value of n=1 is based on data derived from three different studies, which is not in line with the procedures of the Dutch expert panel on probits. However, using the data of a single study (Muthu et al., 1980) would result in n=0.544, leading to unrealistically high AGW-values. As an alternative, using the default values for n (n=1, n=3) would lead to unrealistically low AGW-values. Therefore, the n-value of 1, as used by AEGL, is adopted for derivation of AGW-values.
In contrast to the 10 minute AEGL-2 value that was set equal to the 30 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: The highest concentration yielding no deaths in rats (18 ppm = 25 mg/m³) for 6 hours was used as point of departure for the calculation of the LBW values. An interspecies uncertainty factor of 3 and an intraspecies factor of 10 were applied for reasons provided above. Time scaling was performed using the equation $C^n \times t = k$ and a n-value of 1 was accepted (due to a lack of a better alternative, see above).
In contrast to the 10 minute AEGL-3 value that was set equal to the 30 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.
These values are considered protective since workers were repeatedly exposed for “brief” periods of time to phosphine concentrations up to 35 ppm (49 mg/m³) with no life-threatening effects and workers exposed to >50 ppm (>70 mg/m³) for 2-5 minutes experienced only odor.

Additional toxicological information (including relevant results of a general literature search, if any)

A very steep concentration-response curve is observed for phosphine toxicity. Children are thought to be more sensitive to phosphine exposure. Common clinical signs after exposure to phosphine are headache, vomiting, coughing, shortness of breath, paresthesia, weakness, tremors and jaundice. Pulmonary congestion, pleural effusion, and congestive heart failure may be observed upon post-mortem examination.

In vitro, phosphine reacts with cytochrome c and cytochrome c oxidase, thereby inhibiting mitochondrial

oxygen uptake. In vitro studies have also shown that phosphine can react with the heme moiety of hemoglobin in the presence of oxygen. Cell death and loss of cell membrane integrity accounted for the increased liver enzymes, bronchiolytic effects, cloudy swelling of renal tubular epithelia, and hemorrhagic myocardial lesions.

No reproductive or developmental data were located in the literature.

H314: Causes severe skin burns and eye damage; H330: Fatal if inhaled.

Carcinogenicity and derivation of the CRP value
IARC classification: not classified. No carcinogenic risk potency (CRP) was derived. Fumigation workers exposed long-term to phosphine have a higher incidence of both stable and less stable chromosomal aberrations. Molecular analysis of these lesions suggests that the breakpoints are near proto-oncogenes involved in non-Hodgkin's lymphoma, possibly contributing to the increased incidence of lymphomas in pesticide workers.

Odour and derivation of the LOA value
Odour: pure phosphine is odourless at concentrations up to 283 mg/m^3 (200 ppm). Technical-grade phosphine has garlic-like odour (may be due to impurities). No LOA was derived due to lack of reliable data. Ruth (1986) reported an odor range of 0.028-3.6 mg/m^3.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **NR**	*AEGL-1* NR	*ERPG-1* NR		*IDLH:* 71 mg/m^3 (10 minutes)
AGW level **2.8**	*AEGL-2* 2.8	*ERPG-2* 0.71		
LBW level **5.1**	*AEGL-3* 5.1	*ERPG-3* 7.1		

Stofdocument deel A

CAS-nr: 10025-87-3 **Fosforoxychloride** $POCl_3$ **VN-nr: 1810**

GEVI: X668

Synoniemen: fosforylchloride, fosforyltrichloride (Engels: phosphorus oxychloride) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	NA	NA	NA	NA	NA	NA
Levensbedreigende waarden	LBW (mg/m³)	21	21	16	13	10	5,1

Datum vaststelling: 28-11-2008

Conversiefactor: 1 mg/m³ = 0,157ppm; 1 ppm = 6,38 mg/m³

Explosiegrens: geen data

Geur: muffe, doordringende geur

LOA: onvoldoende betrouwbare gegevens

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze, rokende vloeistof

Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,2

Molecuulmassa: 153,4 g/mol
Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: reactie
Verzadigde dampdruk: 36 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: 1,3 mg/m³

TLV-TWA: 0,64 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: geen informatie

AGW → LBW: irritatie, benauwdheid, longoedeem, larynx- en glottisoedeem

Boven LBW: longoedeem en chemische pneumonitis, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Fosforoxychloride werkt zeer irriterend op de luchtwegen en slijmvliezen.
- Inademing van hoge concentraties kan blijvende longschade veroorzaken. Inademing kan tevens leiden tot larynx- en glottisoedeem, met risico op verstikking door zwellingen in de keel.
- Blootstelling aan fosforoxychloride kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, pijn, ernstige brandwonden

Oogcontact: bijtend, roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen. Blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Inademing/inslikken van fosforoxychloride kan tevens leiden tot larynx- en glottisoedeem, met risico op verstikking door zwellingen in de keel. Intubatie (borgen van vrije luchtwegen), eventueel gevolgd door beademing moeten in ernstige gevallen z.s.m. worden uitgevoerd (door specialisten).

Specifieke behandeling en materialen: geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 10025-87-3 **Phosphorus oxychloride** **$POCl_3$** **UN-nr: 1809**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: Not recommended, in accordance with AEGL

LBW: Same point of departure as for AEGL values but using different uncertainty factors, 2h value added

Date: 28-11-2008 | AEGL document: Final, 2011

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	-
AGW	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	-
LBW	21	21	16	13	10	5.1	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: Exposure-response data were unavailable for developing VRW values for phosphorus oxychloride.

AGW: Exposure-response data were unavailable for developing AGW values for phosphorus oxychloride. Because of the lack of information regarding the exposure-response relationship, estimating AGW values by the reduction of LBW values would be tenuous and difficult to justify.

LBW: In lieu of additional data, the available 4-hr LC_{50} values may be considered for development of the LBW values for phosphorus oxychloride. Because the rat appears to be a slightly more sensitive species, the 4-hr LC_{50} of 48.4 ppm (310 mg/m^3) for rats was used as the basis for the LBW values. The 4-hr LC_{50} value of 32-ppm (200 mg/m^3) reported for rats was not verified and, therefore, was not used as the basis for the LBW values. In the absence of complete data regarding the entire exposure-response curve and under the assumption that the differential between nonlethal and lethal exposures would be small, the lethality threshold was estimated as one-third of the 4-hour rat LC_{50} (i.e., 48.4 ppm/3 = 16.1 ppm (103 mg/m^3)). This is also justified because many respiratory tract irritants have exposure-response relationships in which the transition from progressive irritation and repairable epithelial tissue damage to lethal pulmonary damage occurs abruptly. The limited data suggest that rats and guinea pigs appear to respond similarly to phosphorus oxychloride and phosphorus trichloride. This similarity favours the use of the same UFs for both substances, despite the sparse database. Therefore, as for phosphorus trichloride, an overall uncertainty factor of 10 was applied for phosphorus oxychloride consisting of a factor of 3 for interspecies variability and of 3 for intraspecies variability. The intraspecies uncertainty factor was limited to 3 because a critical mechanism of phosphorus oxychloride toxicity appears to involve irritation and destruction of epithelial tissue with lethality resulting, at least in part, from damage to respiratory epithelium. It is assumed that such a basic contact irritation mechanism would not vary greatly among individuals and that a 3-fold reduction would be sufficient even for individuals with moderately compromised respiratory function. Time-scaling was performed using the $C^n \times t = k$ equation with n = 3 when extrapolating to shorter time points and n = 1 when extrapolating to longer time points. Due to uncertainties in extrapolating from a 4-hour exposure to a 10-minute exposure, the 10-minute LBW value is set equivalent to the 30-minute LBW.

Additional toxicological information (including relevant results of a general literature search, if any)

Most information regarding the toxic response of humans to phosphorus oxychloride is limited to secondary reports that lack quantitative exposure-response data. According to these reports, the chemical appears to be extremely irritating to the respiratory tract and other mucous membranes. Both port-of-entry and systemic effects have been reported. Primary reports describe occupational exposures to phosphorus oxychloride but these involve simultaneous exposures to other irritating chemicals and/or lack definitive exposure concentration/duration terms. The reports affirm signs and symptoms of nasopharyngeal, ocular, and dermal irritation, and ventilatory dysfunction following acute exposures. Concurrent exposures to other chemicals, especially those having the same effects and targets as phosphorus oxychloride, compromise the usefulness of the human exposure data.

The acute lethality of inhaled phosphorus oxychloride likely results from damage of respiratory epithelium and subsequent pulmonary oedema however the precise mechanism of toxicity of inhaled phosphorus oxychloride has not been elucidated.

Definitive quantitative exposure-response toxicity data in animals were limited to lethality data for rats and guinea pigs The available studies affirm the extreme irritation properties of phosphorus oxychloride although the exposures described also resulted in lethality.

No data are available regarding the developmental/reproductive toxicity of phosphorus.

H302: Harmful if swallowed; H314: Causes severe skin burns and eye damage; H330: Fatal if inhaled; H372: Causes damage to organs through prolonged or repeated exposure.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived. Information regarding the potential carcinogenicity of phosphorus oxychloride in humans or experimental animals is not available.	Odour: musty, pungent odour No LOA was derived due to lack of reliable data.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **N.R.**	*AEGL-1* N.R.	*ERPG-1* not derived		*IDLH*: not derived
AGW level **N.R.**	*AEGL-2* N.R.	*ERPG-2* not derived		
LBW level **16**	*AEGL-3* 5.4	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 1314-56-3

Fosforpentoxide

P_2O_5 [42]

VN-nr: 1807

GEVI: 80

Synoniemen: difosforpentaoxide, fosforzuuranhydride (Engels: Phosphorus pentoxide)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,80	0,80	0,80	0,80	0,80	0,80
Alarmeringsgrenswaarden	AGW (mg/m³)	46	32	25	13	6,4	3,2
Levensbedreigende waarden	LBW (mg/m³)	220	150	120	59	30	15

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,169 ppm; 1 ppm = 5,907 mg/m³

Explosiegrens: niet afgeleid
(bij vele reacties kans op brand en explosie)

Geur: lichte fosforgeur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: wit, sterk hygroscopisch poeder, (nagenoeg) reukloos
Brand: zelf niet brandbaar, maar bij vele reacties kans op brand en explosie

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,3-3,0

Molecuulmassa: 142,0 g/mol

Zuurgraad: pH 1 (bij 0,5 g/100 ml)

LogKow:

Wateroplosbaarheid: reactie

Verzadigde dampdruk: 1,3 mbar (bij 388°C)

Overige informatie

Publieke grenswaarde: 1 mg/m³

MAK: 2 mg/m³

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: keelpijn en hoesten

VRW → AGW: branderig gevoel achter het borstbeen

AGW → LBW: kortademigheid

Boven LBW: ademnood, larynx- en glottisoedeem (met risico op verstikking)

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Blootstelling aan fosforpentoxide kan ernstige chemische brandwonden, longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- De stof is bijtend en kan bijtende effecten op de slijmvliezen van ogen en/of hogere luchtwegen veroorzaken.
- In ernstige gevallen kans op verstikking door zwelling in de keel.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, ernstige brandwonden

Oogcontact: bijtend, roodheid en pijn, slecht zien.

Carcinogeniteit

IARC classificatie: niet geclassificeerd.

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding, direct spoedeisende medische hulp inzetten

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen, zo nodig arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

[42] Dit is de empirische formule; de formele formule is $O_{10}P_4$

Stofdocument deel B

CAS-nr: 1314-56-3 **Phosphorus pentoxide** P_4O_{10} **UN-nr: 1807**

Basis for the Dutch Intervention Values

VRW: Based on information as described in ERPG-document, different values are derived, other time-points added

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017 ERPG, 2015

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.80	0.80	0.80	0.80	0.80	0.80	Weight of evidence, threshold for irritation in un-acclimatized humans
AGW	46	32	25	13	6.4	3.2	Analogy with phosphoric acid: Threshold for irritation in animals
LBW	220	150	120	59	30	15	Analogy with phosphoric acid: Threshold for lethality in rats

Derivation of the Dutch Intervention Values

In the absence of toxicity data with phosphorus pentoxide, data are derived from animal studies with smoke of white or red phosphorous $(P4)_n$. Smoke of white and red phosphorous consist of phosphoric acid in a mixture of poly phosphoric acid and ortho-phosphoric acid. One mole of red or white phosphorous can produce 4 moles of phosphoric acid (MW conversion factor 3.2). The values are calculated back to phosphorus pentoxide equivalents by dividing by 2 given that 1 molecule of phosphorus pentoxide is hydrolyzed to produce 2 molecules of phosphoric acid (MW conversion factor 1.38).

VRW: Anecdotal data in humans indicate that concentrations ranging from 3.6 to 11.3 mg phosphorus pentoxide/m³ cause irritation and coughing in unacclimatized workers but were tolerated. Concentrations of 100 mg phosphorus pentoxide/m³ were unbearable, except to acclimatized workers. Concentrations of 0.8 to 5.4 mg phosphorus pentoxide/m³ were noticeable but not uncomfortable. “Momentary” exposure to hydroaerosols of phophoric acid expressed as 1.2, 5.2 and 8.0 mg phosphorus pentoxide/m³ produced irritation in 12 out of 15 healthy adults at the highest concentration, in 3 out of 15 in the middle concentration and no irritation was reported at the lowest concentration. A third study indicates that 131 workers exposed to a mixture of phosphoric acid, phosphorus pentoxide, fluorides and coal tar pitch volatiles in a refinery showed no effects in a 3 to 7-year follow-up longitudinal pulmonary function study where maximum levels of phosphorus pentoxide were 2.2 mg/m³. There is no single study that can serve as PoD for derivation of the VRW. However, based on a weight of evidence approach and the circumstantial data in humans a VRW of 0.8 mg/m³ is proposed. Time scaling was not applied because mild irritant effects generally do not vary greatly over time.

AGW: In the absence of suitable human data, the AGW is based on animal data. Acute inhalation toxicity studies show that 380 mg/m³ phosphorus pentoxide (or 525 mg phosphoric acid equivalents/m³) for 60 minutes causes unmistakable signs of irritation, pulmonary congestion, haemorrhages, and respiratory distress in rats. In mice, 110 mg/m³ phosphorus pentoxide (or 152 mg phosphoric acid equivalents/m³) for 60 minutes also causes unmistakable signs of irritation, congestion and difficulty in breathing. Concentrations of 450 mg/m³ red phosphorus (1422 mg phosphoric acid equivalents/m³, corresponding to 1030 mg phosphorus pentoxide/m³) in the rat and rabbit and 111 mg/m³ red phosphorus (351 mg phosphoric acid equivalents/m³, corresponding to 254.3 mg phosphorous pentoxide/m³) in the mouse did not produce respiratory tract damage after 1 hour exposure and a 14-day observation period. The concentration of 351 mg phosphoric acid equivalents/m³ (corresponding to 254.3 mg phosphorus pentoxide equivalents/m³) was used as PoD for the AGW. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter time points, respectively. The resulting AGW-values are supported by human data: human workplace studies show that a concentration of 100 mg/m³ phosphorus pentoxide was unbearable to un-acclimatised workers.

LBW: Several acute inhalation lethality studies are available with red phosphorous smoke in different laboratory animals and are summarised in the ERPG document. Datasets of two of the five rat lethality studies were considered most relevant. In one study rats were exposed to unformulated pure red phosphorus for 1 hour whole-body in a 10 m^3 chamber at 1422, 2749, 5056 and 6731 mg/m^3 (as phosphoric acid equivalents). Mortality data were 0/12, 2/10, 6/9, and 12/12, respectively. In the second study rats were exposed to red phosphorous some for one hour at concentrations of 6420, 4410, 4030 and 2727 or 4 hours to 1210 mg phosphoric acid equivalents/m^3. Mortality rates were 9/10, 7/10 3/10, 2/10 and 2/10. The mortality data of these two studies resulted in two comparable 1-hour LC_{01} values of 1754 mg/m^3 and 1637 mg/m^3 of phosphoric acid, respectively, and the lowest value was used as PoD. Therefore, the PoD used corresponds to 1186 mg phosphorus pentoxide equivalents/m^3. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter time points, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Phosphorus pentoxide is a corrosive mineral acid that causes irritation and inflammation to the respiratory tract after inhalation and induces cellular toxicity most likely due to its activity as a reducing agent resulting in disruption of oxidative processes.

Phosphorus pentoxide is not reproductive toxic or developmental toxic in animals.

H314: Causes severe skin burns and eye damage.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived	Odour: slight phosphorus-like odour No LOA was derived due to lack of data.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*[43]

VRW level **0.80**	*AEGL-1*[44] 9	*ERPG-1*[45] 1		*IDLH: -*
AGW level **25**	*AEGL-2* 50	*ERPG-2* 10		
LBW level **120**	*AEGL-3* 110	*ERPG-3* 50		

[43] Note that the ERPG and AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG or AEGL, respectively.
[44] Values are proposed AEGL values for red phosphorous and calculated to phosphorus pentoxide equivalents
[45] ERPG states values in ppm and mg/m^3 that do not match. It is unclear which values should apply.

Stofdocument deel A

CAS-nr: 7719-12-2 **Fosfortrichloride** PCl_3 **VN-nr: 1809** **GEVI: 668**

Synoniemen: - (Eng.: Phosphorus (tri)chloride) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	1,9	1,9	1,9	1,9	1,9	1,9
Alarmeringsgrenswaarden	AGW (mg/m³)	14	14	11	9,1	7,2	4,7
Levensbedreigende waarden	LBW (mg/m³)	40	40	32	25	20	10

Datum vaststelling: 28-11-2008

Conversiefactor: 1 mg/m³ = 0,175 ppm; 1 ppm = 5,71mg/m³

Explosiegrens: alleen kans op explosie in contact met andere stoffen

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze, rokende vloeistof
Brand: niet brandbaar, bij vele reacties kans op brand en explosie

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,5

Molecuulmassa: 137,3 g/mol
Zuurgraad: Geen data
LogKow: Geen data
Wateroplosbaarheid: Reactie
Verzadigde dampdruk: 127 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: 2,9 mg/m³
TLV-TWA: 1,14 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: lichte oog- en luchtwegirritatie, branderig gevoel in ogen en keel, druk op de borst, hoesten, hoofdpijn, misselijkheid, braken

AGW → LBW: ernstige oog- en luchtwegirritatie, ernstige branderig gevoel in ogen en keel, benauwdheid, chemische pneumonitis, longoedeem

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Fostortrichloride is irriterend voor de ogen, huid en de luchtwegen.
- Primaire effecten zijn irritatie en schade aan de luchtwegen.
- Blootstelling aan fosfortrichloride kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- De irriterende eigenschappen worden vooral toegekend aan de degradatieproducten van fosfortrichloride: waterstofchloride en fosforigzuur.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, pijn, ernstige brandwonden
Oogcontact: bijtend, roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeed
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen. Blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Ontsmetting bij inademen/inslikken
Inademing/inslikken van fosfortrichloride kan tevens leiden tot larynx- en glottisoedeem, met risico op verstikking (asfyxie) door zwellingen in de keel. Intubatie (borgen van vrije luchtwegen), eventueel gevolgd door beademing moeten in ernstige gevallen z.s.m. worden uitgevoerd (door specialisten). Zet derhalve direct spoedeisende medische hulp in.
Specifieke behandeling en materialen: geen.
Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7719-12-2 **Phosphorus trichloride** **PCl_3** **VN-nr:**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 28-11-2008 | AEGL document: Final 2011

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	1.9	1.9	1.9	1.9	1.9	1.9	Slight irritation
AGW	14	14	11	9.1	7.2	4.7	Irritation (respiratory tract)
LBW	40	40	32	25	20	10	Lethality animals

Derivation of the Dutch Intervention Values

VRW: In the absence of human data concerning VRW type effects, the NOAEL of 3.4 ppm (19.4 mg/m³) for slight to mild irritation, derived from a 1 and 6 hour, 4 week toxicity study in rats, was used as a starting point for the derivation of the VRW. A total uncertainty factor of 10 was applied (3 for intraspecies and 3 for interspecies differences). This factor is considered sufficient, because effects resulting from direct-contact of dissociation products is likely to be similar for any epithelial surface, because the available data suggest small differences between species, and because limited human exposure data suggest that humans can experience 2-to 6-hour exposures of up to 3.6 ppm (21 mg/m³) with no apparent effects. The same VRW values were set for all time points, because contact irritation from exposure to phosphorus trichloride is not expected to vary over time.

AGW: A NOAEL of 11 ppm (63 mg/m³) for respiratory tract irritation, derived from a 6 hours/day, 5 days/week, 4 week rat study was used for the derivation of the AGW. Although the study did not result in a response with a severity at the level of AGW, the histopathological alterations in the respiratory tract may be considered a NOAEL in the absence of any other suitable data. A total uncertainty factor of 10 was applied (3 for intraspecies and 3 for interspecies differences). This factor is considered sufficient, because effects resulting from direct-contact of dissociation products is likely to be similar for any epithelial surface and because the available, but limited data suggest small interspecies differences. Time scaling was performed using the equation $C^n \times t = k$, with n=1 to extrapolate to long term exposures and n=3 to extrapolate to shorter exposure durations. Because extrapolation from >4 hr values to 10 minutes is not justified, the 10 minute value was set equal to the calculated 30 minutes value.

LBW: In the absence of exposure-response data, the lethality threshold was estimated as a three-fold reduction of a 4-hour LC_{50} value (104.3 ppm or 596 mg/m³) in rats resulting in a point of departure of 34.8 ppm (199 mg/m³) for the LBW derivation. Although the LC_{50} of guinea pigs (50.1 ppm; 286 mg/m³) was lower LBW values calculated from guinea pigs would be overly conservative and result in LBW values that are inconsistent with human exposure information.
A total uncertainty factor of 10 was applied, 3 for interspecies differences and 3 for intraspecies differences. The interspecies factor was supported by the fact that limited data regarding human exposure showed that 2 to 6 hour exposures to 14-27 ppm (80-154 mg/m³) were not life threatening. The primary effects of phosphorus trichloride are of a local nature, irritation and subsequent tissue damage and are not considered to differ greatly between individuals. Time scaling was performed using the equation $C^n \times t = k$, with n=1 to extrapolate to long term exposures and n=3 to extrapolate to shorter exposure durations. The 10-minute value was set equal to the calculated 30-minute value because extrapolation from 4 hr values to 10 minutes introduces too large uncertainties.

Additional toxicological information (including relevant results of a general literature search, if any)

The mechanism of the lethality of phosphorus trichloride is currently unknown. It does not, however, appear to

be completely explained by the activity of the irritant degradation products (hydrogen chloride and phosphoric acid). The rapid exothermic reaction in the presence of water may contribute to localized tissue damage and also explain, in part, the greater toxicity of phosphorus trichloride relative to hydrogen chloride and phosphoric acid.

There is no information available regarding the reproductive and developmental toxicity of phosphorus trichloride.

H300: Fatal if swallowed; H314: Causes severe skin burns and eye damage; H330: Fatal if inhaled; H373: May cause damage to organs.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived. There is no information in the available literature regarding the potential carcinogenicity of phosphorus trichloride in humans or animals.	Pungent irritating odour. No LOA could be derived due to lack of data.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **1.9**	*AEGL-1* 1.9	*ERPG-1* 2.9		*IDLH:* 143 mg/m^3 (30 minutes)
AGW level **11**	*AEGL-2* 11	*ERPG-2* 17		
LBW level **32**	*AEGL-3* 32	*ERPG-3* 86		

Stofdocument deel A

CAS-nr: 7664-38-2 **Fosforzuur** H_3PO_4 **VN-nr:** 3453 (100%); 1805 (85% in water)
GEVI: 80

Synoniemen: orthofosoforzuur (Engels: phosphoric acid) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	1,0	1,0	1,0	1,0	1,0	1,0
Alarmeringsgrenswaarden	AGW (mg/m³)	64	44	35	18	8,8	4,4
Levensbedreigende waarden	LBW (mg/m³)	300	210	160	82	41	20

Datum vaststelling: 31-10-2017 Conversiefactor: 1 mg/m³ = 0,245 ppm; 1 ppm = 4,076 mg/m³

Explosiegrens: niet afgeleid

Geur: geurloos
LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: heldere kleurloze hygroscopische kristallen of viskeuze vloeistof
Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,0

Molecuulmassa: 98,0 g/mol

Zuurgraad: pH 1,2 (bij 85 g/100 ml)
LogKow: Geen data
Wateroplosbaarheid: 548 g /100 ml (volledig)
Verzadigde dampdruk: 2 mbar

Overige informatie

Publieke grenswaarde: 1 mg/m³
MAK: 2 mg/m³
TLV-TWA: 1 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: keelpijn en hoest

VRW → AGW: branderig gevoel achter het borstbeen

AGW → LBW: kortademigheid

Boven LBW: ademnood, larynx- en glottisoedeem

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Blootstelling aan fosforzuur kan ernstige chemische brandwonden, longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- De stof is bijtend en kan bijtende effecten op de slijmvliezen van ogen en/of hogere luchtwegen veroorzaken.
- In ernstige gevallen kans op verstikking door zwelling in de keel.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn, blaren, ernstige brandwonden
Oogcontact: roodheid en pijn, slecht zien, hoornvliesbeschadiging, ernstige brandwonden.

Carcinogeniteit

IARC classificatie: niet geclassificeerd.
Fosforzuur in sterke anorganische mist wordt beschouwd als carcinogeen (groep 1)(IARC monograph Volume 54, 1992)
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding, direct spoedeisende medische hulp inzetten

Ontsmetting vloeistof
huid: overmaat stof droog verwijderen, verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen, zo nodig arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7664-38-2 **Phosphoric acid** H_3PO_4 **UN-nr:** 3453/1805

Basis for the Dutch Intervention Values

VRW: Based on information as described in ERPG-document, different values are derived, other time-points added

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017 ERPG,2011

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	1.0	1.0	1.0	1.0	1.0	1.0	Weight of evidence threshold for irritation in un-acclimatised humans.
AGW	64	44	35	18	8.8	4.4	Threshold for irritation in animals
LBW	300	210	160	82	41	20	Threshold for lethality in rats.

Derivation of the Dutch Intervention Values

In the absence of toxicity data with phosphoric acid, data are derived from studies with smoke of white or red phosphorous $(P4)_n$. One mole of red or white phosphorous can produce 4 moles of phosphoric acid. The values are calculated back to phosphoric acid equivalents using a factor of 3.16 (MW conversion factor).

VRW: Anecdotal data in humans indicate that concentrations ranging from 5.0 to 15.6 mg phosphoric acid equivalents/m³ caused coughing among un-acclimatised people. Concentrations of 100 mg/m3 phosphor pentoxide (138 mg phosphoric acid equivalents/m³) were unbearable, except to acclimatised workers. “Momentary” exposure of hydroaerosols of phophoric acid (1.6, 7.2, and 11.0 mg phosphoric acid equivalents/m³) produced irritation in 12 out of 15 healthy adults at the highest concentration, in 3 out of 15 in the middle concentration and no irritation was reported at the lowest concentration. A third study indicates that phosphoric acid mist concentration of 1.0 mg/m³ is irritating to the un-acclimatised worker. There is no single study that can serve as PoD for derivation of the VRW. However, based on a weight of evidence approach and the circumstantial data in humans, a VRW of 1.0 mg/m³ is proposed. Time scaling was not applied because mild irritant effects generally do not vary greatly over time.

AGW: In the absence of suitable human data, the AGW is based on animal data. Acute inhalation toxicity studies show that 380 mg/m³ phosphorus pentoxide (or 525 mg phosphoric acid equivalents/m³) for 60 minutes causes unmistakable signs of irritation, pulmonary congestion, haemorrhages, and respiratory distress in rats. In mice, 110 mg/m³ phosphorus pentoxide (or 152 mg phosphoric acid equivalents/m³) for 60 minutes also causes unmistakable signs of irritation, congestion and difficulty in breathing. Concentrations of 450 mg/m³ red phosphorus (1422 mg phosphoric acid equivalents/m³) in the rat and rabbit and 111 mg/m³ red phosphorus (351 mg phosphoric acid equivalents/m³) in the mouse for one hour did not produce respiratory tract damage after a 14-day observation period. The concentration of 351 mg phosphoric acid equivalents/m³ (1 hr) was used as PoD for the AGW. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the equation Cn × t = k with the default values of n=1 and n=3 when extrapolating to longer and shorter time points, respectively. The resulting AGW-values are supported by human data: human workplace studies show that 138 mg/m³ phosphoric acid equivalent was unbearable to un-acclimatised workers.

LBW: Several acute inhalation lethality studies are available with red phosphorous smoke in different laboratory animals and are summarised in the ERPG document. Datasets of two of the five rat lethality studies were considered most relevant. In one of the two rat studies, rats were exposed to unformulated pure red phosphorus for 1 hour whole-body in a 10 m³ chamber at 1422, 2749, 5056 and 6731 mg/m³ (as phosphoric acid equivalents). Mortality was 0/12, 2/10, 6/9, and 12/12, respectively. In the second study rats were exposed to red phosphorous for one hour at concentrations of 6420, 4410, 4030 and 2727 mg phosphoric acid equivalents/m³ or 4 hours to 1210

mg phosphoric acid equivalents/m^3. Mortality rates were 9/10, 7/10, 3/10, 2/10 and 2/10. The mortality data were used to calculate two 1-hour LC_{01} values of 1754 mg/m^3 and 1637 mg/m^3 of phosphoric acid, respectively, and the lowest value was used as PoD. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter time points, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Phosphoric acid is a corrosive mineral acid that causes irritation and inflammation to the respiratory tract after inhalation and induces cellular toxicity most likely due to its activity as a reducing agent resulting in disruption of oxidative processes.

Phosphoric acid is not reproductive toxic or developmental toxic in animals.

H314: Causes severe burns and eye damage.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

Strong-inorganic-acid mists containing phosphoric acid are carcinogenic to humans (group 1) (IARC monograph 54, 1992).

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: odourless

No LOA was derived due to lack of data.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*[46]

VRW level **1.0**	*AEGL-1*[47] 12	*ERPG-1* 3		*IDLH:* 1000 (30 min)
AGW level **35**	*AEGL-2* 35	*ERPG-2* 30		
LBW level **160**	*AEGL-3* 150	*ERPG-3* 150		

[46] Note that the ERPG and AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG or AEGL,respectively.

[47] Values are proposed AEGL values for red phosphorous and calculated to phosphoric acid equivalents

Stofdocument deel A

CAS-nr: 75-44-5 **Fosgeen** $O=CCl_2$ **VN-nr: 1076**
GEVI: 268

Synoniemen: Carbonyl chloride, carbonyldichloride, chloorkooloxide (Engels: Phosgene) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	2,5	2,5	1,2	0,62	0,31	0,15
Levensbedreigende waarden	LBW (mg/m³)	34	9,4	4,2	1,9	0,82	0,37

Datum vaststelling: November 2015 Conversiefactor: 1 mg/m³ = 0,243 ppm; 1 ppm = 4,11 mg/m³

Explosiegrens: geen data

Geur: typerende geur vergelijkbaar met vers gemaaid gras

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos tot lichtgeel onder druk tot vloeistof verdicht gas

Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 3,4

Molecuulmassa:	98,9 g/mol
Zuurgraad:	Geen data
LogKow:	-0.7 (berekend)
Wateroplosbaarheid:	Reacties
Verzadigde dampdruk:	1550 mbar

Overige informatie

Publieke grenswaarde: 0,08 mg/m³ (8 uur)
MAK: 0,08 mg/m³
TLV-TWA: 0,411 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*onder **AGW***: irritatie van ogen en luchtwegen, hoesten, tranenvloed

AGW → LBW: ademnood, pijn of druk op de borst, longoedeem, piepende ademhaling, dyspnoe, pijnlijk hoesten

Boven LBW: anoxie, circulatoire collaps, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De toxiciteit van fosgeen is te wijten aan acylatie en hydrolyse, wat zorgt voor eiwit- en vetdenaturatie, membraanschade en irritatie.
- De stof werkt bijtend op de luchtwegen. Inademing van de stof kan kortademigheid/ademnood veroorzaken.
- Blootstelling aan fosgeen kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Door snel verdampen kan de vloeistof bevriezing veroorzaken.
- Overlevende van een ernstige intoxicatie kunnen langdurende klachten (neurotoxische gevolgen, hart- en ademhalingsfunctiestoornissen) ondervinden.

Effecten bij blootstelling aan vloeistof

Huidcontact: bij bevriezing: roodheid, pijn en brandwonden

Oogcontact: bij bevriezing: roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

Ontsmetting vloeistof

huid: aan de huid vastgevroren kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, bij bevriezing: blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas).

***Specifieke behandeling en materialen**:* geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 75-44-5 **Phosgene** **$O=CCl_2$** **UN-nr: 1076**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value is adopted, 2 h value added

LBW: Based on a different point of departure as for AEGL, different uncertainty factors, 2h value added.

Date: November 2015 | Final AEGL document, 2002;

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	2.5	2.5	1.2	0.62	0.31	0.15	Irritation of respiratory tract
LBW	34	9.4	4.2	1.9	0.82	0.37	Threshold of lethality in rats

Derivation of the Dutch Intervention Values

VRW: Appropriate data were not available for the derivation of VRW values for phosgene. Odour cannot be used as a warning for potential exposure, because the odor threshold is reported to be between 0.5 and 1.5 ppm (2.1-6.2 mg/m³), a value above or approaching the AGW and LBW values, and tolerance to the pleasant odor occurs rapidly. Furthermore, following odor detection and minor irritation, serious effects may occur after a clinical latency period of 2-24 hours.

AGW: The chemical pneumonia observed in rats exposed to phosgene at 2 ppm (8.2 mg/m³) for 90 minutes was used as starting point for the derivation of the AGW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$, with n=1. This scaling was supported by time-scaling data derived from rat (n=0.93) and mice (n=1.3) lethality studies. The 30 minute value is also adopted for the 10 minute value, because otherwise, a 10 minute AGW would be determined close to concentrations producing alveolar edema in rats. The values are supported by nonlethal toxicity studies with rats exposed to phosgene at 1 ppm (4.11 mg/m³) for 4 h (severe pulmonary edema and body weight loss). The 10 minute value is also supported by the observation of pulmonary edema in rats exposed at 5 ppm (20.55 mg/m³) for 10 minutes. Applying the same uncertainty factors to both potential starting points would yield comparable AGW values.

LBW: LBW values were based on a rat lethality study in which rats were exposed whole-body for 5, 10, 30 and 60 minutes (Zwart et al., 1990). LC_{01}values and the related time scaling factor were calculated using Doseresp, resulting in the following LC_{01} values for a 10 min, 30 min, 1h, 2h, 4h and 8h exposure period, respectively: 202.8 – 56.14 – 24.96 – 11.1 – 4.935 – 2.194 mg/m³ with an n-value of 0.86. Short exposure durations (i.e. ≤5 min) were excluded for analyses, as these were considered less reliable than longer exposure durations. A second rat lethality study (Pauluhn 2006) was also available in which rats were exposed nose-only to phosgene for 10-30-60-240 min. Analysis of this second study resulted in quite similar results: a similar value for n (0.86) and LC_{01} values approximately a factor 2 lower than those of the study of Zwart et al. (1990). Given that human data of workers with a phosgene indicator badge revealed that an exposure below 50 ppm x min (corresponding to 0.4 mg/m³ for 8h exposure period) did not result in signs or symptoms of phosgene toxicity in 78 of 88 individuals, the slightly less conservative data of the study of Zwart were selected for the LBW-derivation. An uncertainty factor of 2 for interspecies and the default intraspecies uncertainty factor of 3 is applied. An interspecies factor of 2 is considered sufficient given the following information: 1) rats are considered more sensitive for phosgene-induced pulmonary effects than dogs, 2) dogs are considered more human-like and a better model for humans (associated with the higher ventilation rate of small rodents and with rodent-specific sensory bronchopulmonary defense reflexes (i.e. reflex bradypnoea)) and 3) evaluation of LC_{50} values showed that LC_{50} values of dogs are higher than those of rats.

Additional toxicological information (including relevant results of a general literature search, if any)

The toxicity of phosgene is due to lipid and protein denaturation, irreversible membrane changes and disruption of enzymatic function. Cellular glycolysis and oxygen uptake are decreased following exposure to phosgene, and it causes an increased permeability of pulmonary vessels and pulmonary oedema. The hydrogen chloride formed by the hydrolysis of phosgene causes initial irritation to the eyes, nasopharynx, and respiratory tract. However, because phosgene's poor water solubility, a minimal amount of hydrogen chloride is formed.

No information is found regarding reproductive or developmental toxicity in rats or humans.

H330 very toxic by inhalation, H314 causes severe burns

Carcinogenicity and derivation of the CRP value
IARC classification: not classified No carcinogenic risk potency (CRP) was derived. Epidemiologic studies in humans have shown no increase in cancer in workers.

Odour and derivation of the LOA value
Odour: typical and pleasant odour. Odour threshold supposedly between 0.5 and 1.5 ppm (2.1 and 6.2 mg/m^3). No LOA was derived due to lack of reliable data.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **NA**	*AEGL-1* NA	*ERPG-1* NA		*IDLH:* 8.22 (30 min.)
AGW level **1.2**	*AEGL-2* 1.2	*ERPG-2* 0.8		
LBW level **4.2**	*AEGL-3* 3.1	*ERPG-3* 4.1		

Stofdocument deel A

CAS-nr: 110-00-9 **Furaan** **C_4H_4O, cyclisch** **VN-nr: 2389**

GEVI: 33

Synoniemen: divinyleenoxyde, furfuraan, oxacyclopentadieen (Eng.: Furan) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	160	113	88	44	22	11
Levensbedreigende waarden	LBW (mg/m³)	480	340	270	130	67	33

Datum vaststelling: 28-11-2008 Conversiefactor: 1 mg/m³ = 0,353 ppm; 1 ppm = 2,83 mg/m³

Explosiegrens: LEL = 2,3 vol%≈ 65 000 mg/m³

Geur: typerende etherische lucht

LOA: 440 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof, die na lang staan bruin wordt

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,9

Molecuulmassa:	68,1 g/mol
Zuurgraad:	Geen data
LogKow:	1,5 (berekend)
Wateroplosbaarheid:	1 g/100 ml (matig)
Verzadigde dampdruk:	670 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***:	irriterende effecten niet uitgesloten
AGW → LBW:	oog- en bovenste luchtwegirritatie tranenvloed, hoesten, duizeligheid, bewustzijnsdaling
Boven LBW:	ademnood, coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Furaan is irriterend voor de huid, ogen en de bovenste luchtwegen.
- Furaan veroorzaakt depressie van het centraal zenuwstelsel.
- De stof heeft een steile concentratie-respons curve.

Effecten bij blootstelling aan vloeistof

Huidcontact: (alleen bij hogere concentraties) roodheid, pijn

Oogcontact: roodheid, pijn

Carcinogeniteit

IARC classificatie: 2B

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen:	frisse lucht, rust, halfzittende houding en arts raadplegen.
ogen:	desgewenst spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof

huid:	verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen
ogen:	minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken:	mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**:* geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 110-00-9 **Furan** **C_4H_4O, cyclisch** **UN-nr: 2389**

Basis for the Dutch Intervention Values

VRW: Not recommended due to insufficient data, in accordance with AEGL.

AGW: Different point of departure as for AEGL, 2 hr value added

LBW: Same point of departure as for AEGL values but using different uncertainty factors, 2 hr value added

Date: 28-11-2008 | AEGL document: Final, 2010

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End Point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	160	110	88	44	22	11	1/3 LBW
LBW	480	340	270	130	67	33	Threshold for lethality (animals)

Derivation of the Dutch Intervention Values

VRW: VRW values are not recommended based on the available information.

AGW: Toxicity signs, including respiratory distress, increased secretory response and death, during exposure in a 1-hour rat inhalation lethality study were observed. However, the specific response at each tested concentration was not described. Furthermore, the dose response curve in the given study was steep; no deaths after 1 hour exposure at 1014 ppm (2873 mg/m³) and 2851 ppm (8077 mg/m³), and 9/10 deaths at 4049 ppm (11470 mg/m³). Based on these two aspects and considering the lack of further data, the AGW was based on 1/3 of the LBW instead of the very conservative approach of the AEGL, using the 1014 ppm (2873 mg/m³) level as point of departure and a total uncertainty factor of 150.

LBW: The LBW is based on the 1-hour rat inhalation study (see AGW for description of study). The exposure concentration of 2851 ppm (8077 mg/m³), the highest non-lethal concentration in male and female rats, was used as starting point for the derivation of the LBW. An overall factor of 10 for intraspecies and interspecies differences (3 each) was implied. An additional modifying factor 3 was applied to compensate for the sparse data set. Time scaling was performed using the equation $C^n \times t = k$, with n=1 to extrapolate to long term exposures and n=3 to extrapolate to shorter exposure durations. In contrast to the 10 min AEGL-3 value, time scaling was also applied for the 10 min AGW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Furan acts as a narcotic agent causing an increase in respiratory rate, decrease of blood pressure, convulsions, complete anesthesia, followed by asphyxia due to inhibition of the medulla. In addition, according to chemical safety data sheet, the substance acts as a local irritant on the eyes, skin and respiratory tract. According to the AEGL document, the liver is the major target organ for furan-induced toxicity following oral exposure. Although there is no direct evidence that inhaled furan causes hepatotoxicity, based on the available literature and PBPK-modeling it may be reasonable to expect that the liver is a target organ of inhaled furan as well. The dose-response curve is very steep, and little can be said about the sensitive subpopulations.

No information available regarding the reproductive and developmental toxicity of furan.

H302: Harmful if swallowed; H315: Causes skin irritation; H332: Harmful if inhaled; H341: Suspected of causing genetic damage; H350: May cause cancer; H373: May cause damage to organs.

Carcinogenicity and derivation of the CRP value

IARC classification: 2B (possibly carcinogenic to humans)

No carcinogenic risk potency (CRP) was derived.

A cancer risk assessment was not conducted because the studies were limited to repeated exposure by oral gavage in rats and mice. Furthermore, if an epigenetic mechanism is responsible for the furan-induced

Odour and derivation of the LOA value

Ethereal odour

Odour threshold: 10 ppm (28 mg/m³) [Nagata (2003)]

LOA = 11.8 * 28 * 1.33 = 440 mg/m³

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 *

hepatocarcinogenicity it is not expected that a one-time exposure up to 8 hours would induce cancer. *In vivo* and *in vitro* data as well as PBPK modeling predictions indicate that the integrated liver exposure to furan metabolites following a single inhalation exposure to the LBW exposure concentrations would not be sufficient to cause genotoxicity.	log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value) Apart from the 10 min LBW, the LOA is higher than the Dutch Intervention values.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH:* not determined
AGW level **88**	*AEGL-2* 19	*ERPG-2* -		
LBW level **270**	*AEGL-3* 54	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 98-01-1 **Furfural** $C_5H_4O_2$ **VN-nr: 1199**

GEVI: 63

Synoniemen: 2-furaldehyde, furaldehyde, fural (Engels: 2-furaldehyde) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	6,8	6,8	6,8	6,8	6,8	6,8
Alarmeringsgrenswaarden	AGW (mg/m³)	64	64	64	64	64	64
32Levensbedreigende	LBW (mg/m³)	1300	870	690	350	170	170

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,250 ppm; 1 ppm = 3,997 mg/m³

Explosiegrens: 2,1 vol% ≈ 84.000 mg/m³

Geur: amandel/brood geur

LOA: 0,38 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot lichtgele vloeistof
Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,00

Molecuulmassa: 96,1 g/mol

Zuurgraad: pH 3,5-4,5

LogKow: 0,4

Wateroplosbaarheid: 8,3 g/100 ml (matig)

Verzadigde dampdruk: 1,5 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 0,80 mg/m³ (huid)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: prikkeling, hoesten, irritatie van ogen en luchtwegen, keelpijn

AGW → LBW: sufheid, kortademigheid

Boven LBW: coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt irriterend op de ogen en de slijmvliezen.
- De stof geeft depressie van het centrale zenuwstelsel. Deze dempende effecten worden in sommige gevallen voorafgegaan door een excitatiefase (opwinding, euforie/'high', delier).

Effecten bij blootstelling aan vloeistof

Huidcontact: droge huid, roodheid en pijn.

Oogcontact: roodheid en pijn, slecht zien.

Carcinogeniteit

IARC classificatie: groep 3
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en onmiddellijk arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 98-01-1 **2-Furaldehyde** $C_5H_4O_2$ **UN-nr: 1199**

Basis for the Dutch Intervention Values

VRW: Based on information as described in ERPG-document, different values are derived, other time-points added

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017 ERPG 2016

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	6.8	6.8	6.8	6.8	6.8	6.8	Eye and nasal irritation in humans
AGW	64	64	64	64	64	64	Eye and respiratory irritation in humans
LBW	1300	870	690	350	170	170	Acute lethality in rat

Derivation of the Dutch Intervention Values

VRW: The VRW-levels were based on results from an occupational health hazard evaluation. Reported symptoms in workers were eye irritation (itching, burning, tearing, and/or redness) and nasal irritation (stuffiness, dryness, soreness and (1 case of) bloody nasal discharge. These symptoms were observed for example during nightshifts with average furfural concentrations of 5.1 and 5.9 ppm (corresponding to 20.4 and 23.6 mg/m³) for the first and second halves of the shift. In addition, investigators performing the health hazard evaluation and present at the industry plant experienced similar symptoms (eye irritation, nasal stuffiness, and dryness of the mouth) during the investigation. At one instance, when half-shift furfural concentrations averaging 13.5 and 16 ppm (corresponding to 54 and 64 mg/m³) occurred, these symptoms were of rapid onset even though the investigators were not continuously in the environment.
An exposure to 20.4 mg/m³ furfural was selected as point of departure for deriving the VRW-levels. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was not applied as respiratory irritation is considered to be concentration-dependent and not exposure duration-dependent.

AGW: Due to complete lack of relevant acute toxicity data for workers exposed to concentrations above 16 ppm (64 mg/m³) and the lack of quantitative information on the impact of exposure concentration and/or exposure duration on the severity of the local effects, a conservative approach was taken. The AGW levels were based on results of two studies. First, an effect level of 64 mg/m³ (half-shift; rapid onset of symptoms) was derived from the occupational health hazard evaluation (see VRW). Observed effects were sub-AGW, though reported to occur rapidly, *i.e.*, within a short period of time. Second, the data of a human ADME study with male volunteers (n=6; 30-55 years) being exposed to concentrations of up to 7.9 ppm (32 mg/m³) for 7.5 hours while sitting were also used for derivation of AGW. Although not explicitly stated, it can be concluded that, apparently no clear adverse effects addressing the level of AGW were noticed.
Based on these data, the AGW-values are set to 64 mg/m³ for all exposure durations. No intraspecies uncertainty factor was applied, given that the observed effects are sub-AGW. Considering the 8-hour exposure to 32 mg/m³ without AGW effects and the rapid onset of sub-AGW symptoms at 64 mg/m³, time-scaling was not applied.

LBW: The LBW-values were based on an acute rat lethality study. Rats (n=5/sex/group) were exposed via whole body inhalation to analytical concentrations of 498, 995, 1198 and 1838 ppm furfural (corresponding to 1991, 3977, 4788 and 7346 mg/m³) for one hour. Mortality was 0/5, 4/5, 2/5, 5/5 (males) and 0/5, 2/5, 4/5, 5/5 (females), respectively. Doseresp was applied to calculate LC_{50} and LC_{01} values. There were no clear differences between males and females. The resultant 1-hour LC_{50} and LC_{01} values (sexes combined) were 4030 mg/m³ and 2078 mg/m³, respectively. The 1-hour LC_{01}

value of 2078 mg/m^3 was selected as point of departure for deriving LBW-values. Applying an overall uncertainty factor of 10 (3x3) for interspecies and intraspecies differences would result in LBW values that are in conflict with human data, *i.e.*, no significant effects in a human ADME study with exposure concentrations of up to 7.9 ppm (32 mg/m^3) for 7.5 hours. In addition, lethality data from multiple species were available. An interspecies uncertainty factor of 1 was applied. The default intraspecies uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$ with the default n = 1 and n= 3, to extrapolate to longer and shorter durations, respectively. Due to conflict with human data (see AGW), the 8-hour LBW-value was set similar to the 4-hour LBW-value.

Additional toxicological information (including relevant results of a general literature search, if any)

Furfural is irritating to the skin, eye and respiratory tract and induces depression of the CNS.

No information on reproductive toxicity upon inhalation exposure available for furfural.

H301: Toxic if swallowed, H312: Harmful in contact with skin, H315: Causes skin irritation, H319: Causes serious eye irritation, H331: Toxic if inhaled, H335: May cause respiratory irritation, H351: Suspected of causing cancer.

Carcinogenicity and derivation of the CRP value

IARC classification: group 3 (not classifiable as to carcinogenicity to humans)

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: aromatic odour resembling almonds or bread

OT: 0.024 mg/m^3 [Ruth, 1986]
LOA = 11.8 * OT * 1.33 = 0.38 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: $I = 2.33 * \log (C/OT_{50}) + 0.5$. A correction factor of 1.33 is applied to this value)

The LOA is below the VRW.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [48]

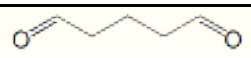
VRW level **6.8**	*AEGL-1* -	*ERPG-1* 8		*IDLH:* 100 ppm (400 mg/m^3) (30 minutes)
AGW level **64**	*AEGL-2* -	*ERPG-2* 40		
LBW level **690**	*AEGL-3* -	*ERPG-3* 200		

[48] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 111-30-8

Glutaaraldehyde



VN-nr: 3265
GEVI: 80

Synoniemen: 1,5-pentaandial, succinaldehyde, glutaaral (Engels: Glutaraldehyde)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m³)**	0,42	0,42	0,42	0,42	0,42	0,42
Alarmeringsgrenswaarden	**AGW (mg/m³)**	9,7	6,7	5,3	4,2	3,4	1,7
Levensbedreigende waarden	**LBW (mg/m³)**	27	18	15	12	9,2	4,6

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,240 ppm; 1 ppm = 4,16 mg/m³

Explosiegrens: 1,5 vol% ≈ 62.000 mg/m³

Geur: Groene appel, stekende geur

LOA: 0,016 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze tot gele viskeuze oplossing
Brand: moeilijk tot niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,00

Molecuulmassa:	100,1 g/mol
Zuurgraad:	3,7 (bij 10g / 100 ml)
LogKow:	-0,4
Wateroplosbaarheid:	volledig
Verzadigde dampdruk:	0,6 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: 0,21 mg/m³
TLV-ceiling: 0,21 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	Geen effect
VRW → AGW:	Irritatie van ogen, neus en keel, tranende ogen, keelpijn en hoesten
AGW → LBW:	Irritatie van ogen, neus en keel, hoofdpijn, kortademigheid
Boven LBW:	Ademnood, sufheid, bloeddrukdaling, bewusteloosheid, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Glutaaraldehyde is als vloeistof en damp sterk irriterend tot bijtend voor alle contactwegen.
- Inademing kan tot een heftige astmatische reactie leiden die wordt veroorzaakt door hetzij een bronchiale hyperreactiviteit dan wel door een respiratoire allergie (de stof is ook een huidallergeen).
- Hoge concentraties kunnen zwellingen in de keel (larynx- en glottisoedeem) veroorzaken, met gevaar op verstikking.
- In zeer hoge (dodelijke) concentraties worden effecten op het centrale zenuwstelsel merkbaar (spiertrekkingen, sufheid tot bewusteloosheid)

Effecten bij blootstelling aan vloeistof

Huidcontact: prikkeling, roodheid en pijn, bijtend, branderig gevoel, brandwonden.

Oogcontact: prikkeling, roodheid en pijn, tranenvloed, branderig gevoel, hoornvliesbeschadiging.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

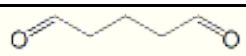
Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding, direct spoedeisende medische hulp inzetten

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen, arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 111-30-8 **Glutaraldehyde**  **UN-nr: 3265**

Basis for the Dutch Intervention Values

VRW: Based on information as described in ERPG-document, different values are derived, other time-points added

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017 | ERPG, 2015

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.42	0.42	0.42	0.42	0.42	0.42	Sensory irritation in human volunteers
AGW	9.7	6.7	5.3	4.2	3.4	1.7	Symptoms of ocular irritation in rats
LBW	27	18	15	12	9.2	4.6	No lethality in rats

Derivation of the Dutch Intervention Values

VRW: VRW values are based on an experimental study on the detection of odour and sensory irritation from exposure to glutaraldehyde vapour in human volunteers. Fifty female volunteers (aged 18 – 35 years) were exposed to 35, 50, 75 or 100 ppb (0.146, 0.208, 0.312 or 0.416 mg/m³) during 15 minutes in an exposure chamber, either in ascending or descending order of concentration (25 subjects each) and with intervals of 45 – 75 minutes between subsequent exposures. In addition, exposure to clean air and an odour control (heptane) were included in the exposure setup. Exposure up to 0.416 mg/m³ was tolerated without eye, nose or throat irritation. Other human volunteer studies reported irritation thresholds of 0.26 ppm (1.08 mg/m³) and 0.3 ppm (1.25 mg/m³). In hospital workers, irritation of the eyes and upper respiratory tract was reported at glutaraldehyde vapour concentrations of 0.2 ppm (0.833 mg/m³), while no symptoms were reported at 0.1 ppm (0.416 mg/m³). Therefore, 0.416 mg/m³ is used as point of departure for the VRW values. An intraspecies uncertainty factor was not applied given the absence of irritation effects in the volunteer study. Time scaling was not applied as respiratory irritation is considered to be concentration-dependent rather than concentration x time-dependent.

AGW: AGW values are based on an acute inhalation study in rats. Groups of 10 rats (5 male, 5 female) were exposed to dynamically generated saturated glutaraldehyde vapour atmosphere in an exposure chamber for 4 hours at ambient temperatures (17°C – 23°C) followed by a 14-days post-exposure observation. Air sampling inside the exposure chambers showed that gluataraldehyde concentrations ranged from 8.1 ppm (33.7 mg/m³) to 22.2 ppm (92.4 mg/m³). At 33.7 mg/m³, blepharospasm (involuntary closing of the eyes) and lacrimation were noted. At higher concentrations also periocular wetness, hyperactivity and audible breathing were noted. All symptoms resolved within a day after exposure. The exposure concentration of 33.7 mg/m³ was used as the point of departure for derivation of the AGW values. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n * t = k$, with the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively

LBW: Acute inhalation studies were available with glutaraldehyde vapour generated at ambient temperature under dynamic (concentrations of 22.2 ppm (92 mg/m³)) and static conditions (concentrations up to 48.1 ppm (200 mg/m³)). The six and four hour exposures to static and dynamic generated saturated concentrations, respectively did not result in mortality in rats. Acute inhalation toxicity studies were also performed, in which rats were exposed to glutaraldehyde vapour generated at elevated temperature (60°C or 65°C) and cooled before exposure. Mortality was observed in these studies. As heating of glutaraldehyde appears to increase the toxicity of the vapour these studies were not used as point of departure for derivation of the LBWs. The

dynamically generated highest concentration of 92 mg/m^3, for a 4 hr exposure, causing no mortality was used as PoD. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n * t = k$, with the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively

Additional toxicological information (including relevant results of a general literature search, if any)

The primary effect of inhalation exposure to glutaraldehyde is irritation of the eyes and upper respiratory tract.

Glutaraldehyde is usually used in aqueous solutions, which contain a mixture of chemical species including the dialdehyde, hemihydrate, dehydrate, and cyclic hemiacetal forms. Depending on temperature and pH, several polymers may also be present. The chemical composition of the mixture affects toxicity and may change with temperature. Exposure to glutaraldehyde vapours generated under elevated temperature appears to result in more severe toxicity than exposure to similar concentrations of the vapour at ambient temperature. Vapour concentrations above approximately 28 ppm (approximately 120 mg/m^3) require heating of the solution.

No evidence for reproductive toxicity upon inhalation of glutaraldehyde was found.

H330: Fatal if inhaled; H301: Toxic if swallowed; H314: Causes severe skin burns and eye damage; H317: May cause an allergic skin reaction; H335: May cause respiratory irritation; H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled

Carcinogenicity and derivation of the CRP value

IARC classification: not classified.

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: pungent, green apple-like

OT: 0.001 mg/m^3 [Cain et.al., 2007]
LOA = 11.8 * 0.001 * 1.33 = 0.016 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: $I = 2.33 * \log (C/OT_{50}) + 0.5$. A correction factor of 1.33 is applied to this value)

The LOA lies well below VRW level.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [49]

VRW level **0.42**	*AEGL-1* -	*ERPG-1* 0.82		*IDLH:* not derived
AGW level **5.3**	*AEGL-2* -	*ERPG-2* 4.1		
LBW level **15**	*AEGL-3* -	*ERPG-3* 20.5		

[49] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 110-54-3 **Hexaan** CH_3-$(CH_2)_4$-CH_3 **VN-nr: 1208**

GEVI: 33

Synoniemen: n-hexaan (Engels: Hexane) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	15.000*	10.000*	10.000*	10.000*	10.000*	10.000*
Levensbedreigende waarden	LBW (mg/m³)	45.000***	31.000**	31.000**	31.000**	31.000**	31.000**

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,279 ppm; 1 ppm = 3,59 mg/m³

Explosiegrens: LEL = 1,0 vol% ≈ 36.000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

** berekende interventiewaarde hoger dan 50% LEL

*** berekende interventiewaarde hoger dan 100% LEL

Geur: typerende (bezine-) geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,3

Molecuulmassa:	86,2 g/mol
Zuurgraad:	Geen data
LogKow:	3,8
Wateroplosbaarheid:	Niet oplosbaar
Verzadigde dampdruk:	160 mbar

Overige informatie

Publieke grenswaarde: 72 mg/m³
MAK: 180 mg/m³
TLV-TWA: 180 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: mogelijk hoofdpijn, duizeligheid, misselijkheid

AGW → LBW: verminderde ademhaling bewustzijnsdaling

Boven LBW: ademstilstand, coma, sterfte

Toxiciteit bij eenmalige inhalatoire blootstelling

- De acute toxiciteit van hexaan is laag.
- Hexaan verorzaakt depressie van het centraal zenuwstelstel.
- De stof heeft een steile concentratie-respons curve.

Effecten bij blootstelling aan vloeistof

Huidcontact: droge huid, roodheid.

Oogcontact: roodheid, pijn.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, arts raadplegen en direct spoedeisende medische hulp inzetten.

ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken en minimaal 20 min. spoelen met veel water of douchen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), daarna naar oogarts brengen

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**:* geen.

Neem contact op met het NVIC (Tel: +31(0)30-274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 110-54-3 **Hexane** **CH_3-$(CH_2)_4$-CH_3** **UN-nr: 1208**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with the AEGL

AGW: One third of LBW values

LBW: AEGL value is adopted, 2h value added

Date: November 2015 | AEGL document: Final, 2013

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	15,000*	10,000*	10,000*	10,000*	10,000*	10,000*	One third of LBW values
LBW	45,000***	31,000**	31,000**	31,000**	31,000**	31,000**	Threshold for lethality in animals

* value higher than 10% of LEL; ** value higher than 50% of LEL; *** value higher than 100% of LEL

Derivation of the Dutch Intervention Values

VRW: Due to insufficient human and animal data addressing the level of effects defined by the VRW, no VRW values are recommended.

AGW: The AGW values for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data. In one study, rats showed reduced respiration associated with narcosis at 10,000 ppm (35,860 mg/m³) for 6 h but not at 3,000 ppm (10,760 mg/m³). This study did not mention how toxicity was assessed and failed to provide specific observations related to toxicity. In another rat study, sedation, hypothermia and ptosis (dropping upper eyelid) were reported at 2,000 ppm (7,170 mg/m³), 4,000 ppm (14,300 mg/m³) or 8,000 ppm (28,700 mg/m³) for 8 h. Nevertheless, no further details were provided and the severity of effects could not be related to the exposure concentration. This approach to derive the AGW is also supported by the steep concentration-response curve demonstrated for butane, a structural analog of n-hexane and CNS depressant. CNS depression is the most relevant adverse effect from acute exposure to n-hexane. Adequate human data were not available and there is considerable uncertainty regarding the no-effect level for AGW level effects in rats and mice as a result of reporting insufficiencies and confounding methodologic issues, respectively.

LBW: As point of departure for the derivation of the LBW-values, a 30 minute exposure level of 86,222 ppm (309,192 mg/m³) from a rat kinetic study was used. At this concentration, rats showed signs of ataxia and decreased motor activity, but no mortality occurred. The available mouse lethality studies were not suitable because of study flaws, including use of static exposure systems with poorly reported methods and results. Therefore, rat data were considered to be the most reliable. The two lethal studies for rats could not be judged properly because of inadequate documentation, and appear to be inconsistent with other reports. For these reasons, the kinetic rat study was selected as a point of departure for LBW effects. A total uncertainty factor of 10 was applied, 3 for interspecies and 3 for intraspecies differences. The effects are attributed to n-hexane itself and no relevant differences in kinetics are assumed, so only small interspecies differences are expected. Mortality from n-hexane exposure is preceded by CNS-depression and the variation in susceptibility for CNS depression is not very great in the human population. In addition, the concentration-response curve is rather steep, indicating that a larger factor is not necessary. A steady state blood concentration for n-hexane was reached in approximately 30 minutes. Hence, no increase of effect-size by exposure duration is expected from 30 minutes to 8 hours and the LBW-values for 30 min, 1, 2, 4, and 8 hours of exposure will be set equal. The 10-minute value will be derived from the 30-minute concentration by time scaling, using the equation $C^n \times t = k$, with n=3.

Additional toxicological information (including relevant results of a general literature search, if any)

Acute toxicity of n-hexane to humans is very low. Visible signs of acute toxicity were only observed in animal toxicity studies and are generally associated with effects on the nervous system and are attributed to n-

hexane itself. The margin between narcotic and fatal concentrations is rather small and a blood steady-state concentration of n-hexane is reached after only 30 minutes.

H304: May be fatal if swallowed and enters airways; H315: Causes skin irritation; H336: May cause drowsiness or dizziness; H361f: Suspected of damaging fertility; H373: May cause damage to organs.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived.	Odour: Hexane has a slight gasoline-like odour. No LOA was derived due to lack of data.

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)***

VRW level **NR**	*AEGL-1* NR	*ERPG-1* Not derived		*IDLH:* 3900 (30 min)
AGW level **10,000**	*AEGL-2* 10,000	*ERPG-2* Not derived		
LBW level **31,000**	*AEGL-3* 31,000	*ERPG-3* Not derived		

Stofdocument deel A

CAS-nr: 87-68-3

Hexachloorbutadieen C_4Cl_6

VN-nr: 2279
GEVI: 60

Synoniemen: HCBD, perchloor-1,3-butadieen (Engels: hexachloro-1,3-butadiene) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	59	18	8,8	4,3	2,1	1,0
Levensbedreigende waarden	LBW (mg/m³)	180	55	26	13	6,3	3,1

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,0920 ppm; 1 ppm = 10,85 mg/m³

Explosiegrens: niet bekend

Geur: terpentijn-achtig

LOA: 188 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: brandgevaar

Molecuulmassa: 260,8 g/mol

Zuurgraad: -

LogKow: 4,8

Wateroplosbaarheid: 0,05 g/100 ml (zeer slecht)

Verzadigde dampdruk: 0,5 mbar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,0

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: 0,22 mg/m³
TLV-TWA: 0,22 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: hoesten, keelpijn

AGW → LBW: branderig gevoel, kortademigheid

Boven LBW: sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De damp is irriterend voor de ogen en slijmvliezen, en bij hogere concentraties irriterend op de luchtwegen.
- Na opname in het lichaam zijn met name de nieren het doelorgaan van deze stof.
- Sterfte kan mogelijk vertraagd optreden.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid

Oogcontact: roodheid, pijn

Carcinogeniteit

IARC classificatie: groep 3
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, en onmiddellijk arts raadplegen.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!) en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 87-68-3 **Hexachloro-1,3-butadiene** C_4Cl_6 **UN-nr: 2279**

Basis for the Dutch Intervention Values

VRW: Not recommended, in contrast to ERPG

AGW: Different rationale than ERPG, different values are derived, other time-points added

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017 ERPG 2004

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	59	18	8.8	4.3	2.1	1.0	One-third of LBW
LBW	180	55	26	13	6.3	3.1	Acute lethality rabbit, rat and guinea pig

Derivation of the Dutch Intervention Values

VRW: VRW-values were not derived for hexachloro-1,3-butadiene. There are no exposure-response data in humans or animals consistent with VRW-level effects. In absence of suitable data, the VRW-levels were set to Not recommended.

AGW: In the absence of human data and due to the limited animal data consistent with AGW-level effects, AGW-values were set to one third of the LBW.

LBW: LBW-values were based on an acute inhalation lethality study in rats, guinea pigs, rabbit and cats. Animals were exposed to hexachloro-1,3-butadiene (whole body exposure concentrations of 240-3290 mg/m^3 for exposure durations ranging from 20 to 420 minutes). Doseresp was applied to calculate the LC_{01} values. Rat LC_{01} values for a 10 min, 30 min, 1h, 2h, 4h and 8h exposure duration were 4139, 1300, 626, 302, 145 and 70 mg/m^3, respectively, and the corresponding n-value was 0.949. Guinea pig LC_{01} values for a 10 min, 30 min, 1h, 2h, 4h and 8h exposure duration were 808, 181, 70.4, 27.4, 10.7 and 4.14 mg/m^3, respectively, and the corresponding n-value was 0.734. Rabbit LC_{01} values for a 10 min, 30 min, 1h, 2h, 4h and 8h exposure duration were 387, 166, 97.5, 57.2, 33.5 and 19.7 mg/m^3, respectively, and the corresponding n-value was 1.299. Calculation of LC_{01} values was not possible for the cat dataset. There is a difference between rat vs. guinea pig and rabbit in sensitivity and n. In absence of information on the representativeness for humans, the data were combined. For each time point, the mean LC_{01} values were calculated based on the three datasets and used as PoD. Combined LC_{01} values for a 10 min, 30 min, 1h, 2h, 4h and 8h exposure duration were 1778, 549, 265, 129, 63 and 31 mg/m^3, respectively, and the corresponding n-value was 0.99. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences.

Additional toxicological information (including relevant results of a general literature search, if any)

Hexachloro-1,3-butadiene is irritating to the mucous membranes. The major systemic target organ is the kidney.

The available data indicate that hexachloro-1,3-butadiene is not toxic for the developing foetus after inhalation, except for a reduction in foetal body weight. There is no information on the potential effects on fertility via the inhalation route in the available literature for this chemical.

No harmonized H-statements for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to its carcinogenicity to humans)

No carcinogenic risk potency (CRP) was derived. Reliable

Odour and derivation of the LOA value

Odour: mild to faint turpentine-like, pungent

OT: 12 mg/m^3 [Ruth, 1986]
LOA = 11.8 * OT * 1.33 = 188 mg/m^3

inhalation data were not available. An inhalation unit risk of 0.22 per mg/m^3 is reported (US EPA), however this value is not used for calculation of the CRP as the unit risk is based on oral data.	(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [50]				
VRW level **NR**	*AEGL-1* -	*ERPG-1* 10.7		*IDLH:* not derived
AGW level **8.8**	*AEGL-2* -	*ERPG-2* 32.1		
LBW level **26**	*AEGL-3* -	*ERPG-3* 106.9		

[50] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 684-16-2 **Hexafluoraceton** CF_3COCF_3 **VN-nr: 2420**
GEVI: 268

Synoniemen: perfluoraceton, perfluor-2-propanon, 1,1,1,3,3,3-hexafluor-2-propanon (Engels: hexafluoroacetone) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	25	8,3	4,1	2,1	1,0	0,52
Levensbedreigende waarden	LBW (mg/m³)	3.300	1.100	550	280	140	69

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,145 ppm; 1 ppm = 6,91 mg/m³

Explosiegrens: geen data

Geur: karakteristieke muffe geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas
Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa: 166 g/mol
Zuurgraad: geen data
LogKow: 1,46
Wateroplosbaarheid: reactie
Verzadigde dampdruk: 5.877 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA:0,691mg/m³ H

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW: hoesten en keelpijn, tranenvloed

AGW → LBW: irritatie van de hogere luchtwegen= keelpijn en hoesten, zwaktegevoel, coördinatiestoornissen, kortademigheid, ademnood, benauwdheid, effecten op de ongeboren vrucht

Boven LBW: sterfte

LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof is sterk irriterend voor de ogen, de huid en de luchtwegen.
- De stof vormt met vocht hydraten die sterk zuur zijn (tasten glas en metaal aan). Zowel HFA als zijn hydraten kunnen worden ingeademd. Via de huid wordt de stof ook goed geabsorbeerd.
- Blootstelling aan hexafluoraceton kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Hexafluoraceton kan embryotoxiciteit veroorzaken.

Effecten bij blootstelling aan vloeistof (i.e., hyrdaten)

Huidcontact: roodheid, pijn en brandwonden. De stof wordt door de huid opgenomen.
Oogcontact: roodheid en pijn, hoornvliesbeschadiging.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: n.v.t. (gas). Er zijn wel hydraten die met water gevormd worden, of zelfs in waterige oplossing kunnen voorkomen. In die gevallen: kleding uittrekken en minstens 20 min. spoelen met veel water of douchen. Bij brandworden arts raadplegen.

ogen: zie hierboven.

inslikken: n.v.t. (gas) **N.B.**: hydraten en waterige oplossing kunnen wellicht wel als vloeistof worden ingeslikt. In dat geval mond spoelen met water (uitspugen!) en direct spoedeisende hulp inzetten.

Specifieke behandeling en materialen*: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 684-16-2 **Hexafluoroacetone** **CF_3COCF_3** **UN-nr: 2420**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: Same point of departure as for AEGL values but using different uncertainty factors, (except 10 min value for which time scaling was applied), 2h value added.

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: November 2015 | AEGL document: Final, 2013

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Inadequate data.
AGW	25	8.3	4.1	2.1	1.0	0.52	Threshold for adverse developmental effects in rats
LBW	3,300	1,100	550	280	140	69	Estimated threshold for lethality in rats

Derivation of the Dutch Intervention Values

VRW: The VRW values were not derived for hexafluoroacetone. There are no adequate exposure-response data in humans or animals consistent with VRW-level effects. The lack of VRW-values does not necessarily mean that exposure below AGW-levels is without any effects.

AGW: A number of studies have reported developmental and reproductive toxicity of hexafluoroacetone after acute inhalation exposure in rats. Testicular atrophy in male rats and developmental toxicity were observed. The developmental toxicity occurred at lower concentrations than the testicular effects, which tended to be reversible. Developmental toxicity was therefore selected as the critical effect for derivation of the AGW values. Exposure of dams (nose-only) to a concentration of 6.9 ppm (47.7 mg/m^3) for 6 hours a day during gestation day 7-16 resulted in a significant decrease in the number of live fetuses per litter. Furthermore, a significant increase in resorptions, malformations and external and skeletal developmental variations was observed. Exposure to 1 ppm (6.91 mg/m^3) for 6 hours/day during during gestation day 7-16 resulted in increased incidence of variations in skeletal development and decreases in fetal body weight. These findings suggest that the fetus is sensitive to exposure to hexafluroroacetone, because maternal toxicity was absent at these concentrations. As the reported resorptions and skeletal effects could also occur after a single exposure (van Raaij, 2003), the 1 ppm (6.91 mg/m^3) level was selected as a NOAEL for adverse developmental effects and was used as point of departure for derivation of the AGW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differencesTime-scaling was performed using the equation $C^n \times t = k$ with an empirical value of n = 1 based on available data.

LBW: Two studies in rats showed that a 4-hour exposure to 200 ppm (1,382 mg/m^3) was without lethality and that mortality increased to 50% at 300 ppm (2,073 mg/m^3) and up to 75% at 400 ppm (2,764 mg/m^3). Therefore the exposure for 4-hour to 200 ppm (1,382 mg/m^3) was used as point of departure for derivation of LBW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differencesTime-scaling was performed using the equation $C^n \times t = k$. From the available data an empirical value of n = 1 was derived.

Additional toxicological information (including relevant results of a general literature search, if any)

The mechanism of toxicity of hexafluoroacetone is unclear due to a lack of data. In one study it was noted that the effects of hexafluroroacetone are mediated with pulmonary damage in rats at air concentrations above minimal lethality levels. Other studies indicate that the substance is a contact irritant with systemic effects (CNS depression, neuromuscular dysfunction, weight loss and renal dysfunction).

There is no data located on developmental toxicity and reproductive effects in humans. Animal studies showed that exposure to hexafluoroacetone can result in testicular atrophy in male rats and developmental and reproductive effects in female rats (see derivation of the AGW).

No harmonised H-statements

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived.	Odour: characteristic musty odour No LOA was derived (due to lack of suitable data)

Other standards and guidelines *(1h values in mg/m³, unless otherwise indicated)*				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH: not determined*
AGW level **4.1**	*AEGL-2* 1.4	*ERPG-2* 6.9		
LBW level **550**	*AEGL-3* 540	*ERPG-3* 346		

Stofdocument deel A

CAS-nr: 302-01-2 **Hydrazine** H_2NNH_2 **VN-nr: 2029**

GEVI: geen

Synoniemen: diamine, diamide (Engels: hydrazine) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,13	0,13	0,13	0,13	0,13	0,13
Alarmeringsgrenswaarden	AGW (mg/m³)	43	30	24	12	5,9	3,0
Levensbedreigende waarden	LBW (mg/m³)	130	90	71	36	18	8,9

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,749 ppm; 1 ppm = 1,34 mg/m³

Explosiegrens: LEL = 1,8 Vol% ≈ 24.000 mg/m³

Geur: stekende ammoniak-achtige geur

LOA: 84 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,1

Molecuulmassa: 32,1 g/mol
Zuurgraad: geen data
LogKow: -2,1
Wateroplosbaarheid: volledig
Verzadigde dampdruk: 21 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 0,013 mg/m³ (huid)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte irritatie van ogen en luchtwegen, bijtend

VRW → AGW: irritatie van ogen, huid en luchtwegen, hoofdpijn, misselijkheid, branderig gevoel in het gelaat

AGW → LBW: schade aan luchtwegen, braken, tremoren, krampen, benauwdheid, kortademigheid, ademnood, verminderde coördinatie, stuiptrekkingen, bewusteloosheid,

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt bijtend op de ogen, de huid en de luchtwegen.
- Blootstelling aan hydrazine kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- De stof kan inwerken op het centrale zenuwstelsel met als gevolg braken, stuiptrekkingen en slaperigheid. Ook de lever, nieren en hartspier lijken doelorganen voor systemische toxiciteit.
- Blootstelling kan tot bewusteloosheid leiden.
- De stof is een sterke huidsensibilisator en vertoont kruisovergevoeligheid met allerlei hydrazine-derivaten.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, brandwonden. De stof wordt door de huid opgenomen.
Oogcontact: bijtend, bindvliesontsteking, tijdelijk verlies van gezichtsvermogen, slecht zien, ernstige brandwonden.

Carcinogeniteit

IARC classificatie: 2B
CRP: 4,5 mg/m³

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding, direct spoedeisende medische hulp inzetten

Ontsmetting vloeistof
huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, spoelen met veel water / kleding verwijderen, direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 302-01-2 **Hydrazine** **H_2NNH_2** **UN-nr: 2029**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Different point of departure as AEGL, 2h value added

LBW: Same point of departure as AEGL, different modifying factor, 2h value added

Date: November 2015 | AEGL document: final, 2010

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.13	0.13	0.13	0.13	0.13	0.13	Threshold for eye and facial irritation in monkeys
AGW	43	30	24	12	5.9	3.0	1/3 LBW
LBW	130	90	71	36	18	8.9	Threshold for lethality in rats

Derivation of the Dutch Intervention Values

VRW: A study in male monkeys showed skin flushing and swollen eyes after 24 hours of exposure to 0.52 mg/m³. This represents the lowest exposure resulting in an effect that could be considered consistent with the definition of a VRW value. A total uncertainty factor of 10 was considered to be sufficient to deal with the variability between species and between individuals. The default value of n = 3 is used to extrapolate from 24-h of exposure to the 8-h VRW time frame. Hydrazine is extremely reactive and the observed sensory irritation effects are considered to be concentration dependent rather than time dependent, This is also demonstrated by the calculated 10 minute-8 hour values, which lie between 0.08 and 0.3 mg/m³. Therefore 0.1 ppm (0.13 mg/m³) was considered appropriate for all VRW durations. The resulting VRW values are in line with available human data, indicating no signs of toxicity in workers when routinely exposed to 0.07-0.12 ppm (0.093-0.16 mg/m³) hydrazine.

AGW: A study in rats showed nasal lesions following a 1 hour exposure to 750 ppm (1,001 mg/m³). This value was considered to be the most appropriate basis for derivation of the AGW. However, the data that were found show some inadequacies in the study designs In an inhalation exposure (nose-only) study exposing pregnant rats to 50 or 500 ppm (67 or 668 mg/m³) on gestation day 9 resulted in no compound-related effects at 50 ppm (67 mg/m³) and significant (48%) embryolethality at 500 ppm (668 mg/m³) hydrazine compared to control animals. Although embryonal death is considered relevant for AGW, this study was not taken as point of departure because: 1) effects were concurrent with maternal toxicity, 2) observed effects were somewhat higher than other datasets and 3) essential study data were lacking.
Based on the above considerations, in contrast to the AEGL, the AGW values were based on 1/3 of the LBW values.

LBW: The results from the various lethality studies were not considered suitable for use in DoseResp to calculate LC_{01} values. In a study in rats an exposure to 3,192 ppm (4,262 mg/m³) was considered as a 1-hour LC_{50} value. A 3-fold reduction of the LC_{50} value is considered to be appropriate to estimate the lethality threshold. Therefore, a value of 1,064 ppm (1,421 mg/m³) for 1 hour was used as the point of departure for the derivation the LBW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. An additional modifying factor of 2 was applied based on the limited dataset. Time-scaling was performed using the equation $C^n \times t=k$, using the default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Hydrazine is an oxygen scavenger and is highly reactive with other chemicals. The various studies demonstrated the acute lethality of hydrazine, however the time to lethality following inhalation exposure appears to be extremely variable. Exposure to hydrazine may result in lethality as long as 14 days following cessation of exposure. A steep concentration-response relationship appeared to be present for hydrazine.

The available data suggest that there may be little margin between lethal effects and nonlethal effects following inhalation exposure to hydrazine. Studies with animals have shown that hydrazine may be metabolized to acetylhydrazine, diacetylhydrazine, ammonia, urea and may form hydrazones with pyruvate and 2-oxoglutarate.
Data on developmental and reproductive toxicity and, genotoxicity are too limited to draw conclusions. An inhalation (nose-only) study with pregnant rats (strain unspecified) revealed that a 1-h exposure to 500 ppm (668 mg/m^3) hydrazine resulted in 48% embryolethality compared to control animals. This effect was concurrent with maternal toxicity.

H350: May cause cancer, H331: Toxic by inhalation, H311: Toxic in contact with skin, H301: Toxic if swallowed, H314: Causes severe skin burns and eye damage, H317: May cause allergic skin reaction

Carcinogenicity and derivation of the CRP value

IARC classification: 2B (possibly carcinogenic to humans)

Derivation of the carcinogenic risk potency (CRP):

10^{-4} risk level after inhalation: $2.0*10^{-5}$ mg/m^3 [MacEwen et al., 1981]

CRP = (10^{-4} risk level * average life span in hours)/DRCF

= ($2.0*10^{-5}$ mg/m^3 * 613,200) /2.8 = 4.5 mg/m^3

Odour and derivation of the LOA value

Odour: pungent ammonia-like odour

OT_{50}: 5.34 mg/m^3 [van Doorn et al., 2002]
LOA = 11.8 * 5.34 * 1.33 = 84 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies above the AGW, VRW and LBW values, except for the 10- and 30-min LBW value.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **0.13**	*AEGL-1* 0.1	*ERPG-1* 0.67		*IDLH: 67 (30 minutes)*
AGW level **24**	*AEGL-2* 17	*ERPG-2* 6.7		
LBW level **71**	*AEGL-3* 46	*ERPG-3* 40		

Stofdocument deel A

CAS-nr: 13463-40-6 **IJzercarbonyl** **$Fe(CO)_5$** **VN-nr: 1994** **GEVI: 663**

Synoniemen: ijzerpentacarbonyl, pentacarbonylijzer (Engels: iron pentacarbonyl) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	0,90	0,62	0,49	0,39	0,31	0,20
Levensbedreigende waarden	LBW (mg/m³)	2,7	1,9	1,5	1,2	0,93	0,61

Datum vaststelling: 24-09-2009 **Conversiefactor**: 1 mg/m³ = 0,123 ppm; 1 ppm = 8,15

Explosiegrens: LEL = 3,7 vol% ≈ 300.000 mg/m³

Geur: nagenoeg reukloos

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: lichtgele tot donkerrode olieachtige vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,2

Molecuulmassa:	195,9 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	Niet oplosbaar
Verzadigde dampdruk:	35 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: 0,82 mg/m³

TLV-TWA: 0,82 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: mogelijk oog- en luchtwegirritatie, hoesten, misselijkheid, braken, hoofdpijn, duizeligheid

AGW → LBW: ernstige luchtwegirritatie met koorts, hoesten en benauwdheid, ernstige effecten op centraal zenuwstelsel niet uitsluitbaar

Boven LBW: coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- IJzercarbonyl veroorzaakt primair effecten in de luchtwegen.
- De long-effecten lijken op metaaldampkoorts en kunnen vertraagd optreden.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid

Oogcontact: bijtend, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 13463-40-6 **Iron pentacarbonyl** **$Fe(CO)_5$** **UN-nr: 1994**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value adopted (except 10 min value for which time scaling was applied), 2hr value added.

LBW: AEGL value adopted (except 10 min value for which time scaling was applied), 2hr value added.

Date: 24-09-2009 | AEGL document, final 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended.
AGW	0.90	0.62	0.49	0.39	0.31	0.20	One third of LBW
LBW	2.7	1.9	1.5	1.2	0.93	0.61	Threshold of animal lethality

Derivation of the Dutch Intervention Values

VRW: Not recommended, because of lack of data and an inadequate margin of safety between levels where VRW type effects were observed and levels causing severe effects or death.

AGW: The AGW values were derived by dividing the LBW values by a factor of 3. This approach is considered appropriate, because of the steep dose-response relationship of iron pentacarbonyl.

LBW: Exposure of rats to 1.0 ppm (8.15 mg/m³), 6 hours/day for 28 days resulted in no clinical signs of toxicity and was taken as point of departure. In the same study, a single 6hr exposure to 2.91 ppm (23.7 mg/m³) resulted in the death of one rat (of ten) and a second exposure to that level caused the death of 5 animals. The remaining 26 exposures did not result in more animal deaths. Since it is uncertain whether the first exposure already could have caused the mortality of 50% observed at day two a benchmark analysis was performed. The LC_{01} and $BMCL_{05}$ values were calculated for the scenarios that the single exposure either caused one or five deaths, where the latter is the conservative scenario. The calculated $BMCL_{05}$ of 0.8 ppm (6.5 mg/m³) for the latter scenario is below the 1.0 ppm that did not cause mortality after 28 exposures. Therefore, 1.0 ppm (8.15 mg/m³) was taken as point of departure. An intraspecies factor of 3 and an interspecies factor of 3 were applied, provided a total uncertainty factor of 10. Time scaling was performed using $C^n * t = k$, with the defaults of n = 3 and n = 1 for extrapolation to shorter and longer exposure durations, respectively. In contrast to the 10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

The available toxicity data indicate that acute inhalation exposure to iron pentacarbonyl results in portal-of entry effects (i.e., airway and lungs) rather than systemic effects and, therefore, variability in response due to dosimetric factors may be limited. Additionally, lethality in rats following acute inhalation exposure to iron pentacarbonyl exhibits a steep exposure-response relationship with little margin between minimal and lethal effects, and little individual variability in the response of test animals.

The substance may also affect the central nervous system leading to headache, dizziness and unconsciousness. Other symptoms after inhalation may be cyanosis, shortness of breath, vomiting.

Iron pentacarbonyl is sensitive to light decomposing into ferric nonacarbonyl and carbon monoxide. Under heating the substance decomposes into ferric oxide and carbon monoxide.

There are no data concerning the reprotoxic effects of iron pentacarbonyl.

No harmonized H-statements for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived due to

Odour and derivation of the LOA value

Odour: Substance is odourless. No LOA was derived.

lack of data.	

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* Not derived		*IDLH:* not established
AGW level **0.49**	*AEGL-2* 0.49	*ERPG-2* Not derived		
LBW level **1.5**	*AEGL-3* 1.5	*ERPG-3* Not derived		

Stofdocument deel A

CAS-nr: 78-82-0 **Isobutyronitril** **CH_3-CH(CH_3)CN** **VN-nr: 2284** **GEVI: 336**

Synoniemen: 2-methylpropaannitril, isopropylcyanide, 2- cyanopreen (Engels: Isobutyronitrile) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	95	66	52	41	33	22
Levensbedreigende waarden	LBW (mg/m³)	350	250	190	97	49	49

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,348 ppm; 1 ppm = 2,87 mg/m³

Explosiegrens: LEL = 1,6 vol% ≈ 46.000 mg/m³

Geur: bittere amandelen

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze vloeistof
Brand: zeer brandgevaarlijk.

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,38

Molecuulmassa:	69,1 g/mol
Zuurgraad:	Geen data
LogKow:	0,46
Wateroplosbaarheid:	Tegenstrijdige data
Verzadigde dampdruk:	Geen data

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 23 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW: irritatie ogen en bovenste luchtwegen, hoofdpijn

AGW → LBW: hoesten, zwelling/verkramping strottenhoofd, benauwdheid, pijn op de borst, misselijkheid, braken, duizeligheid, krachtsverlies, verwardheid, foetale sterfte

Onder LBW: convulsies, ademnood, ademstilstand, coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Isobutyronitril wordt omgezet tot o.a. cyanide.
- Cyanide blokkeert de ademhalingsketen in de cel. Hierdoor wordt de energiehuishouding verstoord en kan lactaatacidose ontstaan.
- Primaire systemische doelorganen zijn het centrale zenuwstelsel en het cardiovasculaire systeem.
- Isobutyronitril veroorzaakt irritatie van de bovenste luchtwegen.
- Verschijnselen kunnen vertraagd optreden.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, ademnood, blauwe lippen of nagels, duizeligheid, slaperigheid, hoofdpijn, zwaktegevoel, krampen.

Oogcontact: irritatie, pijn, slecht zien.

Carcinogeniteit

IARC: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: 100% zuurstof, direct spoedeisende medische hulp inzetten, specifieke behandeling. GEEN mond-op-mondbeademing!

Ontsmetting vloeistof

huid: eerst: zie *Ontsmetting damp - algemeen*, verder: verontreinigde kleding uittrekken, overmaat stof met PEG 400 opdeppen, spoelen en wassen met water en zeep.

ogen: eerst: zie *Ontsmetting damp - algemeen*, verder: uitspoelen met water (evt. contactlenzen verwijderen).

inslikken: eerst: zie *Ontsmetting damp - algemeen*, verder: mond laten spoelen (uitspugen!), GEEN braken opwekken.

Specifieke behandeling en materialen: De benodigde middelen (specifieke antidota zoals 100% zuurstof en o.a. hydroxocobalamine, en natriumthiosulfaat) moeten met gebruiksaanwijzing ter plekke beschikbaar zijn.

Voor aanwijzingen over verdere behandeling zo nodig het NVIC (tel: +31 (0)30 –274 8888) bellen.

Stofdocument deel B

CAS-nr: 78-82-0 **Isobutyronitrile** **CH_3-CH(CH_3)CN** **UN-nr: 2284**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: Different point of departure than AEGL values, using different uncertainty factors, 2h value added, also for 10 min timescaling was applied

LBW: Different point of departure than AEGL values, 2h value added, also for 10 min timescaling was applied and the 4h value was flatlined to the 8h value

Date: November 2015 | AEGL document: Final, 2014

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Insufficient data
AGW	95	66	52	41	33	22	No-effect-level level for fetal toxicity from a developmental toxicity study in rats
LBW	350	250	190	97	49	49	Calculated 1-hr LC_{01} in rats

Derivation of the Dutch Intervention Values

VRW: Data are insufficient for the derivation of VRW values for isobutyronitrile. Absence of VRW values does not imply that exposure below the AGW value is without adverse effects.

AGW: A developmental toxicity study in rats showing a no-effect-level for maternal and fetal mortality of 100 ppm (287 mg/m^3), was used as point of departure for the AGW. Rats were exposed to isobutyronitrile for 6 hour/day on days 6-20 of gestation. A significant increase in the incidence of embryonic resorptions was observed at 300 ppm (860 mg/m^3) and a decrease in fetal body weight was observed at 200 pm (575 mg/m3). One of 21 females dies in the 200 ppm group, while 3 of 21 females in the 300 ppm (860 mg/m3) group died. Although the study involved repeated exposures, fetal death is considered relevant for AGW derivation, as fetal death can also occur during a narrow developmental window and does not necessarily require repeated exposures. This is in contrast to maternal death, which is not considered an acute effect, but a result of repeated exposure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. For time-scaling $C^n \times t = k$ was used, using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.
The approach deviates from the AEGL-2 derivation where the AEGL-2 levels were calculated by dividing the AEGL-3 levels by 3.

LBW: The LBW was based on a rat lethality study. Groups of 5 animals/sex were exposed to isobutyronitrile at actual concentrations of 1248, 1778, and 2709 ppm for 1 hour. The calculated 1-hour LC_{01} of 677 ppm (1945 mg/m^3) in rats was used as point of departure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. For time-scaling $C^n \times t = k$ was used, using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. The 4 hour LBW was flatlined to the 8 hour value, to preclude conflict with the TLV-TWA of 23 mg/m^3.
This approach deviates from the AEGL-3 derivation. AEGL-3 levels were based on the effects observed in a developmental toxicity study.

Additional toxicological information (including relevant results of a general literature search, if any)

Aliphatic nitriles like isobutyronitrile are readily absorbed from the lung and gastrointestinal tract, resulting in systemic toxicity. Most of the systemic toxicity of these nitriles is mediated through hepatic and extrahepatic cytochrome P450 catalyzed oxidation of the carbon alpha to the cyano group producing a cyanohydrin and an aldehyde. The metabolically-liberated cyanide is then conjugated with thiosulfate to form thiocyanate and is excreted in the urine. The toxicity of isobutyronitrile is due to the metabolic liberation of cyanide and signs and

symptoms are similar to those observed after cyanide exposure.

Data concerning human exposure to isobutyronitrile are limited to occupational case reports lacking exposure concentration and duration information. These reports do indicate that clinical signs are consistent with those of cyanide poisoning.

Isobutyronitril is not teratogenic or toxic for reproduction. Fetal effects were only observed in rats at levels that also induced maternal toxicity.

No harmonised H-sentences for human health.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived No reports regarding carcinogenicity were found.	Odour: an almond-like odour No LOA was derived due to lack of data.

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)***

VRW level **NR**	*AEGL-1* NR	*ERPG-1* NR		*IDLH: not derived*
AGW level **52**	*AEGL-2* 5.7	*ERPG-2* 86		
LBW level **190**	*AEGL-3* 18	*ERPG-3* 287		

Stofdocument deel A

CAS-nr: 30674-80-7 **2-Isocyanatoethyl-methacrylaat** **$C_7H_9NO_3$** **VN-nr: 2206** **GEVI: geen**

Synoniemen: 2-propenoinezuur, methacryloylethylisoyanaat (Engels: methacryloyloxyethyl isocyanate) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	3,6	2,5	2,0	0,98	0,49	0,24
Levensbedreigende waarden	LBW (mg/m³)	11	7,4	5,9	2,9	1,5	0,74

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,155 ppm; 1 ppm = 6,456 mg/m³

Explosiegrens: geen data

Geur: Scherp en peperachtige

LOA: niet afgeleid

Fysisch-chemische eigenschappen[51]

Uiterlijk: kleurloze vloeistof
Brand: geen data

Relatieve dichtheid van verzadigd damp-lucht mengsel: 5,35

Molecuulmassa:	155,2 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	Niet oplosbaar
Verzadigde dampdruk:	0,27 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW**:* keelpijn, hoest, hoofdpijn, piepende ademhaling, misselijkheid

AGW → LBW: benauwdheid, vertraagde ademhaling, rode/pijnlijke ogen

Boven LBW: ademnood, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- 2-Isocyanatoethylmethacrylaat heeft een zeer sterk irriterende tot bijtende werking op de slijmvliezen, de longen en ogen.
- Dit uit zich vaak in astma-achtige klachten, vaak met neusloop (rhinitis). Er kan ook sprake zijn van bronchiale hyperreactiviteit.
- De stof is sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn, blaren.

Oogcontact: roodheid en pijn

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en onmiddellijk arts raadplegen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en onmiddellijk arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: mond laten spoelen (uitspugen!), en onmiddellijk arts raadplegen.

***Specifieke behandeling en materialen**: geen.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

[51] In afwezigheid van een Chemiekaart voor deze stof is gebruik gemaakt van ERPG (2004)

Stofdocument deel B

CAS-nr: 30674-80-7 **Methacryloyloxyethyl isocyanate** **$C_7H_9NO_3$** **UN-nr: 2206**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with ERPG

AGW: Different rationale than ERPG, other time-points added.

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added.

Date: 31-10-2017 | ERPG, 2004

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	3.6	2.5	2.0	0.98	0.49	0.24	One-third of LBW
LBW	11	7.4	5.9	2.9	1.5	0.74	Threshold for rat lethality

Derivation of the Dutch Intervention Values

VRW: The VRW values were not derived for methacryloyloxyethyl isocyanate. There are no exposure-response data in humans or animals consistent with VRW-level effects.

AGW: In the absence of human data and due to the limited animal data, AGW-values were set to one third of the LBW. A 13-week rat study is available (0.025, 0.08 and 0.25 ppm (0.16, 0.52 and 1.61 mg/m³) for 6 h/d, 5 d/week for 13 weeks) which shows very slight to slight multifocal hyperplasia of the respiratory epithelial lining of the nasal turbinates in the mid and high concentration group, though evaluation of a recovery group (30 and 92 days post-exposure) showed that the observed effects were reversible. Given the reversibility of the effects and the fact that the nasal lesions were only slight, the observed effects are considered sub-AGW effects. A 2-week rat inhalation study was also performed (0.25, 0.50 or 1.0 ppm (1.61, 3.23 or 6.46 mg/m³) for 6 h/d, 5d/week) in which also effects on the mucosal lining of the nasal passages and nasal turbinates were observed, mainly in the high concentration (6.46 mg/m³) group, though some effects were also noticed in the low concentration group (1.61 mg/m³). A recovery group was not included in this 2-week rat inhalation study. Based on an overall analysis of the available animal data, it was considered more appropriate to set the AGW-values at one-third of the LBW-values.
The study as used for LBW-derivation provides some support for setting the AGW to one-third of the LBW. A 1-hour exposure of rats to the lowest concentration of 10 ppm (65 mg/m³) and a 6-hour exposure to the lowest tested concentration of 2 ppm (13 mg/m³) resulted in slight signs of eye, nasal and respiratory irritation or even no effects. These concentrations are a factor of 2 lower than the concentrations at which lethality was observed.

LBW: A rat lethality study, in which a large number of rats was exposed for two exposure durations (1 and 6 hours), was considered the most relevant study for deriving LBW values. In this study, 10 rats per sex per concentration were exposed by inhalation for 1 hour to 10, 20 and 40 ppm (65, 129 and 258 mg/m³, respectively) of methacryloyloxyethyl isocyanate. Mortality was 0/10, 4/10 and 8/10 (males) and 0/10, 0/10 and 5/10 (females), for the respective concentrations. Further, rats were treated for 6 hours with 2, 4 and 7 ppm (13, 26 and 45 mg/m³, respectively) of methacryloyloxyethyl isocyanate. Mortality was 0/10, 6/10 and 7/10 (males) and 0/10, 3/10 and 7/10 (females), at the respective concentrations. Doseresp was used to calculate LC_{50} and LC_{01} values for both time points. There were no clear differences between males and females and a combined analysis of male+female data was performed. The 1-hour LC_{50} and LC_{01} were 204 and 58.9 mg/m³, respectively. The 6-hour LC_{50} and LC_{01} were 31.8 and 9.4 mg/m³, respectively.
Scaling of the 1-hour LC_{01} value of 58.9 mg/m³ to 6 hours with a default scaling factor of 1 would result in a 6-hour LC_{01} value that is comparable with the calculated 6-hour LC_{01} value of 9.4 mg/m³. Scaling of the 6-hour LC_{01} value to 1 hour with a default scaling factor of 3, however, would result in a 1-hour LC_{01} value that is more than a factor 3 lower than the calculated 1-hour LC_{01} value of 58.9 mg/m³. Therefore, derivation of LBW starting from the 1-hour LC_{01} value of 58.9 mg/m³ does justice

to both calculated LC_{01} values.
The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Isocyanate vapours are irritating to the airways and can cause inflammation resulting in wheezing, gasping, severe distress, even loss of consciousness and fluid in the lungs. Nervous system symptoms that may occur include headache, sleep disturbance, euphoria, incoordination, anxiety, depression and paranoia.

Respiratory sensitization may result in allergic asthma ; from coughing and minor breathing difficulties to bronchitis with wheezing, gasping.

The available data indicate that methacryloyloxyethyl isocyanate is not toxic for reproduction (fertility) after inhalation. There is however no information on the developmental toxicity via the inhalation route in the available literature for this chemical.

No harmonized H-sentences for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

Derivation of the carcinogenic risk potency (CRP):

No carcinogenic risk potency (**CRP**) was derived

Odour and derivation of the LOA value

Odour: Peppery

No LOA was derived due to lack of reliable data.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*[52]

VRW level **NR**	*AEGL-1* -	*ERPG-1* NR		*IDLH:* -
AGW level **2.0**	*AEGL-2* -	*ERPG-2* 0.63		
LBW level **5.9**	*AEGL-3* -	*ERPG-3* 6.34		

[52] Note that the ERPG values as presented here (in mg/m³) are derived using the conversion factors of the ERPG.

Stofducument deel A

CAS-nr: 78-79-5 **Isopreen** $CH_2=C(CH_3)-CH=CH_2$ **VN-nr: 1218**
GEVI: 339

Synoniemen 2-methyl-1,3-butadieen (Engels: isoprene) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	53	53	53	53	53	53
Alarmeringsgrenswaarden	AGW (mg/m³)	5600*	3900*	3100*	2400	1900	1300
Levensbedreigende waarden	LBW (mg/m³)	11000*	7400*	5900*	4700*	3700*	1900

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,353 ppm; 1 ppm = 2,83 mg/m³

Explosiegrens: 1,0 vol% ≈ 28.000 mg/m³
* berekende interventiewaarde hoger dan 10% LEL

Geur: penetrant, scherp
LOA: 2,14 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze zeer vluchtige vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,8

Molecuulmassa:	68,1 g/mol
Zuurgraad:	-
LogKow:	2,4
Wateroplosbaarheid:	0,064 g/100 ml (zeer slecht)
Verzadigde dampdruk:	ca 600 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: 8,5 mg/m³
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: hoesten

VRW → AGW: irritatie ogen, huid en luchtwegen, keelpijn, hoesten

AGW → LBW: sufheid, bewustzijnsdaling

Boven LBW: coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Isopreen werkt irriterend op de ogen, luchtwegen en de huid.
- De stof veroorzaakt effecten op het CZS, met als gevolg bewustzijnsdaling.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid

Oogcontact: roodheid en pijn

Carcinogeniteit

IARC classificatie: groep 2B
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust en arts raadplegen.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en onmiddellijk arts raadplegen.

Specifieke behandeling en materialen*: geen*.

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 78-79-5 **Isoprene** $CH_2=C(CH_3)-CH=CH_2$ **UN-nr: 1218**

Basis for the Dutch Intervention Values

VRW: Based on information as described in ERPG-document, different values are derived, other time-points added

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017 | ERPG 2006

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	53	53	53	53	53	53	Irritation of upper respiratory tract in humans
AGW	5600*	3900*	3100*	2400	1900	1300	Slight lung congestion in rats
LBW	11000 *	7400*	5900*	4700*	3700*	1900	Lethality in rats

* value higher than 10% of LEL

Derivation of the Dutch Intervention Values

VRW: VRW levels were based on results of a human volunteer study in which 10 subjects were exposed to isoprene using 6 concentrations ranging from 5 to 160 mg/m³. Information on the exposure duration or the individual exposure concentrations was not clear. Slight irritation of the mucosa of the nose, larynx or pharynx was perceived at 160 mg/m³. An exposure of 160 mg/m³ was selected as point of departure for the VRW-levels. As the observed effects were minimal, no additional factor was applied to derive a no-effect-level. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was not applied as respiratory irritation is considered to be concentration-dependent rather than concentration x time-dependent.

AGW: AGW levels were based on results of a subacute rat inhalation study with isoprene. Two male and two female rats exposed to isoprene for 6 hours/day for 15 days at 1670 ppm (4726 mg/m³) had no toxic signs and the necropsy was normal, while another group of two male and two female rats exposed for 6 hours/day for 6 days at 6000 ppm (16980 mg/m³) had lungs that were slightly congested. It is noted that the description of the results of this study were very limited. Results of a second subacute inhalation study (well-described) showed no (pulmonary) effects at 7000 ppm (19810 mg/m³) upon exposure of 6h/d, 5d/week for two weeks. In the absence of suitable single exposure experiments, the data of these two subacute studies were used for derivation of the AGW. The exposure of 6 hours to 16980 mg/m³ was selected as point of departure for deriving AGW levels.
The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$ with the default n = 1 and n= 3, to extrapolate to longer and shorter durations, respectively.

LBW: LBW values were based on results from an acute rat lethality study. The reported LC_{16}, LC_{50} and LC_{84}-values for rats after 4 hours exposure were 92,000, 180,000 and 381,000 mg/m³. Because this study reported only these LC_{16}, LC_{50}, and the LC_{84} values obtained by probit analysis and not the individual experimental data, benchmark dose-response modeling is not possible. However, the LC_{01} can be calculated because the mean is known and the standard deviation of the underlying lognormal distribution can be derived from these data. A 4-hour LC_{01} of 37183 mg/m³ for rats was calculated. In the same study LC_{16}, LC_{50} and LC_{84}-values were established for 2-hour exposure to mice as well. These values were 117,000, 157,000, 212,000 mg/m³, respectively, leading to a calculated 2-hour LC_{01} of 78914 mg/m³ for mice. This value is supportive to the 4-hour LC_{01} of 37183 mg/m³ for rats. The rat LC_{01} value was chosen as point of departure for derivation of LBW values, as it resulted in the lowest LBW-values. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the

equation $C^n \times t = k$ with the default n = 1 and n= 3, to extrapolate to longer and shorter durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Isoprene causes irritation of the eyes and respiratory tract. The substance may cause effects on the central nervous system, resulting in lower consciousness.

In a mouse developmental toxicity study, a concentration-related increase in the percentage of fetuses per litter with supernumerary ribs was noted at all dose levels, in presence of maternal toxicity (reduced bw). No such effects were observed in a rat developmental toxicity study.

H341: Suspected of causing genetic defects, H350: May cause cancer

Carcinogenicity and derivation of the CRP value

IARC classification: group 2B (possibly carcinogenic to humans)

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: pungent

Odour threshold: 0.136 mg/m^3 [Nagata 2003]

LOA = 11.8 * OT * 1.33 = 2.14 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is below the VRW

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [53]

VRW level **53**	*AEGL-1* -	*ERPG-1* 14		*IDLH:* -
AGW level **3100**	*AEGL-2* -	*ERPG-2* 2790		
LBW level **5900**	*AEGL-3* -	*ERPG-3* 11160		

[53] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 108-23-6 **Isopropylchloorformiaat** $(CH_3)_2CH\text{-}O\text{-}COCl$ **VN-nr: 2407**

GEVI: geen

Synoniemen: chloormierenzuur isopropylester, isopropylchloorcarbonaat, isopropylchloormethanoaat (Engels: Isopropyl chloroformate)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	21	14	11	9,1	7,2	3,6
Levensbedreigende waarden	LBW (mg/m³)	62	43	34	27	22	11

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,196 ppm; 1 ppm = 5,10 mg/m³

Explosiegrens: LEL = 3,2 vol% ≈ 163.000 mg/m³

Geur: scherp, penetrant

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot lichtgele vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,1

Molecuulmassa:	122,6 g/mol
Zuurgraad:	Geen data
LogKow:	1,0
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	31 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij blootstelling aan damp

*Onder **AGW***: irritatie van de ogen en luchtwegen

AGW → LBW: ernstige irritatie van de ogen en luchtwegen, tranenvloed, keelpijn, hoesten, speekselvloed, druk op de borst, piepende ademhaling, benauwdheid, longoedeem

Boven LBW: ademnood, sterfte

LET OP: de afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij kortdurende blootstelling aan damp

- Isopropylchloorformiaat werkt bijtend op de ogen en luchtwegen.
- Isopropylchloorformiaat kan longoedeem veroorzaken, waarbij de verschijnselen pas na enkele uren kunnen optreden en versterkt kunnen worden door lichamelijke inspanning.
- Isopropylchloorformiaat ontleedt in aanwezigheid van water of vochtige lucht zeer heftig tot chloorwaterstof, CO_2, isopropanol.

Klachten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, brandwonden

Oogcontact: bijtend, tranenvloed, roodheid en pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen, zo nodig arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen:.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 108-23-6 **Isopropyl chloroformate** **$(CH_3)_2$ CH-O-COCl** **UN-nr: 2407**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: Same rationale as for AEGL (one-third of LBW), 2h value added

LBW: Different point of departure than AEGL, 2h value added

Date: November 2015	AEGL document: Interim, 2008

Proposal for the Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Insufficient data
AGW	21	14	11	9.1	7.2	3.6	3-fold reduction of LBW values
LBW	62	43	34	27	22	11	Analogy with methyl chloroformate; Estimated lethality threshold in the rat

Derivation of the Dutch Intervention Values

VRW: VRW values for isopropyl chloroformate are not recommended due to insufficient data. Absence of VRW values does not imply that exposure below the AGW value is without adverse effects.

AGW: No acute inhalation data consistent with the definition of AGW with both exposure concentration and duration parameters were available. Therefore, the AGW values for isopropyl chloroformate are based upon a 3-fold reduction of the LBW values; this is considered an estimate of a threshold for irreversible effects.

Calculation of the AGW values by reducing the LBW values 3 fold is supported by an animal study in which rats were exposed to 0, 25, 50, 100 ppm (0, 127, 255, 510 mg/m^3) isopropyl chloroformiate for 6 hours/days for 5 days. Enlarged bronchial lymph nodes were observed at necropsy in several animals in all treatment groups. Focal alveolar edema and bronchiolitis were observed in several mid concentration and all high-concentration animals. Peribronchiolar mononuclear cell infiltrate was observed in low- and mid-concentration animals and is assumed to have preceded the bronchiolitis observed in the high-concentration animals. Animals from all three treatment groups exhibited focal pulmonary emphysema.

LBW: In contrast to AEGL, LBW values for isopropyl chloroformate are based on data of methyl chloroformate based on ppm-analogy (due to the limited dataset for isopropyl chloroformate).

The LBW of methylchloroformate was based on a study of 5 rats/sex/group exposed to 35, 45, 57, 73 ppm methyl chloroformate for 4 hours. The calculated 4-h $BMCL_{05}$ value in rats (42.4 ppm) was used as the point of departure. This concentration is considered a threshold for lethality and is supported by the fact that no deaths were observed in rats exposed to 45 ppm (177 mg/m^3) for 4 hours. The 4-h $BMCL_{05}$ value of 42.4 ppm methyl chloroformate was used on a ppm-basis as point of departure for isopropyl chloroformate (42.4 ppm, corresponding to 216 mg isopropyl chloroformate/m^3). The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n \times t = k$, with default values of n=1 and n=3 when extrapolating to longer and shorter exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Chloroformates hydrolyze in water or moist air to produce the parent hydroxy compound, hydrogen chloride, carbon dioxide, and a carbonate. They are direct-acting contact irritants, and are corrosive to the eyes, skin, gastrointestinal and respiratory tracts. Inhalation may result in coughing, labored breathing, sore throat, unconsciousness, convulsions, and death. Lung edema frequently occurs, and symptoms of this may not manifest for several hours after exposure and may be aggravated by physical exertion. Ingestion may result in a burning sensation of the digestive tract, nausea, vomiting, and abdominal pain.

No data concerning developmental/reproductive toxicity of isopropyl chloroformate were found.

Carcinogenicity and derivation of the CRP value
IARC classification: not classified No carcinogenic risk potency (CRP) was derived. No data concerning carcinogenicity of isopropyl chloroformate were found.

Odour and derivation of the LOA value
Odour: Pungent No LOA was derived due to lack of information.

Other standards and guidelines (1h values in mg/m3, unless otherwise indicated)				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* ID		*IDLH:* not derived
AGW level **11**	*AEGL-2* 17	*ERPG-2* 25		
LBW level **34**	*AEGL-3* 51	*ERPG-3* 100		

ID Insufficient data

Stofdocument deel A

CAS-nr: 10034-85-2 **Joodwaterstof** **H-I** **VN-nr: 2197**

GEVI: 80

Synoniemen: waterstofjodide (Eng.: Hydrogen iodide) ***Status:*** B-stof

Interventiewaarden		10 min.	30	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	5,3	5,3	5,3	5,3	5,3	5,3
Alarmeringsgrenswaarden	AGW (mg/m³)	720	350	220	140	85	85
Levensbedreigende waarden	LBW (mg/m³)	2200	1000	650	410	250	250

Datum samenstelling: November 2015

Conversiefactor: 1 mg/m³ = 0,188 ppm; 1 ppm = 5,32 mg/m³

Explosiegrens: niet afgeleid

Geur: scherpe doordringende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas

Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 4,6

Molecuulmassa:	127,9 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	234 g/100 ml (zeer goed)
Verzadigde dampdruk:	7600 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling:

Onder VRW:	mogelijk lichte oog- en luchtwegirritatie
VRW → AGW:	oog- en luchtwegirritatie, tranenvloed, hoesten, lichte benauwdheid
AGW → LBW:	ernstige oog- en luchtwegirritatie, pijn op de borst, benauwdheid, longontsteking, longoedeem
Boven LBW:	ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling:

- Empirische gegevens voor blootstelling aan joodwaterstof zijn afwezig. Op basis van verschillende gegevens kan aangenomen worden dat joodwaterstof minder toxisch is vergeleken met andere waterstofhalogenides. Vergeleken met de andere halides is joodwaterstof het beste oplosbaar in water en wordt beter afgevangen in de hogere luchtwegen (neus) dan de andere waterstofhalogenides.
- Inhalatie van joodwaterstof kan mogelijk een type I inhalatie intoxicatie veroorzaken.
- Joodwaterstof veroorzaakt mogelijk irritatie van de slijmvliezen van ogen en luchtwegen.
- Joodwaterstof kan mogelijk bij inhalatie longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, pijn, ernstige brandwonden

Oogcontact: bijtend, roodheid, pijn en slecht zien.

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen:	frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
ogen:	minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid:	n.v.t. (gas), maar in geval van *bevriezingswonden*: aan de huid vastgevroren kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en arts raadplegen.
ogen:	n.v.t. (gas), maar in geval van *bevriezingswonden*: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen. Blijven spoelen tijdens vervoer.
inslikken:	n.v.t. (gas)

Ontsmetting bij inademing

Inademing van jodiumwaterstof kan tevens leiden tot larynx- en glottisoedeem, met risico op verstikking (asfyxie) door zwellingen in de keel. Intubatie (borgen van vrije luchtwegen), eventueel gevolgd door beademing moeten in ernstige gevallen z.s.m. worden uitgevoerd (door specialisten). Vandaar de noodzaak om direct spoedeisende medische hulp in te roepen.

Specifieke behandeling en materialen: geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 10034-85-2 **Hydrogen iodide** **H-I** **UN-nr: 2197**

Basis for the Dutch Intervention Values

VRW: Different point of departure as for AEGL, 2-hr value added

AGW: Analogy with HBr, but different point of departure as for AEGL HI values (interim 2007)

LBW: Analogy with HBr: Same point of departure as for AEGL values but using different value for *n*, 2h value added and 8h value set equal to 4h value

Date: November 2015 | AEGL document: Interim, 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	5.3	5.3	5.3	5.3	5.3	5.3	Slight irritation (nose) in humans (analogy with HBr)
AGW	720	350	220	140	85	85	One third of LBW values (analogy with HBr)
LBW	2200	1000	650	410	250	250	Lethality animals (analogy with HBr)

Derivation of the Dutch Intervention Values

VRW: No empirical data were available for HI. In the absence of data, the HI values were set equal to the HBr values in ppm. HI is predicted to be less toxic than the other hydrogen halides. Being the most water soluble hydrogen halide, it is better scrubbed in the upper nasal passages than the other hydrogen halides. For highly scrubbed chemicals, higher concentrations are necessary to reach the lungs. Thus setting the HI values equal to the HBr values, with support from the entire data base of hydrogen halides is appropriate. The resulting VRW values for HBr were adjusted to the respective mg/m³ values of HI.

Derivation of VRW values for HBr:

For the derivation of the VRW values the threshold for nose irritation in humans inhaling 3 ppm HBr (10 mg/m³) for several minutes was selected as point of departure. This concentration was considered a NOAEL for notable discomfort. An uncertainty factor for intraspecies differences of 3 was considered suitable, because the threshold for sensory irritation is not expected to vary greatly among individuals and the effect of slight (nose) irritation is below the definition of the VRW. Because adaptation to slight irritation occurs, the resulting 1 ppm (3.37 mg/m³) concentration was used for all exposure durations. This value was also considered to be protective to asthmatics, because at low concentrations HBr is scrubbed well in the upper nasal passage. The 1 ppm concentration is supported by the VRW values for other hydrogen halides of 1.0 ppm and 1.8 ppm for HF and HCl, respectively.

AGW: No empirical data were available for HI. In the absence of data, the HI values were set equal to the HBr values in ppm. HI is predicted to be less toxic than the other hydrogen halides. Being the most water soluble hydrogen halide, it is better scrubbed in the upper nasal passages than the other hydrogen halides. For highly scrubbed chemicals, higher concentrations are necessary to reach the lungs. Thus setting the HI values equal to the HBr values, with support from the entire data base of hydrogen halides is appropriate. The resulting AGW values for HBr were adjusted to the respective mg/m³ values of HI.

Derivation of the AGW values for HBr:

The AGW values for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data. The only study of HBr that addressed effects that meet the definition of an AGW, severe nasal lesions, was a study on hydrogen halides by Stavert et al. (1991). Nevertheless, this study was not considered a suitable basis for derivation of AGW values because 8% of the animals died after exposure to HBr at 1300 ppm (4375 mg/m³), only one concentration was tested and the number of animals tested was not specified.

LBW: No empirical data were available for HI. In the absence of data, the HI values were set equal to the

HBr values in ppm. HI is predicted to be less toxic than the other hydrogen halides. Being the most water soluble hydrogen halide, it is better scrubbed in the upper nasal passages than the other hydrogen halides. For highly scrubbed chemicals, higher concentrations are necessary to reach the lungs. Thus setting the HI values equal to the HBr values, with support from the entire data base of hydrogen halides is appropriate. The resulting LBW values for HBr were adjusted to the respective mg/m^3 values of HI.

Derivation of the LBW values for HBr:

The basis for the LBW values was the 1-hour $BMCL_{05}$ of 1239 ppm (4170 mg/m^3) and the BMC_{01} of 1456 ppm (4900 mg/m^3) for HBr in rats. The 1-hour $BMCL_{05}$ of 1239 ppm (4170 mg/m^3) was chosen as the point of departure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. In contrast to the AEGL, the basis for time scaling, using the equation $C^n \times t = k$, was derived from data from the more robuste dataset of the toxicological comparable chemical, HCl, providing an n-value of 1.48 to scale to shorter and longer time points. To maintain consistency with other hydrogen halogenides, the 8 hour value was set equal to the 4 hour value, as performed for the most potent hydrogen halogenide HF.

Additional toxicological information (including relevant results of a general literature search, if any)

Information on the toxicological mechanisms, dose response curves, and/or other aspects are entirely based on the HBr documentation. Although the data base for HBr is also sparse, additional data on the toxicity of HBr relative to those of hydrogen fluoride (HF) and hydrogen chloride (HCl) were available for comparison purposes. The databases for HCl and HF are robust. For the endpoint of lethality, the relative toxicities to the rat and mouse are in the order of HF>HBr>HCl. When considering sublethal concentrations the severity and extent of the lesions to the upper respiratory tract were in the order HF>HCl>HBr, although the severity and extent of the lesions were very similar among the three chemicals. The data also showed that all three chemicals are well scrubbed in the upper respiratory passages. Individuals with asthma may respond to exposure to respiratory irritants such as HBr and HI with increased bronchial responsiveness, but no information on the relative susceptibility to healthy individuals was located. Stress and physical activity may cause greater deposition and pulmonary irritation than when an individual is at rest.

No information regarding reproductive and/or developmental toxicity located for either HI or HBr.

Although hydrogen iodide is (strong) irritating agent, no risk sentences are yet allocated to the substance. The absence of harmonized H-statements is therefore no indication for the toxicity of HI. For comparison reasons the H-statements for HBr are summarized: H314: Causes severe skin burns and eye damage.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

No information on genotoxicity and chronic toxicity/-carcinogenicity in animals was located for either HI or HBr.

Odour and derivation of the LOA value

HI appears to have a sharp penetrating odour. However, no information on threshold levels is available.

No LOA was derived due to lack of reliable data.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **5.3**	*AEGL-1* *5.3*	*ERPG-1* *No data*		*IDLH: no data*
AGW level **220**	*AEGL-2* *120*	*ERPG-2* *No data*		
LBW level **650**	*AEGL-3* *640*	*ERPG-3* *No data*		

Stofdocument deel A

CAS-nr: 20770-41-6 **Kaliumfosfide** K_3P **VN-nr: 2012**

GEVI: geen

Synoniemen: trikaliumfosfide (Engels: potassium phosphide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	74	25	12	6,2	3,1	1,5
Levensbedreigende waarden	LBW (mg/m³)	130	44	22	11	5,6	2,8

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,162 ppm; 1 ppm = 6,169 mg/m³

Explosiegrens: geen data
Kans op explosie door reactie met water of zuren.

Geur: typerende geur (geur als bij fosfine)
LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: geen data
Brand: Niet brandbaar. Echter, bij contact met vocht kans op brand en explosie.

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa: 148,3 g/mol

Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: reactie
Verzadigde dampdruk: geen data

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling
(gebaseerd op vrijkomen fosfine)

*Onder **AGW***: irritatie aan ogen, huid, neus en luchtwegen, hoofdpijn, misselijkheid, braken, zwakte, paresthesie, duizeligheid, tremor

AGW → LBW: benauwdheid, longoedeem, bewustzijnsdaling, hartritmestoornissen, nier- en leverfunctiestoornissen

Boven LBW: convulsies, cardiovasculaire collaps, myocardinfarct, ademnood, coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Kaliumfosfide kan bij contact met vocht uit de lucht of luchtwegen omgezet worden in fosfine. De toxiciteit van kaliumfosfide wordt bepaald door de vorming van fosfine.
- Fosfine verstoort door effecten op de celademhaling de zuurstofopname en energievoorziening van de cel.
- Fosfine werkt irriterend op de ogen, huid en luchtwegen.
- Blootstelling aan kaliumfosfide kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Kinderen zijn mogelijk gevoeliger voor toxiciteit door fosfine.

Effecten bij blootstelling aan vloeistof
Huidcontact: roodheid
Oogcontact: roodheid, pijn, slecht zien

Carcinogeniteit
IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
ogen: spoelen met water (evt. contactlenzen verwijderen).

Ontsmetting vaste stof
huid: verontreinigde kleding uittrekken, afspoelen met water.
ogen: spoelen met water (evt. contactlenzen verwijderen).
inslikken: mond laten spoelen (uitspugen!), rust, GEEN mond-op-mondbeademing, actieve kool (carbomix) toedienen, en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*
Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 20770-41-6 **Potassium phosphide** K_3P **UN-nr: 2012**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 16-10-2018 | AEGL document: Final 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	(insufficient data)
AGW	74	25	12	6.2	3.1	1.5	Irritation nasal mucosa rats (phosphine)
LBW	130	44	22	11	5.6	2.8	Lethality rats (phosphine)

Derivation of the Dutch Intervention Values

VRW: No data are available for potassium phosphide. As toxicity of potassium phosphide is due to phosphine, which is formed due to reaction of potassium phosphide with moisture, data on phosphine could be used to derive intervention values. However, no appropriate data were available for derivation of VRW values for phosphine. Therefore VRW values are not recommended. This does not imply that exposure below AGW is without adverse effects.

AGW: Since no appropriate data exist for potassium phosphide, AGW values for phosphine will be used (on ppm-basis) to derive AGW values for potassium phosphide. The use of phosphine as a surrogate for potassium phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because one mole of phosphine is produced for every mole of potassium phosphide, no molar adjustment factor was needed.

Derivation of AGW values for phosphine

The phosphine AGW values were based on red mucoid nasal discharge in rats exposed to 10 ppm (14 mg/m³) phosphine for 6 hours, corresponding to 61.7 mg/m³ potassium phosphide. Since this endpoint is less severe than effects defined by AGW, the resulting values should be protective. The default uncertainty factor of 3 was applied to account for interspecies variability. An uncertainty factor of 10 was applied to account for intraspecies variability since the human data suggest that children may be more sensitive than adults when exposed to presumably similar phosphine concentrations. For example, in two reports, exposed children died, but exposed adults survived. Time scaling was performed using the equation $C^n \times t = k$, and an n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine).

LBW: Since no appropriate data exist for potassium phosphide, LBW values for phosphine will be used (on ppm-basis) to derive LBW values for potassium phosphide. The use of phosphine as a surrogate for potassium phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because one mole of phosphine is produced for every mole of potassium phosphide, no molar adjustment factor was needed.

Derivation of LBW values for phosphine

The highest concentration yielding no deaths in rats (18 ppm = 25 mg/m³) for 6 hours was used as point of departure for the calculation of the LBW values, corresponding to 111 mg/m³ potassium phosphide. The default uncertainty factor of 3 for interspecies and an intraspecies factor of 10 were applied for reasons provided above. Time scaling was performed using the equation $C^n \times t = k$ and a chemical specific n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine). These values are considered protective since workers were repeatedly exposed for “brief” periods of time to phosphine concentrations up to 35 ppm (49 mg/m³) with no life-threatening effects and workers exposed to >50 ppm (>70 mg/m³) for 2-5 minutes experienced only odour.

Additional toxicological information (including relevant results of a general literature search, if any)

When potassium phosphide reacts with moisture, phosphine gas will be formed. Phosphine is considered to induce acute toxic effects following oral and inhalation exposure. Children are thought to be more vulnerable to phosphine exposure. Common clinical signs after exposure to phosphine are headache, vomiting, coughing, shortness of breath, paresthesia, weakness, tremors and jaundice. Pulmonary congestion, pleural effusion, and congestive heart failure may be observed upon post-mortem examination.

In vitro, phosphine reacts with cytochrome c and cytochrome c oxidase, thereby inhibiting mitochondrial oxygen uptake. In vitro studies have also shown that phosphine can react with the heme moiety of hemoglobin in the presence of oxygen. Cell death and loss of cell membrane integrity accounted for the increased liver enzymes, bronchiolytic effects, cloudy swelling of renal tubular epithelia, and hemorrhagic myocardial lesions.

No reproductive or developmental data were found.

No harmonised H sentences available.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not evaluated No carcinogenic risk potency (CRP) was derived. No data concerning carcinogenicity of potassium phosphide are available. Fumigation workers exposed long-term to phosphine have a higher incidence of both stable and less stable chromosomal aberrations. Molecular analysis of these lesions suggests that the breakpoints are near proto-oncogenes involved in non-Hodgkin's lymphoma, possibly contributing to the increased incidence of lymphomas in pesticide workers.	Odour: no information. Pure phosphine is odourless at concentrations up to 200 ppm. Technical-grade phosphine has a garlic-like odour (may be due to impurities). For phosphine, no LOA was derived due to lack of reliable data. Ruth (1986) reported an odour range of 0.028-3.6 mg/m^3 for phosphine.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [54]

VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH:* not derived
AGW level **12**	*AEGL-2* 12	*ERPG-2* -		
LBW level **22**	*AEGL-3* 22	*ERPG-3* -		

[54] Note that the AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL.

Stofdocument deel A

CAS-nr: 8008-20-6 **Kerosine** **C9-C16 koolwaterstoffen** **VN-nr: 1223** **GEVI: 30**

Synoniemen: kerosine, kookpuntenbenzine, lichtpetroleum (Engels: jet propellant fuels (JP-8)) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	120	120	120	120	120	120
Alarmeringsgrenswaarden	AGW (mg/m³)	450	310	250	250	250	250
Levensbedreigende waarden	LBW (mg/m³)	NA	NA	NA	NA	NA	NA

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,141 ppm; 1 ppm =7,07 mg/m³

Explosiegrens: LEL = 0,6 Vol% ≈ 42.500 mg/m³

Geur: sterke, karakteristieke geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot amber kleurige vloeistof
Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,01

Molecuulmassa: ≈ 170 g/mol
Zuurgraad: geen data
LogKow: 3,3 – 6
Wateroplosbaarheid: Niet
Verzadigde dampdruk: 3 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 200 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: lichte irritatie van ogen en luchtwegen

AGW → LBW: hoesten, oogirritatie, irritatie van de bovenste luchtwegen, hoofdpijn, duizeligheid, verwardheid, bewustzijnsdaling

Boven LBW: sterfte door inhalatie onwaarschijnlijk

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt ontvettend en irriterend op de ogen, de huid en de luchtwegen.
- De stof kan inwerken op het centrale zenuwstelsel met als gevolg hoofdpijn, duizeligheid, verwardheid en bewustzijnsdaling.
- Blootstelling kan tot bewusteloosheid leiden.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, pijn, irritatie en uitdroging. Wordt door de huid opgenomen

Oogcontact: roodheid, pijn

Carcinogeniteit

IARC classificatie: geen classificatie
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: Let op: aspiratiegevaar! Mond laten spoelen (uitspugen!), GEEN braken opwekken, en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 8008-20-6 **jet propellant fuels (JP-8)** **C9-C16 hydrocarbons** **UN-nr: 1223**

Basis for the Dutch Intervention Values

VRW: Different point of departure than AEGL, uncertainty factor added, 2h value added.

AGW: Different point of departure than AEGL, uncertainty factors added, 2h value added.

LBW: Not determined.

Date: November 2015 | AEGL Document: Final, 2011

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	120	120	120	120	120	120	Threshold for irritation in humans (extrapolated from mouse RD_{50} test)
AGW	450	310	250	250	250	250	Threshold for eye irritation in rats and mice
LBW	ND	ND	ND	ND	ND	ND	Not determined

Derivation of the Dutch Intervention Values

The proposed Dutch Intervention Values are based on a mixture of aliphatic and aromatic hydrocarbons, of which jet fuel 5 (JP-5) and jet fuel 8 (JP-8) are the primary fuels. Short term exposure values are extrapolated from a large database encompassing many jet fuels and a robust set of repeated exposure studies.

VRW: The VRW value is based on a study in mice. Exposure to JP-8 (vapour and aerosol) at 681, 1,090 1,837 and 3,565 mg/m^3 for 30 min resulted in a dose-dependent decrease of the respiratory rate with 22%, 38%, 46% and 50%, respectively. Based on these data, a RD_{50} level of 2,876 mg/m^3 was derived. In contrast to AEGL, the RD_{10} is considered to be a more appropriate point of departure (PoD) for the VRW than the RD_{50}. BMD analyses were performed on the original data to calculate a BMD of 355 mg/m3 for a 10% decrease in the respiratory rate (RD_{10}). Since stimulation of the N. trigeminus is considered to be conservative PoD for JP-8 an overall UF of 3 is considered to be sufficient. Because slight sensory irritation is believed to be a concentration effect independent of time, the derived VRW value was applied to all exposure durations.

AGW: In contrast to AEGL-2, the AGW value is based on a study in rats indicating that exposure to JP-5 (vapour and aerosol) at 2,500 mg/m3 for 1 hour resulted in undefined eye irritation in rats and eye irritation in mice which resolved after termination of exposure. Exposure at 5,000 mg/m3 for 1 hour resulted in ocular irritation (indicated by mild lacrimation, eye closure and pawing at the eye lids), lethargy and delayed righting reflex in rats. The value of 2.500 mg/m3 is considered relevant for the AGW-level and is used a point of departure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Timescaling to shorter duration was performed using the default value of n=3, as narcotic systemic effects need some time to develop. The 1-h value was set equal to the 2-, 4- and 8-hour values.

LBW: In a study it is reported that the highest vapor concentration that could be attained was 3,430 mg/m^3. It is not apparent that concentrations high enough to cause death can be attained. On the basis of the likelihood that lethal concentrations cannot be attained and sustained under ambient conditions, LBW values were not determined.

Additional toxicological information (including relevant results of a general literature search, if any)

Aliphatic and alicyclic hydrocarbons cause CNS depression (narcosis) and asphyxia by interactions with neuronal membranes and myelin interactions following acute exposures to high concentrations. Exposure to high concentrations can also result in excitement, loss of equilibrium, stupor and coma. Recovery from the CNS effects is usually rapid and complete.

No studies on developmental toxicity in humans were located. Studies in animals show that kerosene (meaning JP-5 and JP-8) is not considered to be a carcinogenic, genotoxic or reproductive or developmental toxicant.

H304: May be fatal if swallowed and enters airways

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived It is noted that some components in the mixture are recognized carcinogens: IARC has classified benzene as carcinogenic to humans (1).	Odour: Strong characteristic odour Odour Threshold: 0.58 mg/m^3 [ATSDR, 1998] No LOA was derived (due to lack of suitable data)

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **120**	*AEGL-1* 290	*ERPG-1* -		*IDLH: 4,500 (30 min)*
AGW level **250**	*AEGL-2* 1,100	*ERPG-2* -		
LBW level **ND**	*AEGL-3* ND	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 463-51-4 **Keteen** $H_2C=C=O$ **VN-nr: geen** **GEVI: geen**

Synoniemen: Carbomethaan, carbometheen, ethenon (Eng.: ketene) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	2,1	1,5	1,2	0,92	0,73	0,39
Levensbedreigende	LBW (mg/m³)	6,3	4,4	3,5	2,8	2,2	1,2
Datum vaststelling: November 2015			Conversiefactor: 1 mg/m³ = 0,57 ppm; 1 ppm = 1,75 mg/m³				

Explosiegrens: LEL = 5,5 Vol% ≈ 96.000 mg/m³

Geur: stekend

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,5

Molecuulmassa:	42,0 g/mol
Zuurgraad:	geen data
LogKow:	geen data
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	geen data

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 0,86 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling:

*Onder **AGW***: lichte irritatie van luchtwegen en ogen, hoesten, keelpijn
AGW → LBW: longschade, bemoeilijkte ademhaling
Boven LBW: long oedeem, ademnood, sterfte

LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling:

- Primaire effecten op de longen. Schade treedt diep in de longen op (alveolair gebied).
- Inhalatie veroorzaakt ook irritatie aan ogen, huid en luchtwegen.
- Vormt in contact met vocht (slijmvliezen) azijnzuur. Zeer steile dosis-respons relatie, waarbij de respons vertraagd kan optreden.
- Blootstelling aan keteen kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en verstrekt worden door lichamelijke inspanning.
- Wordt in dezelfde categorie van extreem toxische gassen geplaatst als fosgeen

Effecten bij blootstelling aan vloeistof:

Huidcontact: roodheid, pijn
Oogcontact: bijtend, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: (gas) minimaal 20 min. spoelen met veel water of douchen, arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: n.v.t. (gas).

***Specifieke behandeling en materialen**:* geen (100% zuurstof).

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr : 463-51-4 **Ketene** **$H_2C=C=O$** **UN-nr: none**

Basis for the Dutch Intervention Values

VRW: Not recommended.

AGW: Same rationale as for AEGL (one-third of LBW), 2h value added

LBW: Different point of departure as for AEGL, 2hr value added.

Date: November 2015 | AEGL document, final (2014)

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Insufficient data
AGW	2.1	1.5	1.2	0.92	0.73	0.39	One third of LBW
LBW	6.3	4.4	3.5	2.8	2.2	1.2	Threshold of animal lethality

Derivation of the Dutch Intervention Values

VRW: The VRW value was not derived due to a lack of adequate data. Therefore, VRW values were not recommended. It is noted that effects may occur below the AGW.

AGW: A study in mice reported no clear signs of toxicity at a 7 hr exposure to a concentration of 1 ppm (1.75 mg/m³) ketene or a 4.5 hr exposure to a concentration of 12 ppm (21 mg/m³) ketene. It is unclear whether the concentrations used in this study would result in latent lung damage after a single exposure. These data are therefore considered unsuitable for derivation of the AGW values. In absence of relevant data, the AGW values are estimated by dividing the LBW values by a factor 3. This reduction is considered an estimate of the threshold for irreversible effects. The concentration-response relationship that was found in the studies was steep, therefore a reduction by a factor 3 is considered to be appropriate.

LBW: The LBW is based on the lowest concentration at which acute lethality was seen, i.e. 12 ppm (21 mg/m³) (4.5 h/d): all mice survived the first 4.5-hour exposure period, while 3/7 mice died during the second 5.5 h on the subsequent day. Although the time of death during the second exposure is not given, these deaths are considered to be caused by the second subsequent exposure. Therefore, the 4.5 hour exposure to 12 ppm (21 mg/m³) is considered to provide a threshold for lethality and is used as point of departure for LBW. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n \times t = k$, with default values of n=1 and n=3 when extrapolating to longer and shorter exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Ketene has a high toxic potency with main effects on the lungs and CNS. Severe damage to the lungs (at the alveolar level) was observed at lethal concentrations. The CNS effects might be due to cerebral anoxia secondary to severe alveolar damage. Steep concentration-response curve and time-response relationships appeared to be present for ketene.

Effects and mode of action of ketene has similarities to phosgene. Delay in toxicity is observed with ketene, as toxicity of ketene occurs through acetylation of functional groups of proteins and enzymes (e.g. in the lungs).

Data on developmental and reproductive toxicity, genotoxicity and carcinogenicity are too limited to draw conclusions.

No harmonized H-statements for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: Sharp, pungent.

No LOA was derived due to lack of data.

Other standards and guidelines (1h values in mg/m³, unless otherwise indicated)

VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH:* 8.75 (30 min)
AGW level **1.2**	*AEGL-2* 0.11	*ERPG-2* -		
LBW level **3.5**	*AEGL-3* 0.33	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 16842-03-8 **Kobalthydrocarbonyl** $HCo(CO)_4$ **VN-nr: -** **GEVI: -**

Synoniemen: tetracarbonylhydrocobalt (Engels: cobalthydrocarbonyl) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	2,9	2,0	1,0	0,51	0,26	0,13
Levensbedreigende waarden	LBW (mg/m³)	7,4	5,1	2,6	1,3	0,64	0,32

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,140 ppm; 1 ppm = 7,16 mg/m³

Explosiegrens: geen data

Geur: geen data

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: lichtgeel gas

Brand: geen data

Relatieve dichtheid gas (lucht =1): 5.93

Molecuulmassa: 172,0 g/mol

Zuurgraad: Waterige oplossingen reageren sterk zuur

LogKow: geen data

Wateroplosbaarheid: 0,5 g/100 ml

Verzadigde dampdruk: geen data

Overige informatie

Publieke grenswaarde: 0,1 mg/m³ (als kobalt)

MAK: niet afgeleid

TLV-TWA: 0,1 mg/m³ (als kobalt)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: prikkeling, hoofdpijn, duizeligheid, misselijkheid, braken, irritatie ogen

AGW → LBW: branderig gevoel, kortademigheid

Boven LBW: ademnood, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Kobalt hydrocarbonyl veroorzaakt irritatie van de luchtwegen
- De stof is bij gewone temperatuur (18 °C) instabiel; aan de lucht dimeriseert de stof naar dikobalt octacarbonyl, wat vervolgens uiteenvalt in koolstofmonoxide en (metallisch of geïoniseerd) kobalt.
- De stof is sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact!

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid

Oogcontact: bijtend, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas).

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 16842-03-8 **Cobalthydrocarbonyl** **$HCo(CO)_4$** **UN-nr: -**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with ERPG

AGW: Different rationale than ERPG, other time-points added.

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added.

Date: 31-10-2017 | ERPG 2005

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	2.9	2.0	1.0	0.51	0.26	0.13	Gross lung damage in rats
LBW	7.4	5.1	2.6	1.3	0.64	0.32	Acute lethality in rats

Derivation of the Dutch Intervention Values

VRW: The VRW values were not derived for cobalt hydrocarbonyl. There are no exposure-response data in humans or animals consistent with VRW-level effects.

AGW: The AGW values were based on an acute inhalation study in rats. Nine groups of rats (n=5/group, males) were exposed for 30 minutes to cobalt hydrocarbonyl in concentrations varying from 7 to 236 mg/m^3 (measured as dust, expressed as cobalt). A control group was also included. Acute pulmonary irritation (as measured by pulmonary edema and gross lung damage) was assessed 24 h after single exposure. At a 30-min exposure of 7 and 26 mg/m^3 (expressed as cobalt), corresponding to 20.4 and 75.9 mg/m^3 cobalt hydrocarbonyl, 1/5 and 1/5 rats, respectively, showed pulmonary edema, and 1/5 and 2/5 rats, respectively, showed gross lung damage. The incidence of pulmonary edema was not different as compared to control animals (2/38), however, the incidence of gross lung damage (i.e. hemorrhage, edema, consolidation, congestion, pleuritis, bronchiectasis, emphysema or atelectasis) in the 75.9 mg/m^3 exposure group was higher than in control animals (5/31).
A 30-min exposure to 20.4 mg/m^3 (threshold for gross lung damage) was used as point of departure for deriving the AGW. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter durations, respectively.

LBW: The LBW values were based on an acute inhalation study in rats (the same study as used for AGW, though based on a different experiment). Ten groups of rats (n=5/group, males) were exposed for 30 minutes to cobalt hydrocarbonyl in concentrations varying from 7 to 408 mg/m^3 (measured as dust, expressed as cobalt). All of the deaths occurred during the exposure, or within 3 days post exposure. Doseresp was used to calculate LC_{50} and LC_{01} values. The 30-min LC_{50} and LC_{01}-values were 121 mg/m^3 and 17.5 mg/m^3 (expressed as cobalt), respectively, corresponding to 353 mg/m^3 and 51 mg/m^3, respectively, when expressed as cobalt hydrocarbonyl. The 30-min LC_{01} of 51 mg/m^3 cobalt hydrocarbonyl was used as point of departure. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter durations, respectively.
Two non-published studies in rats and mice supported these findings. In one study rats (n=10/group) were exposed for 30 min to 110 and 210 mg/m^3. No animals versus 7 animals died at the low and high dose group, respectively. In the second study rats and mice (n=5/group) were exposed for 15, 30 and 60 min to 82 mg/m^3. No rats died in these exposures, and no mice died in the 15- or 30-minute exposures. In mice 3/5 animals died in the 60 min exposure. Though, in one subchronic toxicity study with rats exposure to 9 mg/m^3 for 13 weeks, 5 days/week and 6 hours/day did not lead to death, all other data support the values as proposed. Furthermore, the data are in line with the values as derived for the structurally related compound nickel carbonyl.

Additional toxicological information (including relevant results of a general literature search, if any)

Cobalt hydrocarbonyl induces respiratory irritation and sensitization.

Gaseous cobalt hydrocarbonyl already reacts in the air at normal temperature, splitting off hydrogen to form dicobalt octacarbonyl. This is also unstable in air and decomposes to form cobalt and carbon monoxide.

There are no data on reproductive toxicity upon inhalation for cobalt hydrocarbonyl.

No harmonised H-sentences for human health.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived	Odour: no data No LOA was derived.

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)*** [55]

VRW level **NR**	*AEGL-1* -	*ERPG-1* NR		*IDLH:* 20 mg/m³ (for cobalt metal, dust and fume, expressed as Co) (30 minutes)
AGW level **1.0**	*AEGL-2* -	*ERPG-2* 0.9		
LBW level **2.6**	*AEGL-3* -	*ERPG-3* 3		

[55] Note that the ERPG values as presented here (in mg/m³) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 630-08-0 **Koolmonoxide** **C-O** **VN-nr: 1016**

GEVI: 263

Synoniemen: carbon monoxide (Engels: carbon monoxide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	490	180	97	59	39	32
Levensbedreigende waarden	LBW (mg/m³)	2.000	700	390	240	170	160

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,859 ppm; 1 ppm = 1,17 mg/m³

Explosiegrens: LEL=10,9 Vol% ≈ 127.000 mg/m³

Geur: reukloos

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas
Brand: zeer brandgevaarlijk, in combinatie met lucht explosief

Relatieve dichtheid gas (lucht = 1): 0,97

Molecuulmassa:	28,0 g/mol
Zuurgraad:	geen data
LogKow:	1,8
Wateroplosbaarheid:	niet
Verzadigde dampdruk:	35.000 mbar

Overige informatie

Publieke grenswaarde:
29 mg/m³
MAK: 35 mg/m³
TLV-TWA: 29 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: lichte hoofdpijn, benauwdheid (bij inspanning)

AGW → LBW: benauwdheid, hoofdpijn, misselijkheid, pijn op de borst, snelle hartslag, wazig zien, duizeligheid, verwardheid, spierzwakte, foetale letaliteit

Boven LBW: coma en sterfte

LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Koolmonoxide bindt reversibel aan hemoglobine waarbij HbCO gevormd wordt, leidend tot een verminderde bindingscapaciteit van hemoglobine voor zuurstof. Als gevolg hiervan neemt het zuurstoftransport in het bloed en de afgifte van zuurstof in de weefsels af. Hypoxie kan leiden tot lokale weefselschade. In organen met een hoge zuurstofbehoefte, zoals hart en hersenen, treden de eerste effecten op.
- De stof kan inwerken op het centrale zenuwstelsel met als gevolg (bandvormige) hoofdpijn, misselijkheid, verwardheid, maligne hartritmestoornissen en bewusteloosheid.
- Na een ernstige acute blootstelling kunnen ook vertraagde effecten optreden op het zenuwstelsel optreden, zoals psychose, parkinsonisme, paralyse en neuropathie. De effecten kunnen gepaard gaan met psychische effecten, zoals irritabiliteit, concentratieproblemen, schrijf- en leesproblemen en emotionele verarming.
- Gevoelige groepen zijn o.a. hart- en COPD patiënten, patiënten met een hersenaandoening, rokers, kinderen, en foetussen.

Effecten bij blootstelling aan vloeistof

Huidcontact: n.v.t.

Oogcontact: n.v.t.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht (bij voorkeur 100% zuurstof), rust, en direct spoedeisende medische hulp inzetten.
ogen: n.v.t. (gas).

Ontsmetting vloeistof n.v.t. (gas).
Specifieke behandeling en materialen*:* onmiddellijk zuurstof 100% toedienen, zo nodig via hyperbare zuurstoftherapie (daarvoor is opname in een ziekenhuis noodzakelijk).
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 630-08-0 **Carbon monoxide** **C-O** **UN-nr: 1016**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 06-10-2016 | AEGL document: Final, 2010

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	-
AGW	490	180	97	59	39	32	Cardiac effects in humans with coronary artery disease. (4% COHb)
LBW	2,000	700	390	240	170	160	Threshold for significant increased likelihood of fatality in humans. (40% COHb)

Derivation of the Dutch Intervention Values

VRW: VRW values are not recommended because susceptible persons may experience more serious effects (equivalent to AGW effects) at concentrations, which do not yet cause VRW effects in the general population. In addition, CO exposures encountered frequently in everyday life are at or above the concentration range, in which a VRW level would have to be set.

AGW: For the derivation of AGW values a level of 4% COHb was chosen based on studies in humans. At the level of 4% COHb patients with coronary artery disease may experience a reduced time until onset of angina (chest pain) during physical exertion. Patients with coronary artery disease must be considered the most susceptible group. Therefore, AGW values derived on effects in coronary artery disease patients are likely to protect other susceptible subpopulations: i.e., children, elderly people and fetuses. A mathematical model (CFK-model) was used to calculate external exposure concentrations resulting in a COHb of 4 % in a 70-kg man with a starting COHb of 0.75% due to endogenous CO production at the end of exposure periods of 10-minutes, 30-minutes, 1-hour, 4-hours and 8-hours. The exposure concentrations for the respective durations are 424 ppm (491 mg/m^3), 150 ppm (176 mg/m^3), 83 ppm (97 mg/m^3), 33 ppm (39 mg/m^3) and 27 ppm (32 mg/m^3). Interpolation of the data was used to derive the corresponding concentration for a 2-hour exposure, namely 50 ppm (59 mg/m^3). Since AGW values were based on experimental data on the most susceptible subpopulation (patients with coronary artery disease), they were considered protective also for other subpopulations and a total uncertainty factor of 1 was considered sufficient.

LBW: Based on a weight-of-evidence analysis of numerous lethal human cases and their COHb levels at their time of death, a lethality threshold of 40% COHb was derived. This level of 40 % COHb was used as the basis for LBW derivation. This point of departure is supported by studies in animals reporting minimum lethal COHb levels in rats and mice of about 50-70 %. Using a mathematical model (CFK-model), external exposure concentrations resulting in a COHb of 40% at the end of exposure periods of 10-minutes, 30-minutes, 1-hour, 4-hours and 8-hours. Various experimental studies in healthy human subjects support the 40% COHb-level. The default intraspecies uncertainty factor of 3 was considered sufficient to account for intraspecies differences. No interspecies uncertainty factor was applied, leading to a total uncertainty factor of 3.
The exposure concentrations for the respective durations are 1,707 ppm (1,997 mg/m^3), 603 ppm (706 mg/m^3), 333 ppm (390 mg/m^3), 146 ppm (171 mg/m^3) and 134 ppm (157 mg/m^3). Interpolation of the data was used to derive the corresponding concentration for a 2-hour exposure, namely 240 mg/m^3.

Additional toxicological information (including relevant results of a general literature search, if any)

Carbon monoxide binds to hemoglobin forming COHb and thereby renders the hemoglobin molecule less able to bind with oxygen. Due to this mechanism, the oxygen transport by the blood and the release of bound oxygen in the tissues are decreased. Tissue damage results from local hypoxia. Organs with a high

oxygen requirement, such as the heart and the brain, are especially sensitive for this effect. Patients with coronary artery disease, children and fetuses are more susceptible for lethal effects of CO than healthy adults.

Studies on developmental toxicity show that a concentration above 22% COHb could result in stillbirths and it was concluded that acute carbon monoxide poisoning during pregnancy may increase the risk of stillbirths.

H331: Toxic if inhaled, H360D: May damage the unborn child, H372: Causes damage to organs through prolonged or repeated exposure

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived.	Odour: odourless gas No LOA was derived.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **NR**	*AEGL-1* NR	*ERPG-1* 230		*IDLH:1,400 mg/m^3 (30 min)*
AGW level **97**	*AEGL-2* 97	*ERPG-2* 410		
LBW level **390**	*AEGL-3* 380	*ERPG-3* 580		

Stofdocument deel A

CAS-nr: 7439-97-6 **Kwik** **Hg** **VN-nr: 2809**
GEVI: 86

Synoniemen: kwikzilver, hydrargyrum (Engels: mercury) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	3,1	2,1	1,7	1,3	0,67	0,33
Levensbedreigende waarden	LBW (mg/m³)	16	11	8,9	4,5	2,2	2,2

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,120 ppm; 1 ppm = 8,34 mg/m³

Explosiegrens: geen data

Geur: (nagenoeg) reukloos

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: glanzende zilverkleurige zware vloeistof
Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,00

Molecuulmassa: 200,6 g/mol

Zuurgraad: Geen data
LogKow: Geen data
Wateroplosbaarheid: $5{,}6.10^{-6}$ g/100 ml (niet)
Verzadigde dampdruk: 0,002 mbar

Overige informatie

Publieke grenswaarde: 0,02 mg/m³
MAK: 0,02 mg/m³
TLV-TWA: 0,025 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: keelpijn en hoesten, rode, branderige ogen, ademnood.

AGW → LBW: pijn op de borst, koorts, buikpijn, misselijkheid, braken, kortademigheid, respiratoir falen, effect op de ongeboren vrucht.

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Kwik veroorzaakt irritatie van ogen en (bovenste) luchtwegen en bij hoge concentratie ernstige acute effecten op de longen zoals bronchitis, bronchiolitis en pneumonitis, welke kunnen uitmonden in longoedeem, pneumothorax, respiratoir falen en uiteindelijk de dood.
- Acute inhalatoire intoxicaties kunnen gepaard gaan met metaaldampkoorts (met o.a. koorts, malaisegevoel, spierpijn), gecombineerd met gastrointestinale klachten (dorst, misselijkheid en braken, diarree). Deze symptomen verdwijnen meestal binnen een week.
- De stof kan embryotoxiciteit veroorzaken
- (kleine) kinderen zijn extra gevoelig voor de toxische effecten van kwikdampen; de fatale gevallen betreffen meestal kinderen jonger dan 30 maanden.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid

Oogcontact: prikkeling, roodheid

Carcinogeniteit

IARC classificatie: 3
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, en onmiddellijk arts raadplegen.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en zo nodig arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan (oog)arts raadplegen.
inslikken: mond laten spoelen (uitspugen!) en zo nodig arts raadplegen.

Specifieke behandeling en materialen: Bij vergiftiging door deze stof is specifieke eerste hulp mogelijk. Als antidotum kan o.a. DMSA of DMPS worden toegediend.

Neem contact op met het NVIC (Tel: 030 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 7439-97-6 **Kwik** **Hg** **UN-nr: 2809**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with the AEGL.

AGW: AEGL value is adopted, 2h value added.

LBW: AEGL value is adopted, 2h value added.

Date: 16-10-2018 | AEGL, interim (2010)

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	(insufficient data)
AGW	3.1	2.1	1.7	1.3	0.67	0.33	Embryotoxicity in rats
LBW	16	11	8.9	4.5	2.2	2.2	Threshold of lethality in rats

Derivation of the Dutch Intervention Values

VRW: Mercury vapour is odourless and produces no irritation or early warning signs. Accidental human exposures show that even lethal exposures may be tolerated for several hours without apparent warning signs. Because there are no signs of notable discomfort or irritation at low concentrations and studies that document asymptomatic, non-sensory effects that meet the definition of VRW are not available, VRW values are not recommended.

AGW: The AGW is based on a teratogenicity study in which pregnant Long-Events rats were exposed to mercury vapour at concentrations of 0, 1, 2, 4, or 8 mg/m^3 for 2 hours/day for 10 days. A single 2-hour exposure to 4 mg/m^3 is used as point of departure. This is a NOAEL for developmental effects, including increased resorption, decreased litter size and decreased neonatal weight observed at the concentration of 8 mg/m^3. Further, no increase in miscarriages or stillbirths was observed in a study of pregnant women occupationally exposed to low concentrations of mercury (0.025-0.6 mg/m^3). It is assumed that exposure was up to 8 hours daily. Only the default uncertainty factor of 3 for intraspecies differences was applied. Additional application of an interspecies factor of 3 would result in a 4- and 8-hour AGW of 0.22 and 0.11 mg/m^3, respectively which are considered to be too low in comparison with the human data. Time scaling was performed using $C^n \times t = k$, with the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively.

LBW: The LBW is based on an acute lethality study in which rats were exposed to 26.7 mg/m^3 mercury vapour. A 1-hour exposure did not result in lethality. Extending the exposure period for another hour (at approximately the same concentration) resulted in 62.5% mortality. A 1-hour exposure to 26.7 mg/m^3 was selected as point of departure. A total uncertainty factor of 3 was applied based on a weight of evidence approach: a larger uncertainty factor would result in values incompatible with the overall data. Reversible behavioural changes were observed in male and female Wistar rats inhaling 17.2 mg/m^3 for 2 hours/day for 22 exposures. Values derived using a total uncertainty factor of 3 are further supported by the human non-lethal concentrations estimated in accidental exposures (up to 15 mg/m^3 for 0.75 hours) and measured in occupational settings (0.4-2.0 mg/m^3). Time scaling was performed using $C^n \times t = k$, with the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively. Because the 8-hour time-scaled value of 1.1 mg/m^3 appears low in comparison to accidental non-lethal exposures and is lower than some chronic occupational exposures, the 8-hour value was set equal to the 4-hour value.

Additional toxicological information (including relevant results of a general literature search, if any)

Mercury can bind to a variety of proteins, including those involved in producing cell injury or cell death. The central nervous system is probably the most sensitive target for elemental mercury vapour exposure. Within the kidney, the primary toxic effect is on the epithelial cells of the proximal tubules.

Unborn children, infants, and children are considered most susceptible. Mercury rapidly passes the blood-brain barrier and reaches the foetal brain.

Mercury is an embryotoxicant.

H330: Fatal if inhaled, H360D: May damage the unborn child, H372: Causes damage to organ through

prolonged and repeated exposure

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: 3 (not classifiable as to carcinogenicity to humans) No carcinogenic risk potency (CRP) was derived	Odour: odourless No LOA was derived because mercury is odourless

Other standards and guidelines *(1h values in mg/m³, unless otherwise indicated)* [56]				
VRW level NR	*AEGL-1* NR	*ERPG-1* -		*IDLH:* 10 mg/m³ (30 minutes)
AGW level 1.7	*AEGL-2* 1.7	*ERPG-2* 2		
LBW level 8.9	*AEGL-3* 8.9	*ERPG-3* 4.1		

[56] Note that the AEGL and ERPG values as presented here (in mg/m³) are derived using the conversion factors of the AEGL and ERPG, respectively.

Stofdocument deel A

CAS-nr: geen

Magnesiumaluminiumfosfide

Mg_3AlP_3

VN-nr: 1419

GEVI: geen

Synoniemen: trimagnesiumaluminiumtrifosfide (Engels: magnesium aluminum phosphide)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	32	11	5,3	2,7	1,3	0,67
Levensbedreigende waarden	LBW (mg/m³)	58	19	9,6	4,8	2,4	1,2

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,125 ppm; 1 ppm = 8,020 mg/m³

Explosiegrens: geen data
Kans op explosie door reactie met water of zuren.

Geur: typerende geur (geur als bij fosfine)

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: vaste stof

Brand: Niet brandbaar. Echter, bij contact met vocht kans op brand en explosie.

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa: 192,8 g/mol

Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: reactie
Verzadigde dampdruk: geen data

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

(gebaseerd op vrijkomen fosfine)

*Onder **AGW***: irritatie aan ogen, huid, neus en luchtwegen, hoofdpijn, misselijkheid, braken, zwakte, paresthesie, duizeligheid, tremor

AGW → LBW: benauwdheid, longoedeem, bewustzijnsdaling, hartritmestoornissen, nier- en leverfunctiestoornissen

Boven LBW: convulsies, cardiovasculaire collaps, myocardinfarct, ademnood, coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Magnesiumaluminiumfosfide kan bij contact met vocht uit de lucht of luchtwegen omgezet worden in fosfine. De toxiciteit van magnesiumaluminiumfosfide wordt bepaald door de vorming van fosfine.
- Fosfine verstoort door effecten op de celademhaling de zuurstofopname en energievoorziening van de cel.
- Fosfine werkt irriterend op de ogen, huid en luchtwegen.
- Blootstelling aan magnesiumaluminiumfosfide kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Kinderen zijn mogelijk gevoeliger voor toxiciteit door fosfine.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid
Oogcontact: roodheid, pijn

Carcinogeniteit

IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
ogen: spoelen met water (evt. contactlenzen verwijderen).

Ontsmetting vaste stof
huid: verontreinigde kleding uittrekken, afspoelen met water.
ogen: spoelen met water (evt. contactlenzen verwijderen).
inslikken: mond laten spoelen (uitspugen!), rust, GEEN mond-op-mondbeademing, actieve kool (carbomix) toedienen, en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*
Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: none **Magnesium aluminum phosphide** **Mg_3AlP_3** **UN-nr: 1419**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 16-10-2018 | AEGL document: Final 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	(insufficient data)
AGW	32	11	5.3	2.7	1.3	0.67	Irritation nasal mucosa rats (phosphine)
LBW	58	19	9.6	4.8	2.4	1.2	Lethality rats (phosphine)

Derivation of the Dutch Intervention Values

VRW: No data are available for magnesium aluminum phosphide. As toxicity of magnesium aluminum phosphide is due to phosphine, which is formed due to reaction of magnesium aluminum phosphide with moisture, data on phosphine could be used to derive intervention values. However, no appropriate data were available for derivation of VRW values for phosphine. Therefore VRW values are not recommended. This does not imply that exposure below AGW is without adverse effects.

AGW: Since no appropriate data exist for magnesium aluminum phosphide, AGW values for phosphine will be used (on ppm-basis) to derive AGW values for magnesium aluminum phosphide. The use of phosphine as a surrogate for magnesium aluminum phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because three moles of phosphine are produced for every mole of magnesium aluminum phosphide, a molar adjustment factor of 3 was applied to the magnesium aluminum phosphide AGW values.

Derivation of AGW values for phosphine

The phosphine AGW values were based on red mucoid nasal discharge in rats exposed to 10 ppm (14 mg/m³) phosphine for 6 hours, corresponding to 26.73 mg/m³ magnesium aluminum phosphide. Since this endpoint is less severe than effects defined by AGW, the resulting values should be protective.

The default uncertainty factor of 3 was applied to account for interspecies variability. An uncertainty factor of 10 was applied to account for intraspecies variability since the human data suggest that children may be more sensitive than adults when exposed to presumably similar phosphine concentrations. For example, in two reports, exposed children died, but exposed adults survived. Time scaling was performed using the equation $C^n \times t = k$, and an n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine).

LBW: Since no appropriate data exist for magnesium aluminum phosphide, LBW values for phosphine will be used (on ppm-basis) to derive LBW values for magnesium aluminum phosphide. The use of phosphine as a surrogate for magnesium aluminum phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because three moles of phosphine are produced for every mole of magnesium aluminum phosphide, a molar adjustment factor of 3 was applied to the calcium phosphide LBW values.

Derivation of LBW values for phosphine

The highest concentration yielding no deaths in rats (18 ppm = 25 mg/m³) for 6 hours was used as point of departure for the calculation of the LBW values, corresponding to 48.12 mg/m³ magnesium aluminum phosphide. The default uncertainty factor of 3 for interspecies and an intraspecies factor of 10 were applied for reasons provided above. Time scaling was performed using the equation $C^n \times t = k$ and a chemical specific n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine). These values are considered protective since workers were repeatedly exposed for “brief” periods of

time to phosphine concentrations up to 35 ppm (49 mg/m^3) with no life-threatening effects and workers exposed to >50 ppm (>70 mg/m^3) for 2-5 minutes experienced only odour.

Additional toxicological information (including relevant results of a general literature search, if any)

When magnesium aluminum phosphide reacts with moisture, phosphine gas will be formed. Phosphine is considered to induce acute toxic effects following oral and inhalation exposure. Children are thought to be more vulnerable to phosphine exposure. Common clinical signs after exposure to phosphine are headache, vomiting, coughing, shortness of breath, paresthesia, weakness, tremors and jaundice. Pulmonary congestion, pleural effusion, and congestive heart failure may be observed upon post-mortem examination.

In vitro, phosphine reacts with cytochrome c and cytochrome c oxidase, thereby inhibiting mitochondrial oxygen uptake. In vitro studies have also shown that phosphine can react with the heme moiety of hemoglobin in the presence of oxygen. Cell death and loss of cell membrane integrity accounted for the increased liver enzymes, bronchiolytic effects, cloudy swelling of renal tubular epithelia, and hemorrhagic myocardial lesions.

No reproductive or developmental data were found.

No harmonised H sentences available.

Carcinogenicity and derivation of the CRP value

IARC classification: not evaluated.

No carcinogenic risk potency (CRP) was derived.

No data concerning carcinogenicity of magnesium aluminium phosphide are available.

Fumigation workers exposed long-term to phosphine have a higher incidence of both stable and less stable chromosomal aberrations. Molecular analysis of these lesions suggests that the breakpoints are near proto-oncogenes involved in non-Hodgkin's lymphoma, possibly contributing to the increased incidence of lymphomas in pesticide workers.

Odour and derivation of the LOA value

Odour: no information.

Pure phosphine is odourless at concentrations up to 200 ppm. Technical-grade phosphine has a garlic-like odour (may be due to impurities).

For phosphine, no LOA was derived due to lack of reliable data. Ruth (1986) reported an odour range of 0.028-3.6 mg/m^3 for phosphine.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [57]

VRW level **NR**	*AEG-1* NR	*ERPG-1* -		*IDLH:* not derived
AGW level **5.3**	*AEGL-2* 5.3	*ERPG-2* -		
LBW level **9.6**	*AEGL-3* 9.5	*ERPG-3* -		

[57] Note that the AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL.

Stofdocument deel A

CAS-nr: 12057-74-8 **Magnesiumfosfide** Mg_3P_2 **VN-nr: 2011**

GEVI: geen

Synoniemen: trimagnesiumdifosfide (Engels: magnesium phosphide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	34	11	5,6	2,8	1,4	0,70
Levensbedreigende waarden	LBW (mg/m³)	61	20	10	5,1	2,5	1,3

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,178 ppm; 1 ppm = 5,611 mg/m³

Explosiegrens: geen data
Kans op explosie door reactie met water of zuren.

Geur: typerende geur (geur als bij fosfine)
LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: gele tot groene kristallen of grijsgroene pellets
Brand: Niet brandbaar. Echter, bij contact met vocht kans op brand en explosie.

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa: 134,9 g/mol
Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: reactie
Verzadigde dampdruk: geen data

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling
(gebaseerd op vrijkomen fosfine)

*Onder **AGW***: irritatie aan ogen, huid, neus en luchtwegen, hoofdpijn, misselijkheid, braken, zwakte, paresthesie, duizeligheid, tremor

AGW → LBW: benauwdheid, longoedeem, bewustzijnsdaling, hartritmestoornissen, nier- en leverfunctiestoornissen

Boven LBW: convulsies, cardiovasculaire collaps, myocardinfarct, ademnood, coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Magnesiumfosfide kan bij contact met vocht uit de lucht of luchtwegen omgezet worden in fosfine. De toxiciteit van magnesiumfosfide wordt bepaald door de vorming van fosfine.
- Fosfine verstoort door effecten op de celademhaling de zuurstofopname en energievoorziening van de cel.
- Fosfine werkt irriterend op de ogen, huid en luchtwegen.
- Blootstelling aan magnesiumfosfide kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Kinderen zijn mogelijk gevoeliger voor toxiciteit door fosfine.

Effecten bij blootstelling aan vloeistof
Huidcontact: roodheid
Oogcontact: roodheid

Carcinogeniteit
IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
ogen: spoelen met water (evt. contactlenzen verwijderen).

Ontsmetting vaste stof
huid: verontreinigde kleding uittrekken, afspoelen met water.
ogen: spoelen met water (evt. contactlenzen verwijderen).
inslikken: mond laten spoelen (uitspugen!), rust, GEEN mond-op-mondbeademing, actieve kool (carbomix) toedienen, en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*
Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 12057-74-8 **Magnesium phosphide** **Mg_3P_2** **UN-nr: 2011**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 16-10-2018 AEGL document: Final 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	(insufficient data)
AGW	34	11	5.6	2.8	1.4	0.70	Irritation nasal mucosa rats (phosphine)
LBW	61	20	10	5.1	2.5	1.3	Lethality rats (phosphine)

Derivation of the Dutch Intervention Values

VRW: No data are available for magnesium phosphide. As toxicity of magnesium phosphide is due to phosphine, which is formed due to reaction of magnesium phosphide with moisture, data on phosphine could be used to derive intervention values. However, no appropriate data were available for derivation of VRW values for phosphine. Therefore VRW values are not recommended. This does not imply that exposure below AGW is without adverse effects.

AGW: Since no appropriate data exist for magnesium phosphide, AGW values for phosphine will be used (on ppm-basis) to derive AGW values for magnesium phosphide. The use of phosphine as a surrogate for magnesium phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because two moles of phosphine are produced for every mole of magnesium phosphide, a molar adjustment factor of 2 was applied to the magnesium phosphide AGW values.

Derivation of AGW values for phosphine

The phosphine AGW values were based on red mucoid nasal discharge in rats exposed to 10 ppm (14 mg/m³) phosphine for 6 hours, corresponding to 28.1 mg/m³ magnesium phosphide. Since this endpoint is less severe than effects defined by AGW, the resulting values should be protective. The default uncertainty factor of 3 was applied to account for interspecies variability. An uncertainty factor of 10 was applied to account for intraspecies variability since the human data suggest that children may be more sensitive than adults when exposed to presumably similar phosphine concentrations. For example, in two reports, exposed children died, but exposed adults survived. Time scaling was performed using the equation $C^n \times t = k$, and an n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine).

LBW: Since no appropriate data exist for magnesium phosphide, LBW values for phosphine will be used (on ppm-basis) to derive LBW values for magnesium phosphide. The use of phosphine as a surrogate for magnesium phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because two moles of phosphine are produced for every mole of calcium phosphide, a molar adjustment factor of 2 was applied to the calcium phosphide LBW values.

Derivation of LBW values for phosphine

The highest concentration yielding no deaths in rats (18 ppm = 25 mg/m³) for 6 hours was used as point of departure for the calculation of the LBW values, corresponding to 50.5 mg/m³ magnesium phosphide. The default uncertainty factor of 3 for interspecies and an intraspecies factor of 10 were applied for reasons provided above. Time scaling was performed using the equation $C^n \times t = k$ and a chemical specific n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine). These values are considered protective since workers were repeatedly exposed for “brief” periods of time to phosphine concentrations up to 35 ppm (49 mg/m³) with no life-threatening effects and workers exposed to >50 ppm (>70 mg/m³) for 2-5 minutes experienced only odour.

Additional toxicological information (including relevant results of a general literature search, if any)

When magnesium phosphide reacts with moisture, phosphine gas will be formed. Phosphine is considered to induce acute toxic effects following oral and inhalation exposure. Children are thought to be more vulnerable to phosphine exposure. Common clinical signs after exposure to phosphine are headache, vomiting, coughing, shortness of breath, paresthesia, weakness, tremors and jaundice. Pulmonary congestion, pleural effusion, and congestive heart failure may be observed upon post-mortem examination.

In vitro, phosphine reacts with cytochrome c and cytochrome c oxidase, thereby inhibiting mitochondrial oxygen uptake. In vitro studies have also shown that phosphine can react with the heme moiety of hemoglobin in the presence of oxygen. Cell death and loss of cell membrane integrity accounted for the increased liver enzymes, bronchiolytic effects, cloudy swelling of renal tubular epithelia, and hemorrhagic myocardial lesions.

No reproductive or developmental data were found.

H300: Fatal if swallowed; H311:Toxic in contact with skin; H330: Fatal if inhaled

Carcinogenicity and derivation of the CRP value

IARC classification: not evaluated.

No carcinogenic risk potency (CRP) was derived.

No data concerning carcinogenicity of magnesium phosphide are available.

Fumigation workers exposed long-term to phosphine have a higher incidence of both stable and less stable chromosomal aberrations. Molecular analysis of these lesions suggests that the breakpoints are near proto-oncogenes involved in non-Hodgkin's lymphoma, possibly contributing to the increased incidence of lymphomas in pesticide workers.

Odour and derivation of the LOA value

Odour: no information.

Pure phosphine is odourless at concentrations up to 200 ppm. Technical-grade phosphine has a garlic-like odour (may be due to impurities).

For phosphine, no LOA was derived due to lack of reliable data. Ruth (1986) reported an odour range of 0.028-3.6 mg/m^3 for phosphine.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [58]

VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH:* not derived
AGW level **5.6**	*AEGL-2* 5.5	*ERPG-2* -		
LBW level **10**	*AEGL-3* 9.9	*ERPG-3* -		

[58] Note that the AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL.

Stofdocument deel A

CAS-nr: 108-31-6 **Maleinezuuranhydride** $C_4H_2O_3$ **VN-nr: 2215**

GEVI: 80

Synoniemen: 2,5-furaandion, dihydro-2,5-dioxofuraan, cis-1,2-etheendicarbonzuuranhydride (Engels: maleic anhydride)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	6,8	6,8	6,8	6,8	6,8	6,8
Alarmeringsgrenswaarden	AGW (mg/m³)	61	42	33	26	21	14
Levensbedreigende waarden	LBW (mg/m³)	180	130	100	79	63	41

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,245 ppm; 1 ppm = 4,081 mg/m³

Explosiegrens: 1,4 vol% ≈ 57.000 mg/m³

Geur: stekende geur

LOA: 28,9 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot witte hygroscopische kristallen, pellets, schilfers of brokken [59]

Brand: moeilijk brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,00

Molecuulmassa:	98,1 g/mol
Zuurgraad:	Geen informatie
LogKow:	Geen informatie
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	0,33 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: 0,41 mg/m³

TLV-TWA: 0,01 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: hoesten, niezen

VRW → AGW: irritatie van de ogen en luchtwegen, keelpijn, kortademigheid

*Boven **AGW***: ernstige irritatie van de ogen en luchtwegen, pijn achter het borstbeen, longoedeem, ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof is bijtend voor de ogen en de luchtwegen.
- Bij hoge concentraties treedt ontsteking van de oogleden, tranenvloed en zelfs permanente hoornvliesbeschadigingen.
- Inademing van grote hoeveelheden kan longoedeem veroorzaken, echter uitsluitend na verschijnselen van bijtende effecten op de slijmvliezen van ogen en/of hogere luchtwegen.
- De stof is sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact!

Effecten bij blootstelling aan vloeistof

Huidcontact: prikkeling, roodheid en pijn, bijtend, branderig gevoel, brandwonden

Oogcontact: roodheid en pijn, bijtend, ernstige brandwonden, verlies van gezichtsvermogen

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en onmiddellijk arts raadplegen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

[59] De stof kan ook verhandeld/getransporteerd worden in gesmolten vorm: dit betreft een kleurloze vloeistof met een temperatuur van 65°C

Stofdocument deel B

CAS-nr: 108-31-6 **Maleic anhydride** **$C_4H_2O_3$** **UN-nr: 2215**

Basis for the Dutch Intervention Values

VRW: Based on information as described in ERPG-document, different values are derived, other time-points added

AGW: Different rationale than ERPG, different values are derived, other time-points added

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017 ERPG 2005

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	6.8	6.8	6.8	6.8	6.8	6.8	Slight nasal and ocular irritation in human
AGW	61	42	33	26	21	14	One-third of LBW
LBW	180	130	100	79	63	41	Threshold for lethality rats

Derivation of the Dutch Intervention Values

Since maleic anhydride hydrolyzes to maleic acid, some of the experimental studies, especially those involving inhalation, may have had an acid component. It is not possible to separate the toxicities of the anhydride and the acid for inhalation exposures. However, an assumption may be made that exposures resulting from an emergency situation would also have the same relative composition of acid and anhydride.

VRW: The VRW was based on a human volunteer study in which the extent of subjective response to vapours of maleic anhydride were determined. Healthy volunteers were included and the exposure was performed in an inhalation chamber. The study consisted of three experimental runs. I: Six subjects were exposed for 5 minutes to varying concentrations (in a random order; individual concentrations not specified) to evaluate sensory response to the actual concentration in the inhalation chamber; II: Six subjects were exposed for one hour to 6 ppm (24.5 mg/m³) to evaluate the possible increase of sensory response as noted over a longer period of time; III: Five subjects were exposed for four hours to 5 ppm (20.4 mg/m³).
Five minute exposures to concentrations of 2.5 ppm (10.2 mg/m³) did not elicit sensory response to vapours of maleic anhydride. Responses at 5 ppm (20.4 mg/m³) were few and recorded as “slight”. Five minute exposures to concentrations of 20 ppm (81.6 mg/m³) were distinctly unpleasant, and exposure to 30 ppm (122 mg/m³) was intolerable to some subjects. No increase in irritation occurred on longer periods up to four hours of exposure to 20.4 mg/m³. No significant effect on respiratory function was observed.
The 4 hour exposure to 20.4 mg/m³ was used as point of departure for the VRW. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Timescaling was not applied. This approach was considered appropriate because mild irritant effects generally do not vary greatly over time, which was also confirmed in the above mentioned human volunteer study.

AGW: The only human data that could be considered for AGW with both concentration and duration parameters are from the same human volunteer study used as starting point for the VRW. However, using either the 20 or the 30 ppm value as PoD in combination with time scaling, would lead to AGW values conflicting with VRW values. Animal data showing signs comparable to the definition for the AGW are from the acute inhalation study in rats used for the LBW derivation (see rationale LBW). In this study no animals died at the highest concentration of 165 mg/m³, but all appeared sluggish during exposure and, at the highest concentration and many animals were observed to have squinted eyes and blood-encrusted noses. This was also the only concentration causing no mortality. The results were supported by a study with one fixed dose (4400 mg/m³) in various animals (see rationale LBW). Therefore, the AGW values for maleic acid anhydride will be based upon a 3-fold reduction in the LBW values.

LBW: The LBW values are based on an acute rat inhalation study. Rats (n=15/sex/conc) were exposed for six hours whole body to average vapour concentrations of 5 or 165 mg/m^3. Observations were continued for 24 hour post-exposure. No animals died at either concentration, but all appeared sluggish during exposure and, at the higher concentration, many animals were observed to have squinted eyes and blood-encrusted noses The 165 mg/m^3 for six hours was used as POD for deriving the LBW. As this was the highest concentration tested in the acute rat inhalation study and no deaths were observed, an overall uncertainty factor of 3 was considered sufficient. Time scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter time points, respectively.
The resulting LBW-values are supported by a second acute inhalation study in which 10 mice, 4 rats, 1 cat, 1 rabbit and 1 guinea pig were exposed to a single exposure of a static atmosphere of 4400 mg/m^3 for one hour. All animals experienced irritation of the eyes and respiratory airways. The guinea pig and 2 of 10 mice died due to bronchopneumonia. All rats and the rabbit and cat survived. Further, the LBW values are supported by the LBW values of similar anhydrides such as acetic anhydride.

Additional toxicological information (including relevant results of a general literature search, if any)

Maleic anhydride has an irritating effect on the eyes and respiratory tract.

Multigeneration and teratology studies with inhalation exposure do not point towards adverse effect on reproduction or development.

H302: Harmful if swallowed, H314: Causes severe skin burns and eye damage, H317: May cause an allergic skin reaction, H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: pungent odour

OT: 1.84-1.96 mg/m^3 [Ruth, 1986]
LOA = 11.8 * OT * 1.33 = 28.9 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is between the VRW and AGW.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated) [60]

VRW level **6.8**	*AEGL-1* -	*ERPG-1* 0.8		*IDLH:* 10 mg/m^3 (30 minutes)
AGW level **33**	*AEGL-2* -	*ERPG-2* 8.0		
LBW level **100**	*AEGL-3* -	*ERPG-3* 80.2		

[60] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 78-85-3 **Methacrylaldehyde** $CH_2=C(CH_3)-CHO$ **VN-nr: 2396** **GEVI: 336**

Synoniemen: 2-methyl-2-propenal, isobutenal, 2-methylacroleine (Engels: Methacrylaldehyde) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,55	0,55	0,55	0,55	0,55	0,55
Alarmeringsgrenswaarden	AGW (mg/m³)	15	10	8,1	6,4	5,1	3,4
Levensbedreigende waarden	LBW (mg/m³)	25	17	14	11	8,6	5,6

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,343 ppm; 1 ppm = 2,92 mg/m³

Explosiegrens: LEL = 2,6 vol% ≈ 76.000 mg/m³

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,2

Molecuulmassa:	70,1 g/mol
Zuurgraad:	geen data
LogKow:	1,0
Wateroplosbaarheid:	6 g/100 ml (matig)
Verzadigde dampdruk:	160 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: oog- en bovenste luchtwegirritatie, keelpijn, hoesten

AGW → LBW: oog- en bovenste luchtwegirritatie, benauwdheid

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Methacrylaldehyde werkt sterk irriterend op voornamelijk de bovenste luchtwegen en ogen.
- De effecten van methacrylaldehyde op de luchtwegen worden mogelijk veroorzaakt doordat de stof reageert met eiwitten in de slijmvliezen in de neus en keelholten.
- Sterfte door blootstelling aan methacrylaldehyde kan optreden als gevolg van zeer ernstige schade in de luchtwegen.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, brandwonden

Oogcontact: bijtend, roodheid en pijn, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, spoelen met veel water / kleding verwijderen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 78-85-3 **Methacrylaldehyde** **$CH_2=C(CH_3)-CHO$** **UN-nr: 2396**

Basis for the Dutch Intervention Values

VRW: AEGL value adopted, 2h value added

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 16-12-2010 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.55	0.55	0.55	0.55	0.55	0.55	Eye irritation in humans
AGW	15	10	8.1	6.4	5.1	3.4	Severe eye irritation in animals
LBW	25	17	14	11	8.6	5.6	Threshold lethality in animals

Derivation of the Dutch Intervention Values

VRW: The VRW values are based on a NOAEL of 0.19 ppm (0.55 mg/m³) for eye irritation in 10 healthy human subjects. The non-dominant eye was exposed to concentrations of 0, 0.09, 0.19, and 0.29 ppm (0, 0.26, 0.55, and 0.83 mg/m³) for 20 minutes in a series of 8 sessions. The blink frequency was recorded as a measure of irritation and the subjects reported the perceived intensity of any eye discomfort or irritation. The number of complaints about irritation and its perceived intensity were not different at any exposure level relative to the controlled exposure to clean air. Blink frequency was statistically higher during exposure to the highest concentration of 0.286 ppm (0.83 mg/m³) making it the LOAEL for this effect. The blink frequency NOAEL of 0.19 ppm (0.55 mg/m³) was considered the point of departure for all VRW values. No uncertainty factor was considered necessary because the blink frequency is not a perceived effect, but rather an objective measurement that is a precedent to perceived irritation. The VRW was held constant across all exposure durations because mild irritation is not expected to vary over time.

AGW: The AGW values are based on a rat study in which rats (10/group/sex) were exposed to methacrylaldehyde by inhalation at 1, 4.9, and 15.3 ppm (2.9, 14, and 45 mg/m³) 6 hr/day, 5 days/week for 13 weeks. The highest concentration of 15.3 ppm (45 mg/m³) for 6-hr exposure was used as the point of departure. Animals exposed to 4.9 or 15.3 ppm (14 or 45 mg/m³) were observed keeping their eyes half-closed during exposure and in animals exposed to 15.3 ppm (45 mg/m³) salivation was observed occasionally. The latter was considered indicative of substantial irritation. No single or shorter term exposure studies were available. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n \times t = k$, with default values of n=1 and n=3 when extrapolating to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-2 value that was set equal to the 30 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: The LBW values are based on the 90% mortality observed in rats after a single 6 hr exposure to 77 ppm (225 mg/m³). The other two concentrations tested for the full 2 weeks (5 hr/day; 6 days/week; 5 rats/sex/group) were 5 and 19 ppm (15 and 55 mg/m³). No mortality was observed at either of these concentrations. One-third of the 77 ppm lethal concentration (25.7 ppm; 75 mg/m³) was used to estimate the threshold for lethal effects of methacrylaldehyde. This was considered appropriate based on the reported LC_{50} values in other studies [4-hr LC_{50} values of 125 ppm and 195 ppm (365 and 569 mg/m³)]. Also in the same study no mortality was observed after exposure for 2 weeks to 5 or 19 ppm (15 or 55 mg/m³) 5 hr/day; 6 days/week; 5 rats/sex/group.
Cause of death was lesions in the respiratory tract which were comprised of necrosis of the olfactory and respiratory epithelium in the nasal turbinates, extensive epithelial ulceration of the larynx and trachea, and necrosis of the bronchiolar epithelium in the lung. Signs of respiratory irritation in rats were gasping and closed or half-closed eyes during inhalation exposure.
The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n \times t = k$, with default values of n=1 and n=3 when extrapolating to longer and shorter exposure durations, respectively. In contrast to the 10

minute AEGL-3 value that was set equal to the 30 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Methacrylaldehyde is highly irritating to mucous membranes, especially the upper respiratory tract and the eyes. Animals have been found gasping and closing their eyes following methacrylaldehyde exposure. Lesions in the upper respiratory tract indicate the irritation of the mucous membranes, probably resulting from reactivity toward sulfhydryl groups in receptor proteins in the nasal mucosa. Acrolein is the most toxic of the 2-alkenals (including methacrylaldehyde, crotonaldehyde, pentenal, and hexenal) and is also the most reactive toward sulfhydryl groups.

No information has been found concerning the reproductive or developmental toxicity of methacrylaldehyde.

No harmonized H-statements for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

No studies on the carcinogenicity of methacrylaldehyde were found.

Odour and derivation of the LOA value

Odour: Pungent odour

No LOA was derived due to a lack of data.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **0.55**	*AEGL-1* 0.58	*ERPG-1* not derived		*IDLH:* not derived
AGW level **8.1**	*AEGL-2* 8.2	*ERPG-2* not derived		
LBW level **14**	*AEGL-3* 14	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 126-98-7 **Methacrylonitril** **$CH_2=C(CH_3)C\equiv N$** **VN-nr: 3079** **GEVI: 336**

Synoniemen: MAN, 2-methyl-2-propeennitril, isopropeencyanide (Engels: methacrylonitrile) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	5,6	5,6	5,6	5,6	5,6	5,6
Alarmeringsgrenswaarden	AGW (mg/m³)	47	33	26	21	16	8,1
Levensbedreigende waarden	LBW (mg/m³)	140	98	78	62	49	25

Datum vaststelling: november 2015

Conversiefactor: 1 mg/m³ = 0,358 ppm; 1 ppm = 2,79 mg/m³

Explosiegrens: LEL = 1,7 vol% ≈ 47.000 mg/m³

Geur: Bittere amandelen

LOA: 310 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof.
Brand: zeer brandgevaarlijk.

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,1

Molecuulmassa:	67,1 g/mol
Zuurgraad:	Geen data
LogKow:	0,7
Wateroplosbaarheid:	2,6 g/100 ml (matig)
Verzadigde dampdruk:	86 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 2,8 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie
VRW → AGW: irritatie ogen en bovenste luchtwegen, hoofdpijn
AGW → LBW: hoesten, zwelling/verkramping strottenhoofd, benauwdheid, pijn op de borst, misselijkheid, braken, duizeligheid, krachtsverlies, verwardheid
Boven LBW: convulsies, ademnood, ademstilstand, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Methacrylonitril wordt omgezet tot o.a. cyanide.
- Cyanide blokkeert de ademhalingsketen in de cel. Hierdoor wordt de energiehuishouding verstoord en kan lactaatacidose ontstaan.
- Primaire systemische doelorganen zijn het centrale zenuwstelsel en het cardiovasculaire systeem.
- Methacrylonitril veroorzaakt irritatie van de bovenste luchtwegen.
- Verschijnselen kunnen vertraagd optreden.

Effecten bij blootstelling aan vloeistof

Huidcontact: prikkeling, roodheid, pijn, verwarring, misselijkheid, duizeligheid, sufheid, bewusteloosheid, toevallen.

Oogcontact: tranenvloed, roodheid en pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: 100% zuurstof, direct spoedeisende medische hulp inzetten, specifieke behandeling. GEEN mond-op-mondbeademing!

Ontsmetting vloeistof

huid: eerst: zie *Ontsmetting damp - algemeen*, verder: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep.

ogen: spoelen met water (evt. contactlenzen verwijderen).

inslikken: eerst: zie *Ontsmetting damp - algemeen*, verder: mond laten spoelen (uitspugen!), GEEN braken opwekken.

Specifieke behandeling en materialen: De benodigde middelen (specifieke antidota zoals 100% zuurstof en o.a. hydroxocobalamine, evt. gevolgd door natriumthiosulfaat) moeten met gebruiksaanwijzing ter plekke beschikbaar zijn.

Voor aanwijzingen over verdere behandeling zo nodig het NVIC (tel: +31 (0)30 –274 8888) bellen..

Stofdocument deel B

CAS-nr: 126-98-7 **Methacrylonitrile** **$CH_2=C(CH_3)C\equiv N$** **UN-nr: 3079**

Basis for the Dutch Intervention Values

VRW: Different rationale than AEGL (NR for all time points), values derived for all time points

AGW: Same rationale (one-third of LBW) as for AEGL (except 10 min value for which time scaling was applied), 2h value added

LBW: Different PoD, other UFs, 10 min value for which time scaling applied and 2-hr value added

Date: November 2015 | AEGL document: Final, 2014

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	5.6	5.6	5.6	5.6	5.6	5.6	Olfactory fatigue in humans
AGW	47	33	26	21	16	8.2	One-third of LBW
LBW	140	98	78	62	49	25	Threshold for lethality in rats

Derivation of the Dutch Intervention Values

VRW: In contrast to the AEGL, which concluded that the substance elicits poor warning properties, the data from a study with human volunteers (Pozzani et al. 1968) were considered suitable for deriving VRWs for methacrylonitrile. The study was designed to assess sensory response to methacrylonitrile vapors in humans. Olfactory fatigue was observed after a few minutes of exposure to methacrylonitrile at 2 ppm (5.60 mg/m³) for 10 minutes. No uncertainty factor to account for intraspecies differences was considered necessary because olfactory fatigue is not a perceived effect, but rather an objective measurement that is a precedent to perceived irritation. The VRW was held constant across all exposure durations because the observed effects are not expected to vary over time.

AGW: No inhalation data on methacrylonitrile consistent with the definition of AGW are available. Therefore, the AGWs for methacrylonitrile were estimated by dividing the LBWs by 3.

LBW: A comparison of the 4-h LC_{50} values for the various species tested by Pozzani et al. (1968) suggest that mice and rabbits are sensitive species. Despite the fact that mice and rabbits are the most sensitive species, rats are considered to be more alike to humans. So, in contrast to the EAGL, the no effect level for rats of 176 ppm (491 mg/m³) after 4 hour exposure was used as starting point for the LBW. The no effect level was chosen over the LC_{50} values because it is preferable to use an empirical value rather than estimating a no-effect level by adjusting an LC_{50} value. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. For time-scaling $C^n \times t = k$ was used, using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Methacrylonitrile may cause irritation or burning of the eyes and skin. The toxicity of methacrylonitrile is due to the metabolic release of cyanide. Signs of exposure may include weakness, headache, confusion, nausea, vomiting, convulsion, dilated pupils, weak pulse, shallow and gasping breathing, and cyanosis. Methacrylonitrile is readily absorbed through the respiratory and gastrointestinal tracts, and skin.

No evidence of developmental/reproductive toxicity of methacrylonitrile was found.

H301: Toxic if swallowed; H311: Toxic in contact with skin; H331: Toxic if inhaled; H317: May cause an allergic skin reaction

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Methacrylonitrile is structurally similar to acrylonitrile, a

Odour and derivation of the LOA value

Odour: bitter almonds

An odour threshold of 7 ppm (19.5 mg/m³) was reported in literature [AEGL TSD].

known rat and probable human carcinogen (IARC, 1987); however, there is no evidence of carcinogenic activity of methacrylonitrile,	LOA = 11.8 * OT_{50} * 1.33 = 310 mg/m^3 (The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*				
VRW level **5.6**	*AEGL-1* NR	*ERPG-1* not derived		*IDLH:* not derived.
AGW level **26**	*AEGL-2* 2.7	*ERPG-2* not derived		
LBW level **78**	*AEGL-3* 8.7	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 67-56-1 **Methanol** **CH_3-OH** **VN-nr: 1230**

GEVI: 336

Synoniemen: methylalcohol, houtgeest (Engels: methanol) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	1.300	890	710	560	450	350
Alarmeringsgrenswaarden	AGW (mg/m³)	53.000**	18.000*	9.600*	5.900	3.200	2.200
Levensbedreigende waarden	LBW (mg/m³)	80.000**	28.000*	15.000*	8.900*	4.700	3.100

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,751 ppm; 1 ppm = 1,33 mg/m³

Explosiegrens: LEL=5,5 Vol%≈ 73.200 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

** berekende interventiewaarde hoger dan 50% LEL

Geur: typerende zoete alcoholachtige geur

LOA: 12 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,01

Molecuulmassa: 32,0 g/mol
Zuurgraad: geen data
LogKow: -0,7
Wateroplosbaarheid: volledig
Verzadigde dampdruk: 128 mbar

Overige informatie

Publieke grenswaarde: 133 mg/m³ H
MAK: 266 mg/m³ H
TLV-TWA: 266 mg/m³ H

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: hoesten

VRW → AGW: irritatie van de ogen, hoofdpijn, misselijkheid, slaperigheid, duizeligheid.

AGW → LBW: ernstige irritatie van de ogen en de luchtwegen, wazig zien, verlies van gezichtsvermogen, sufheid, kortademigheid, verwardheid

Boven LBW: bewustzijnsdaling, benauwdheid, metabole acidose, toevallen, bewusteloosheid

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Methanol werkt bijtend op ogen, huid en luchtwegen.
- Methanol werkt op het centrale zenuwstelsel en de oogzenuw met als gevolg bewustzijnsverlies en gezichtsverlies
- Blootstelling kan metabole acidose, falende ademhalingsfunctie en de dood tot gevolg hebben. De uitwerking kan vertraagd intreden.
- Personen met een lage folium Status, zoals zwangere vrouwen, zijn mogelijk een gevoelige groep, doordat zij vatbaarder zijn voor de gezondheidseffecten van methanol.

Effecten bij blootstelling aan vloeistof

Huidcontact: droge huid, pijn.
Stof wordt door de huid opgenomen!

Oogcontact: roodheid, pijn, slecht zien, afwijkingen van het hoornvlies.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, specifieke behandeling en onmiddellijk arts raadplegen

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.

ogen: zie hierboven.

inslikken: mond laten spoelen (uitspugen!), specifieke behandeling, GEEN braken opwekken, en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: ethanol* of *fomepizole*.

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 67-56-1 **Methanol** **CH_3-OH** **UN-nr: 1230**

Basis for the Dutch Intervention Values

VRW: AEGL value adopted (except 10 min value for which time scaling was applied), 2hr value added

AGW: Different point of departure as for AEGL, 2h value added

LBW: Different point of departure as for AEGL, 2h value added

Date: 06-10-2016 | AEGL document: Interim 2, 2005

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	1,300	890	710	560	450	350	The NOEL for neurobehavioral, and neuropsychological effects
AGW	53,000**	18,000*	9,600*	5,900	3,200	2,200	PK model based on the threshold for serious methanol poisoning in humans
LBW	80,000**	28,000*	15,000 *	8,900*	4,700	3,100	PK model based on the threshold for lethality in humans.

* value higher than 10% of LEL; ** value higher than 50% of LEL

Derivation of the Dutch Intervention Values

VRW: An experimental study in humans reported that volunteers were exposed in a pharmacokinetic study to a single concentration of 800 ppm (1,064 mg/m³) for 8 hours. The subjects were asked if they experienced any symptoms. None of the subjects reported a problem. Other studies reported headaches, dizziness and blurred vision after occupational exposure to 1,060 ppm (1,410 mg/m³). The described effects in these studies are considered to be discomfort level effects. Therefore the concentration of 800 ppm (1,064 mg/m³) for 8 hours was selected as point-of-departure for derivation of the VRW values. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. The equation $C^n \times t = k$ was used to derive exposure duration-specific values, using the default value n=3 for extrapolation from 8 hours to shorter exposure durations. In contrast to the 10 minute AEGL-1 value, time scaling was also applied for the 10 minutes VRW value.

AGW: A study in mice shows developmental toxic effects. A repeated 7-hour/day exposure study during gestational days 6 to 15 caused a dose-related, significant increase in cervical ribs at 2,000 ppm (2,660 mg/m³) or higher. In a different study mice were exposed to different concentration-time combinations on gestational day 7. The results support that no effects are observed at a concentration of 2,000 ppm (2,660 mg/m³) for 5 hours as well as 7 hours. The exposure to the concentration of 2,000 ppm (2,660 mg/m³) for 7 hours was therefore considered. Experiments show that the AGW level effects are caused by methanol itself and not by a metabolite. The corresponding end-of-exposure blood concentration in mice was used and was measured as 487 mg/L. A proposal for consideration on the classification of methanol as a substance which may damage the unborn child was rejected. It was concluded that the concentrations of methanol leading to developmental toxicity would be lethal in humans. The AGW values are therefore based on toxicity data in humans. Based on various case studies it can be concluded that peak blood methanol concentrations have been above 1,000 mg/L in all fatal cases. Several published clinical practice guidelines on treatment of methanol poisoning state that peak blood methanol concentration >500 mg/L indicate serious poisoning. The peak blood methanol concentration of 500 mg/L was used as the basis for the derivation of the AGW values. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Using a total uncertainty factor of 3 a blood methanol concentration of 167 mg/L was derived as the basis for calculation of exposure concentrations. A pharmacokinetic model (PK model) was used to determine the appropriate time periods that would lead to a blood methanol concentration of 167 mg/L. This results in a concentration of 40,000 ppm (53,000 mg/m³), 14,000 ppm (18,000 mg/m³), 7,200 ppm (9,600 mg/m³), 2,400 ppm (3,200 mg/m³), and 1,600 ppm (2,200 mg/m³) for respectively a 10 min, 30 min, 1 h, 4 h and 8 h exposure. A 2-hour value of 4,400 ppm (5,900 mg/m³) was derived by interpolation of the results.

LBW: The derivation of the LBW values was based on published clinical practice guidelines on treatment of methanol poisoning, which state that a peak blood methanol concentration of ≥ 800 mg/L is considered lethal. The peak blood methanol concentration of 800 mg/L was used as the basis for the derivation of the LBW values. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Using a total uncertainty factor of 3 a blood methanol concentration of 267 mg/L was derived as the basis for calculation of exposure concentrations. In two studies, a pharmacokinetic model (PK model) was used to determine the appropriate time periods that would lead to a blood methanol concentration of 250 mg/L. This results in a concentration of 60,000 ppm (79,800 mg/m^3), 21,000 ppm (27,930 mg/m^3), 11,000 ppm (14,630 mg/m^3), 3,500 ppm (4,655 mg/m^3), and 2,300 ppm (3,059 mg/m^3) for respectively a 10 min, 30 min, 1 h, 4 h and 8 h exposure. A 2-hour value of 6,722 ppm (8,940 mg/m^3) was derived by interpolation of the results.

Additional toxicological information (including relevant results of a general literature search, if any)

The effects of exposure to methanol appear fast after exposure, which suggest that these effects are probably caused by methanol itself and not by a metabolite. The first effects on humans are related to central nervous system (CNS) effects. Experimental evidence shows that after exposure one of the metabolites, formic acid, is responsible for metabolic acidosis and ocular toxicity. Populations with a less than optimal folate Status (for example, pregnant women, the elderly, individuals with poor-quality diet and alcoholics) may be more susceptible to the health effects of methanol.

Several studies on the developmental and reproductive toxicity of methanol were carried out. These studies include single and repeated inhalation exposure studies. The exposures of rats and mice during the period of embryogenesis induced a wide range of concentration-dependent teratogenic and embryolethal effects. The evidence from animal studies provide a strong presumption that methanol could interfere with reproduction in humans. A proposal for consideration by the RAC on the classification of methanol as a substance which may damage the unborn child was rejected in 2014. The RAC concluded that the concentrations of methanol leading to developmental toxicity would be lethal.

H301: Toxic if swallowed; H311: Toxic in contact with skin; H331: Toxic if inhaled; H370: Causes damage to organs

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: characteristic sweet alcoholic odour

OT_{50}: 0.76 mg/m^3 [Hellman and Small, 1974]
LOA = 11.8 * 0.76 * 1.33 = 12 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is below the VRW, therefore subjects will be aware of the odour below the level where health effects may be expected.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **710**	*AEGL-1* 710	*ERPG-1* 270		*IDLH: 7,980 mg/m^3 (30 min)*
AGW level **9.600**	*AEGL-2* 2.800	*ERPG-2* 1.300		
LBW level **15.000**	*AEGL-3* 9.600	*ERPG-3* 6.700		

Stofdocument deel A

CAS-nr: 74-89-5 **Methylamine** **CH_3-NH_2** VN-nr: 1061

GEVI: 23

Synoniemen: aminomethaan,methaanamine, MMA (Engels: methylamine) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	19	19	19	19	19	19
Alarmeringsgrenswaarden	AGW (mg/m³)	210	120	83	57	40	28
Levensbedreigende waarden	LBW (mg/m³)	1200	660	450	320	220	140

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,773 ppm; 1 ppm = 1,29 mg/m³

Explosiegrens: LEL = 4,9 vol% ≈ 63.000 mg/m³

Geur: scherp, vis- of ammoniak-achtig

LOA: 0,706 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos onder druk tot vloeistof verdicht gas

Brand: zeer brandgevaarlijk

Relatieve dichtheid van gas: 1,07

Molecuulmassa:	31,1 g/mol
Zuurgraad:	pK_a 10,65 bij 25°C
LogKow:	-0,6
Wateroplosbaarheid (bij 25°C):	108 g/100 ml (zeer goed)
Verzadigde dampdruk:	3140 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: 13 mg/m³

TLV-TWA: 6,5 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	mogelijk lichte irritatie ogen, huid en bovenste luchtwegen
VRW → AGW:	irritatie ogen, huid en bovenste luchtwegen, hoesten, niezen, tranenvloed
AGW → LBW:	irritatie van onderste luchtwegen, benauwdheid, longoedeem, verlies van gezichtsvermogen, coördinatieproblemen, lethargie
Boven LBW:	convulsies, ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Methylamine werkt irriterend tot bijtend op de ogen, de huid en de luchtwegen, waarschijnlijk door het sterk alkalische karakter van de stof.
- Depressie van het centraal zenuwstelsel kan ontstaan.
- Inademing kan, uitsluitend na verschijnselen van bijtende effecten op de slijmvliezen van de ogen en/of hogere luchtwegen, longontsteking en/of longoedeem veroorzaken. Dit kan pas na enkele uren optreden en wordt versterkt door lichamelijke inspanning.
- Expositie van de ogen aan het gas kan cornea oedeem veroorzaken.
- In ernstige gevallen bestaat kans op verstikking door zwellingen in de keel.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, branderig gevoel, ernstige brandwonden, mogelijk ernstige bevriezingsverschijnselen zoals pijn, blaren, wonden.

Oogcontact: bijtend, tranenvloed, slecht zien, ernstige brandwonden, permanent verlies van gezichtsvermogen

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: aan de huid vastgevroren kleding NIET lostrekken, spoelen met veel water / kleding uittrekken en onmiddellijk arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas).

Specifieke behandeling en materialen

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 74-89-5 **Methylamine** **CH_3-NH_2** **UN-nr: 1061**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 16-12-2010 AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	19	19	19	19	19	19	Mild (nasal) irritation in rats
AGW	210	120	83	57	40	28	Reversible nasal lesions in rats
LBW	1200	600	450	320	220	140	Lethality thresholds in rats

Derivation of the Dutch Intervention Values

VRW: The VRW was based on a rat study. Point of departure was a single 6-hour exposure to 75 ppm (97 mg/m³). Exposures were actually repeated for two-weeks (10 exposures) and resulted in mild irritation of the nasal turbinates. Repeat exposure to higher concentrations (250 ppm (323 mg/m³) and/or 750 ppm (970 mg/m³)) caused more severe nasal lesions and /or systemic toxicity and mortality. A single 6-hour exposure to 75 ppm (97 mg/m³) is expected to cause no more than mild irritation. A total uncertainty factor of 10 was applied to the point of departure, including 3 for interspecies uncertainty and 3 for human variability, because mild nasal irritation from an alkaline irritant gas is a direct surface-contact effect not involving metabolism, and is not likely to vary greatly between species or among humans. A modifying factor of 0.5 was used since the point of departure was a repeated exposure. Application of these uncertainty and modifying factors to point of departure yields a VRW value of 15 ppm (19 mg/m³). The resulting VRW value of 15 ppm (19 mg/m³) was adopted for 10 minutes to 8 hours because mild sensory irritation is not expected to vary greatly over time.

AGW: AGW values were derived from a repeat exposure study. Ten exposures of male CD rats to 250 ppm (323 mg/m³), 6 hours/day, caused reversible lesions of the anterior respiratory tract. The severity of the lesions (focal erosion and ulceration of the nasal turbinate mucosa) was attributed to the repeated exposure scenario, *i.e.*, repeated local irritation. Lesions did not extend into the trachea or lungs. Lesions following a single exposure would be less severe and also reversible. A total uncertainty factor of 10 was applied, including 3 for interspecies uncertainty and 3 for human variability, because nasal irritation from an alkaline irritant gas is a direct surface-contact effect not involving metabolism, and is not likely to vary greatly between species or among humans. Time scaling was performed using $C^n \times t = k$, with the chemical specific value for n of 1.9, derived from rat lethality data (see derivation LBW values). Lethality data were used to time-scale the AGW values because local irritation is considered the first step leading to pulmonary irritation and death.

LBW: The LBW was based on lethality data from a study in which rats were exposed to concentrations of 17,600-35,300 ppm (22,800- 45,700 mg/m³) for 6 minutes, 10,600-17,400 ppm (13,700-22,500 mg/m³) for 20 minutes, or 4100-8670 ppm (5,310- 11,200 mg/m³) for 60 minutes. The probit-analysis based dose-response program of ten Berge (2006) was used to calculate the LC_{01} at each LBW exposure duration. The program incorporated all of the data at the 6-, 20-, and 60-minute time points. The data indicated a time-scaling value of 1.9. A total uncertainty factor of 10 was applied, including 3 for interspecies uncertainty and 3 for human variability, because lethality from an alkaline irritant gas is a direct surface-contact effect not involving metabolism, and is not likely to vary greatly between species or among humans. Time-scaling was used to derive a 2-hr LBW, using the equation $C^n x\ t = k$.

Additional toxicological information (including relevant results of a general literature search, if any)

The accidental poisoning (undefined exposure time or concentration) of 35 people was described in which six

people died within 10 days of exposure, mainly due to lung chemical burns and tissue death. Other effects included difficulty breathing, chemical burns of the nose, mouth, eyes, and exposed skin, coma, dizziness, headache, nausea, black stool, high body temperature, rapid heart rate, and circulatory failure.

The mechanism of methylamine toxicity has not been defined, although its irritant properties are likely related to its high alkalinity (pKa of 10.65 at 25°C) and corrosiveness to exposed tissues such as skin, eyes, and the respiratory mucosa. Thus, methylamine has been reported to cause respiratory and ocular irritation in both humans and animals and at sufficiently high concentrations methylamine causes breathing difficulties, lesions of the eyes and lungs, and death associated with lung lesions. Methylamine vapor is also associated with systemic effects in exposed animals (e.g., neurotoxicity, pathological alterations of the liver, thymus, spleen, and brain), the etiology of which is less clear.

Several aliphatic amines (e.g. ethylamine, diethylamine, triethylamine, dimethylamine, dimethylethylamine) have been reported to cause visual effects after exposure for several hours (hazy vision, blurred objects, blue halos, blue or grey vision). These effects were due to edema of the corneal epithelium. A group of amines, including dimethylamine, has been reported to cause vision disturbances in workers exposed for several hours to concentrations too low to cause discomfort or disability.

Methylamine is metabolized in mammals by semicarbazide-sensitive amine oxidase (SSAO), to form formaldehyde, hydrogen peroxide, and ammonia. Elevated levels of endogenous methylamine and/or increased SSAO activity, and the increased levels of the methylamine metabolites, are believed to cause vascular endothelial damage, and are associated with a number of disease states (diabetes, heart disease, non-diabetic obesity, Alzheimer's disease, cerebral arteriopathy, inflammatory liver disease, atherosclerosis, and congestive heart failure). Individuals with increased SSAO activity may therefore be a sensitive sub-population. Several studies indicate that SSAO activity is greater in human than rodent tissues.

No studies were located that evaluated methylamine developmental or reproductive toxicity to humans.

H315: Causes skin irritation, H318: Causes serious eye damage, H332: Harmful if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

No studies were found that examined the carcinogenic potential of methylamine. Under acidic (e.g. stomach) conditions, the related compounds dimethylamine and trimethylamine can react with nitrite to form dialkylnitrosamines, which are known carcinogens. However, neither dimethylamine nor trimethylamine have shown carcinogenic activity in long-term animal studies.

Odour and derivation of the LOA value

Odour: pungent, fishy odour, that becomes similar to that of ammonia at higher concentrations.

Olfactory fatigue to methylamine occurs readily.

OT_{50}: 0.045 mg/m^3 [AEGL (2008), Ruijten (2005)]

LOA = 11.8 * OT_{50} * 1.33 = 0.706 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is below the VRW; therefore subjects can be aware of the odour below the level where health effects may be expected.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **19**	*AEGL-1* 19	*ERPG-1* 13		*IDLH:* 130 (30 minutes)
AGW level **83**	*AEGL-2* 83	*ERPG-2* 130		
LBW level **450**	*AEGL-3* 450	*ERPG-3* 650		

Stofdocument deel A

CAS-nr: 74-83-9 **Methylbromide** **CH_3Br** **VN-nr: 1062**

GEVI: 26

Synoniemen: broommethaan, monobroommethaan (Engels: methyl bromide) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	3700	1500	840	470	260	260
Levensbedreigende waarden	LBW (mg/m³)	13.000	5200	2900	1600	920	520

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,253 ppm; 1 ppm = 3,95 mg/m³

Explosiegrens: LEL = 10 vol% ≈ 400.000 mg/m³

Geur: vrijwel geen geur; geur is beschreven als zoet en chloroformachtig, fruitig

LOA: 1240 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas

Brand: moeilijk brandbaar

Relatieve dichtheid gas: 3,3

Molecuulmassa: 95 g/mol
Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: 1,5 g/100 ml (matig)
Verzadigde dampdruk: 1900 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: 4,0 mg/m³
TLV-TWA: 4,0 mg/m³ (huid)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: geen informatie

AGW → LBW: keelpijn, hoesten, misselijkheid, braken, hoofdpijn, duizeligheid, zwaktegevoel, lever- en nierschade, benauwdheid, longoedeem, hartritmestoornissen

Boven LBW: convulsies, coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Methylbromide is veroorzaakt effecten op het CZS en de luchtwegen.
- Methylbromide kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Methylbromide kan lever- en nierschade veroorzaken.
- Bij blootstelling aan lage concentraties kunnen de effecten vertraagd optreden.

Effecten bij blootstelling aan vloeistof

Huidcontact: bij bevriezing: ernstige bevriezingsverschijnselen zoals pijn, blaren en wonden

Oogcontact: bij bevriezing: pijn ernstige brandwonden

Carcinogeniteit

IARC classificatie: 3

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, GEEN mond-op-mondbeademing, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: aan de huid vastgevroren kleding NIET lostrekken, minimaal 20 min. spoelen met veel water of douchen en ONMIDDELLIJK arts raadplegen..

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas)

Specifieke behandeling en materialen

Neem contact op met het NVIC (tel: +31 (0)30 – 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 74-83-9 **Methyl bromide** CH_3Br **UN-nr: 1062**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 24-09-2009	AEGL document: Final, 2012

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended due to insufficient data
AGW	3700	1500	840	470	260	260	Threshold of neurotoxic effects
LBW	13,000	5200	2900	1600	920	520	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: Because methyl bromide is not detectable by sensory irritation at concentrations below the AGW, a VRW was not derived.

AGW: For methyl bromide, the endpoint of neurotoxicity, leading to an inability to escape is the most relevant endpoint for the AGW. Because of the steep dose-response curve for such effects, a NOAEL for neurotoxicity is the appropriate endpoint for the AGW. Studies with the dog and rat (the mouse was considered unusually sensitive due to its high tissue levels of the liver enzyme GST) indicate that 200 ppm (790 mg/m³) for 4 hours is a NOAEL for clinical signs indicative of neurotoxicity. Because uptake of methyl bromide is greater in rodents than in humans (based on comparative respiratory rates and comparisons with methyl chloride) and because GST levels in rodents are higher than in humans, resulting in more rapid production of toxic metabolites, an interspecies uncertainty factor of 1 was applied. Humans differ in their capacity to metabolize methyl bromide, but, toxicologically, the difference is considered to be less than 3-fold. An intraspecies uncertainty factor of 3 was applied. The resulting 4-hour value of 67 ppm (260 mg/m³) was time scaled to the other exposure durations using $C^n \times t = k$ and an n value of 1.2 (based on lethality data in the rat). Because the time scaled 8-hour value of 37 ppm (150 mg/m³) is close to the chronic NOAEL of 33 ppm (130 mg/m³) for mice and less than the 5-day NOAEL of 55 ppm (220 mg/m³) for clinical signs and tissue lesions in dogs and 36-week NOAEL of 55 ppm (220 mg/m³) for neurobehavioral parameters and nerve conduction velocity in rats, this is considered as a too high value. Therefore, the 8-hour value was set equal to the 4-hour value.

LBW: The LBW values were based on the $BMCL_{05}$ of 701 ppm (2770 mg/m³) in a 4-hour exposure of rats. This value (701 ppm, 2770 mg/m³) was also the highest nonlethal value in the study. The 4-hour 701 ppm (2770 mg/m³) concentration was adjusted by inter and intraspecies uncertainty factors of 1 and 3, respectively as for the AGW above, and time scaled using $C^{1.2} \times t = k$, based on lethality data in the rat. The 8-hour LBW value of 520 mg/m³ is supported by repeat-dose studies in which dogs exposed to 156 or 158 ppm (616 or 624 mg/m³) for 7 hours/day did not exhibit severe clinical signs until the second or third day of exposure. There were no remarkable histopathological lesions in the dogs at autopsy following a 4-day exposure, but cerebellar lesions were observed following 6 days of exposure to 158 ppm (624 mg/m³).

Additional toxicological information (including relevant results of a general literature search, if any)

Inter-individual variation in the rate of metabolism of methyl halides has been observed in humans. At least two distinct populations of humans with differences in the rate of metabolism of the structurally-similar methyl chloride have been identified. Fast metabolism may lead to the formation of toxic metabolites that can exert their action before they can be eliminated whereas slow metabolizers would be expected to be less susceptible to the toxic effects of methyl halides. For the related chemical, methyl chloride, uptake while inhaling 50 ppm differed less than 3-fold among slow and fast metabolizers. Elimination was rapid by both groups following termination of the exposure. Elimination was more rapid by those volunteers with the lower

blood and expired air concentrations. The authors explained the difference in the two groups by a two-fold difference in the rate at which they metabolized methyl chloride. They considered the difference of questionable toxicological significance. In general, populations that have kidney or liver disease, anemia, or neurological deficits may be more susceptible to the toxic effects of methyl chloride.

Methyl bromide has been responsible for many occupational poisoning incidents, reflecting its wide use as a fumigant. Although many occupational and accidental exposures to methyl bromide have occurred, few cases accurately document exposure concentrations or durations. Methyl bromide is practically odourless, even at lethal concentrations. Descriptive symptoms indicate methyl bromide acts on the central nervous system (headache, visual disturbance, mental disturbance, nausea, vomiting, etc.) and directly on the lungs (lung edema).

Studies with rats and rabbits indicate that inhalation exposure up to 70 ppm (280 mg/m^3) during gestation does not result in any significant developmental effects.

H301: Toxic if swallowed; H315: Causes skin irritation; H319: causes serious eye irritation; H331: Toxic if inhaled; H335: May cause respiratory irritation; H341: Suspected of causing genetic defects; H373: May cause damage to organs.

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to its carcinogenicity to humans).

No carcinogenic risk potency (CRP) was derived.

Methyl bromide tested positive in numerous mutagenicity and genotoxicity tests. Mutagenicity did not require metabolic activation which is consistent with the direct-acting alkylation of DNA. Alkylation suggests that methyl bromide may be carcinogenic, but carcinogenicity has not been established following chronic studies with rats and mice.

Odour and derivation of the LOA value

Odour: Methyl bromide is practically odourless, even at lethal concentrations. Reported odour thresholds are variable: 20-1000 ppm (79-4000 mg/m^3). The odour has been described as sweetish and chloroform-like, but additional descriptions include musty or fruity at concentrations above 1000 ppm (4000 mg/m^3) or faintly acrid at around 500 ppm (2000 mg/m^3).

Using the lowest odour threshold to derive the LOA would provide,

LOA = 11.8 * 79 * 1.33 = 1240 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies in the range of the AGW and LBW.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **NR**	*AEGL-1* NR	*ERPG-1* NR		*IDLH:* 990 (30 min)
AGW level **840**	*AEGL-2* 830	*ERPG-2* 200		
LBW level **2900**	*AEGL-3* 2900	*ERPG-3* 790		

Stofdocument deel A

CAS-nr: 79-22-1 **Methylchloorformiaat** CH_3-O-COCl **VN-nr: 1238**

GEVI: 663

Synoniemen: chloormierenzuur methylester, methylchloorcarbonaat, methylchloormethanaat (Engels: methyl chloroformate)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	16	11	8,8	7,0	5,6	2,8
Levensbedreigende waarden	LBW (mg/m³)	48	33	26	21	17	8,3

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,254 ppm; 1 ppm = 3,93 mg/m³

Explosiegrens: LEL = 6,7 vol% ≈ 263.000 mg/m³

Geur: stekend

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot lichtgele vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,3

Molecuulmassa: 94,5 g/mol

Zuurgraad: Geen data

LogKow: 0,1

Wateroplosbaarheid: reactie

Verzadigde dampdruk: 137 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: 0,79 mg/m³

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: irritatie van de ogen en luchtwegen

AGW → LBW: ernstige irritatie van de ogen en luchtwegen, tranenvloed, keelpijn, hoesten, speekselvloed, druk op de borst, piepende ademhaling, benauwdheid, longoedeem

Boven LBW: ademnood, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Methylchloorformiaat werkt bijtend op de ogen en luchtwegen.
- Methylchloorformiaat kan longoedeem veroorzaken, waarbij de verschijnselen pas na enkele uren kunnen optreden en versterkt kunnen worden door lichamelijke inspanning.
- Methylchloorformiaat ontleedt in aanwezigheid van water of vochtige lucht zeer heftig tot chloorwaterstof, CO_2, methanol.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, brandwonden

Oogcontact: bijtend, tranenvloed, roodheid en pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen, zo nodig arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen:.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 79-22-1 **Methyl chloroformate** **CH_3-O-COCl** **UN-nr: 1238**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: November 2015 | AEGL document: Interim, 2008

Proposal for the Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Insufficient data
AGW	16	11	8.8	7.0	5.6	2.8	3-fold reduction of LBW values
LBW	48	33	26	21	17	8.3	Estimated lethality threshold in the rat

Derivation of the Dutch Intervention Values

VRW: VRW values for methyl chloroformate are not recommended due to insufficient data. Absence of VRW values does not imply that exposure below the AGW value is without adverse effects.

AGW: No acute inhalation data consistent with the definition of AGW with both exposure concentration and duration parameters were available. Therefore, the AGW values for methyl chloroformate are based upon a 3-fold reduction of the LBW values; this is considered an estimate of a threshold for irreversible effects. This approach is justified based on the steep concentration curve with regard to lethality (4-hour rat LC_{50}: 51-53 ppm (200-208 mg/m³), 0% mortality in rats exposed to 45 ppm (177 mg/m³) and 80% mortality in rats exposed to 57 ppm (224 mg/m³) for 4 hours; 1-hour rat LC_{50}: 100 ppm (292 mg/m³); rats exposed to 26 ppm (102 mg/m³) for 1 hour were clinically normal and showed no mortality).
Furthermore this approach is supported by data from an animal study in which rats were exposed to 35, 45, 57, 73 ppm (138, 177, 224, 287 mg/m³) methyl chloroformate for 4 hours. Histopathological examination showed increased permeability in the alveolar septa and corresponding damage to bronchial epithelium; this effect was noted in all treatment groups.

LBW: LBW values were based on a study of 5 rats/sex/group exposed to 35, 45, 57, 73 ppm (138, 177, 224, 287 mg/m³) methyl chloroformate for 4 hours. The calculated 4-hr $BMCL_{05}$ value in rats (42.4 ppm (167 mg/m³)) was used as the point of departure for methyl chloroformate LBW values. This concentration is considered a threshold for lethality and is supported by the fact that no deaths were observed in rats exposed to 45 ppm (177 mg/m³) for 4 hours. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n \times t = k$, with default values of n=1 and n=3 when extrapolating to longer and shorter exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Case reports of methylchloroformate toxicity exist; however, details of exposure concentration and duration are unreported. Signs of exposure included ocular and upper respiratory irritation followed by a latent period which ultimately led to pulmonary edema. For the workers in these reports the latency periods were 36 hours.

Chloroformates hydrolyze in water or moist air to produce the parent hydroxy compound, hydrogen chloride, carbon dioxide, and a carbonate. They are direct-acting contact irritants, and are corrosive to the eyes, skin, gastrointestinal and respiratory tracts. Inhalation may result in coughing, labored breathing, sore throat, unconsciousness, convulsions, and death. Lung edema frequently occurs, and symptoms of this may not manifest for several hours after exposure and may be aggravated by physical exertion. Ingestion may result in a burning sensation of the digestive tract, nausea, vomiting, and abdominal pain.

No data concerning developmental/reproductive toxicity were located in the available literature.

H302: Harmful if swallowed; H312: Harmful in contact with skin; H314: Causes severe skin burns and eye damage; H330:Fatal if inhaled.

Carcinogenicity and derivation of the CRP value

Odour and derivation of the LOA value

IARC classification: not classified No carcinogenic risk potency (CRP) was derived. No data concerning carcinogenicity of methyl chloroformate were found.	Odour: Unpleasant, acrid No LOA was derived due to lack of information.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*				
VRW level **?**	*AEGL-1* NR	*ERPG-1* NR		*IDLH:* not derived
AGW level **8.8**	*AEGL-2* 8.6	*ERPG-2* 7.9		
LBW level **26**	*AEGL-3* 26	*ERPG-3* 20		

Stofdocument deel A

CAS-nr: 74-87-3 **Methylchloride** CH_3Cl **VN-nr: 1063**

GEVI: 23

Synoniemen: chloormethaan, monochloormethaan, R40 (Engels:Methyl Chloride) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	3.500	2.400	1.900	1.500	1.200	790
Levensbedreigende waarden	LBW (mg/m³)	12.000	8.000	6.400	5.000	4.000	2.600

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,476 ppm; 1 ppm = 2,10 mg/m³

Explosiegrens: LEL=7,1 vol% ≈ 150.000 mg/m³

Geur: zoete, etherische geur (geur is zeer zwak)

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa:	50,5 g/mol
Zuurgraad:	Geen data
LogKow:	0,9
Wateroplosbaarheid:	0,5 g/100 ml (slecht)
Verzadigde dampdruk:	4900 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: 100 mg/m³ (huid)
TLV-TWA: 100 mg/m³ (huid)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: geen informatie

AGW → LBW: misselijkheid, braken, problemen met zicht (wazig zien, dubbelzien, accommodatie-stoornissen), hoofdpijn, duizeligheid, coördinatiestoornissen, verwardheid, bewustzijnsdaling

Boven LBW: spierzwakte, tremoren, convulsies, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Methylchloride veroorzaakt effecten op het CZS.
- Methylchloride vormt onder invloed van licht fosgeen (zie effecten aldaar).
- Uit dierstudies blijkt dat methylchloride reprotoxische effecten kan veroorzaken.
- Het optreden van anemie, lever- en nierschade en effecten op het cardiovasculair system zijn beschreven.
- Effecten kunnen vertraagd optreden.

Effecten bij blootstelling aan vloeistof

Huidcontact: bevriezingsverschijnselen zoals roodheid, pijn, blaren (en systemische effecten zoals genoemd bij inhalatie toxiciteit)

Oogcontact: slecht zien, bij bevriezing: irritatie, roodheid en pijn

Carcinogeniteit

IARC classificatie: 3
CRP : niet afgeleid

Beknopte medische informatie

Ontsmetting *gas*

algemeen: frisse lucht, rust en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: aan de huid vastgevroren kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas).

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 74-87-3 **Methyl Chloride** CH_3Cl **UN-nr: 1063**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted(except 10 min value for which time scaling was applied), 2h value added

Date: 24-09-2009 | AEGL document: Interim, 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	(insufficient data)
AGW	3,500	2,400	1,900	1,500	1,200	790	NOAEL for clinical signs and tissue lesions in rats; Transient impaired ability to escape in humans (supportive study).
LBW	12,000	8,000	6,400	5,000	4,000	2,600	Threshold of lethality rats

Derivation of the Dutch Intervention Values

VRW: Clinical studies show that single exposures of healthy adults to 200 ppm (420 mg/m³) for 3 or 3.5 hours and 5-day repeated exposures of exercising adults to 150 ppm (320 mg/m³) for 7.5 hours/day are without adverse neurotoxic effects. The subjects included both “fast” and “slow” methyl chloride metabolizers. These exposures failed to elicit physiological, neurological, behavioural, or clinical symptoms. None of these exposures produced mild, transient effects that define the VRW and therefore VRW values were not recommended.

AGW: The AGW values were based on several rat studies; a monitoring study was used as support. The basis for the AGW was the absence of clinical signs in rats exposed to 1,500 ppm (3,150 mg/m³) for 6 hours/day for one day or 90 days. Based on the greater blood uptake by rodents compared with humans, an interspecies uncertainty factor of 1 was applied. Although humans differ in the rate at which they metabolize methyl chloride, the difference does not appear to be toxicologically significant. Furthermore, genetically, most humans are rapid metabolizers, the most susceptible group. Therefore, an intraspecies uncertainty factor of 3 is sufficient. In the absence of time-scaling information, time scaling was performed using the equation $C^n \times t = k$, and default n values of 3 for shorter durations and 1 for longer durations In contrast to the 10 minute AEGL-2 value that was set equal to the 30 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.
Accidental exposures to 1,000 – 2,000 ppm (2,100 – 4,200 mg/m³) and a repeated exposure to 2,000 – 4,000 ppm (4,200 – 8,400 mg/m³) resulted in transient symptoms of blurring of vision, dizziness, headache, and nausea in workers. Exposure durations were not reported, but appeared to be throughout the work day. Application of an intraspecies uncertainty factor of 3 to the mean value of 1,500 ppm (3,150 mg/m³) in this occupational monitoring report results in 500 ppm (1,050 mg/m³), a value similar to the 4- and 8-hour AGW values.

LBW: Data on lethality are limited to LC_{50} values for the mouse, a particularly sensitive species. Because of the higher respiratory rate in mice and the higher levels of glutathione in mouse liver and kidney, particularly the male mouse, compared with human tissues, the mouse is not considered an appropriate surrogate for human response to methyl chloride. Based on data from a monitoring study in which humans withstood repeated exposures to 1,000-4,000 ppm (2,100 – 8,400 mg/m³), the 6-hour LC_{50} of 2,200 ppm (4,600 mg/m³) in male mice is not realistic for application to humans. Two studies reported no deaths in rats during the first 4 days of 5- and 12-day exposures to 5,000 ppm (10,500 mg/m³) for 6 hours/day. A single 6-hour exposure to 5,000 ppm (10,500 mg/m³) was considered the point of departure for lethality. Inter- and intraspecies uncertainty factors of 1 and 3, respectively, were applied as for the AGW above. Time-scaling was performed using the equation $C^n \times t = k$, and default n values of 1 and 3. In contrast to the 10 minute AEGL-3 value that was set equal to the 30 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

The mechanism of neurotoxicity of methyl chloride is unclear, but most probably involves the conjugation of methyl chloride with glutathione and/or the production of toxic metabolites such as formaldehyde and methanethiol as well as lipid peroxidation. A lack of glutathione may impair the ability of tissues to suppress lipid peroxidatin reactions. Acute exposures of rats and mice cause significant reductions in glutathione levels in numerous organs including the liver, kidney, lung, and brain.

Human and animal studies show that methyl chloride is rapidly absorbed from the lungs. While the principal route of absorption of methyl chloride is by inhalation, it can be absorbed through the skin.

Methyl chloride is extensively distributed throughout the body. Blood and alveolar air levels are difficult to correlate with exposure.

At least two distinct populations of humans with differences in the rate of metabolism of methyl chloride have been identified, attributed to the genetic polymorphism of glutathione transferase T1 (GST). Depending on the presence or absence of glutathione-S-transferase, humans may be “fast metabolizers” or “slow metabolizers” of methyl chloride. There may be a third phenotype, non-conjugators. Fast metabolism may lead to the formation of toxic metabolites that can exert their action before they can be eliminated. Slow metabolizers would be expected to be less susceptible to the toxic effects of methyl chloride. Because the elimination of methyl chloride is rapid in both populations, the difference is of questionable toxicological significance. Among Caucasians, the majority of individuals possess at least one copy of the GST gene; 10-25% are non-conjugators. Approximately 60% of Orientals lack the gene.

In general, populations that have kidney or liver disease, anemia, or neurological deficits may be more susceptible to the toxic effects of methyl chloride. Persons with a deficiency of glucose-6-phosphate dehydrogenase may have reduced levels of GSH. Additionally, accidental exposures suggest that infants are more susceptible than adults. However, in the latter case, death of an infant was due to acute pneumonia resulting from vomiting and aspiration after methyl bromide inhalation.

No studies were located regarding reproductive or developmental effects in humans after inhalation of methyl chloride. However, methyl chloride has been shown to be a reproductive toxicant in a variety of animal studies. Inhalation exposure of F-344 male rats to methyl chloride at concentrations >1000 ppm (2100 mg/m^3) resulted in testicular degeneration, epididymal inflammation, and sperm granuloma formation. Fertility may be decreased at 500 ppm (1,050 mg/m^3). Recovery occurred by week 16 postexposure.

H351: suspected of causing cancer; H373: may cause damage to organs through prolonged or repeated exposure

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: 3 (not classifiable as to carcinogenicity to humans). No carcinogenic risk potency (CRP) was derived.	Odour: ethereal or sweet. Several sources state that the odour is very faint and may not be noticed by individuals at concentrations that are life-threatening. Since data on odour thresholds are conflicting no LOA has been derived.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **NR**	*AEGL-1* NR	*ERPG-1* NR		*IDLH:* 4,200 (30 minutes)
AGW level **1,900**	*AEGL-2* 1,900	*ERPG-2* 840 ppm		
LBW level **6,400**	*AEGL-3* 6,300	*ERPG-3* 2,100 ppm		

Stofdocument deel A

CAS-nr: 75-09-2 **Methyleenchloride** CH_2-Cl_2 **VN-nr: 1593**

GEVI: 60

Synoniemen: DCM, dichloormethaan (Engels: methylene chloride) ***Status*: A-stof**

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	1.000	810	710	620	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	6.000	4.200	2.000	740	350	210
Levensbedreigende waarden	LBW (mg/m³)	42.000	30.000	24.000	19.000	17.000	7.400

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,283 ppm; 1 ppm = 3,53 mg/m³

Explosiegrens: LEL = 13 Vol% ≈ 459.000 mg/m³

Geur: scherp, zoete, chloroformachtige geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vluchtige vloeistof
Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,9

Molecuulmassa:	84,9 g/mol
Zuurgraad:	geen data
LogKow:	1,3
Wateroplosbaarheid:	1,3 g/100 ml (matig)
Verzadigde dampdruk:	470 mbar

Overige informatie

Publieke grenswaarde:
niet afgeleid
MAK: 177 mg/m³ H
TLV-TWA: 177 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen gegevens

VRW → AGW: verwardheid, licht gevoel in het hoofd en spraakproblemen.

AGW → LBW: duizeligheid, misselijkheid, hoofdpijn, ademhalingsproblemen, langzamere motoriek en reactievermogen, bewustzijnsdaling, foetale letaliteit

Boven LBW: hypoxie, coma en sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Afhankelijk van de blootstellingsduur en de hoogte van de acute blootstelling kan de stof leiden tot depressie van het CZS en tot COHb-vorming.
- Bij kortere blootstellingsduren kan wanneer CZS depressie optreedt ook COHb effecten optreden bij toenemende concentraties.
- Bij langere blootstellingsduren kan wanneer COHb effecten optreden ook CZS depressie optreden bij toenemende concentraties.
- CZS depressie is gecorreleerd aan methyleen chloride zelf en kan kort na blootstelling intreden met als gevolg depressie van de ademhaling, maligne hartritmestoornissen en bewusteloosheid.
- Methyleenchloride wordt voornamelijk gemetaboliseerd in de lever, waarbij onder meer koolstofmonoxide (CO) wordt gevormd met als gevolg CO vergiftiging en COHb-vorming. Als gevolg hiervan neemt het zuurstoftransport in het bloed en de afgifte van zuurstof in de weefsels af. Hypoxie kan leiden tot lokale weefselschade. In organen met een hoge zuurstofbehoefte, zoals hart en hersenen, treden de eerste effecten op.
- De piekconcentratie van COHb met de daarbij behorende effecten kan uren na de blootstelling optreden.
- De stof werkt irriterend op de ogen, de huid en de luchtwegen.
- Na een ernstige acute blootstelling kunnen ook vertraagde effecten optreden op het zenuwstelsel optreden, zoals psychose, parkinsonisme, paralyse en neuropatie. De effecten kunnen gepaard gaan met psychische effecten, zoals irritabiliteit, concentratieproblemen, schrijf- en leesproblemen en emotionele verarming.
- Gevoelige groepen zijn o.a. hartpatiënten, patiënten met een hersenaandoening, COPD patiënten, rokers, kinderen, zwangere vrouwen en foetussen.

Effecten bij blootstelling aan vloeistof

Huidcontact: droge huid, roodheid, branderig gevoel
Oogcontact: roodheid en pijn

Carcinogeniteit

IARC classificatie: 2A
CRP: 46.600 mg/m³

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht (bij voorkeur 100% zuurstof), rust, en onmiddellijk arts raadplegen
Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken en spoelen en wassen met water en zeep.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, rust en onmiddellijk arts raadplegen.
***Specifieke behandeling en materialen**: 100% zuurstof.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 75-09-2 **Methylene chloride** $CH_2 – Cl_2$ **UN-nr: 1593**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 06-10-2016 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	1,000	810	710	620	NR	NR	NOEL for light-headedness and enunciation difficulties in humans.
AGW	6,000	4,200	2,000	740	350	210	Absence of AGW-related CNS effects in humans (10-30 min values) or cardiac effects in humans with coronary artery disease. (4% COHb) (1-8 hour values)
LBW	42,000	30,000	24,000	19,000	17,000	7,400	Lethality threshold based on CNS effects in rats (10 min-4 hour values) or the threshold for significant increased likelihood of fatality in humans (40% COHb) (8 hour value)

Derivation of the Dutch Intervention Values

VRW: For the derivation of the VRW values a study in humans was used. In the study 1-h exposures to concentrations of 868 and 986 ppm (3,064 respectively 3,482 mg/m³) may lead to light-headedness and difficulties in enunciation, whereas these effects were absent at a 1-h exposure to 514 ppm (1,815 mg/m³). Therefore, 514 ppm (1,815 mg/m³) was used as point of departure for the derivation of the VRW values. The human brain concentration following a 1-h exposure to 514 ppm (1,815 mg/m³) was calculated to be 0.063 mM, using a human PBPK-model. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. The human PBPK-model was used to calculate external exposure concentrations resulting in a maximum brain concentration of 0.021 mM at the end of exposure periods of 10-minutes, 30-minutes, 1-hour, 4-hours and 8-hours. The exposure concentrations for the respective durations are 290 ppm (1,024 mg/m³), 230 ppm (812 mg/m³), 200 ppm (706 mg/m³), 160 ppm (565 mg/m³) and 140 ppm (494 mg/m³). Interpolation of the data was used to derive the corresponding concentration for a 2-hour exposure, namely 175 ppm (618 mg/m³). VRW values at 4- and 8-h are not recommended because the exposure concentrations are at or above the corresponding AGW concentration values.

AGW: The AGW values are derived based on two different endpoints: formation of carboxyhemoglobin (COHb) and CNS-depression. The critical effect changes from CNS-depression to COHb formation from shorter to longer exposure durations. A PBPK-model was used to estimate the critical endpoint in relation to exposure duration and to derive the respective AGW values from internal dose metrics.
The available experimental human data address neurobehavioural endpoints that are sensitive, subtle effects that may be indicative of more severe effects at higher concentrations. In the absence of more adequate data the highest concentration-time combination tested (751 ppm (2,652 mg/m³) for 230 min) is regarded as appropriate PoD for CNS-depression. The methylene chloride concentration in brain (internal dose metric for CNS-depression) equivalent to a 230-min exposure to the NOAEL of 751 ppm (2,652 mg/m³) was estimated to be 0.137 mM using a human PBPK-model. Because effects observed at 751 ppm (2,651 mg/m³) are very mild and occur at an exposure concentration that is far below the level that would impair the ability to escape, an intraspecies factor of 1, instead of the default factor of 3 is considered sufficient. This results in a maximum target concentration of methylene chloride in human brain of 0.137 mM. The human PBPK-model was used to determine the methylene chloride concentrations in the air for up to 8-hours that will result in a maximum brain concentration of 0.137 mM. The AGW values for methylene chloride that are based on the formation of COHb have to be in compliance with the AGW values for carbon monoxide that are set at a maximum COHb level of 4%. The human PBPK-model was used to

calculate the concentration-time curves for methylene chloride exposure resulting in a maximum COHb level of 4% for subjects lacking GSST-1 who show a higher formation of COHb.
AGW values for the 10- and 30-min time periods, respectively 1,700 ppm (6,004 mg/m^3) and 1,200 ppm (4,238 mg/m^3), are based on CNS-effects, whereas the values for the 1-, 4- and 8-h time periods, respectively 560 ppm (1,987 mg/m^3), 100 ppm (353 mg/m^3) and 60 ppm (212 mg/m^3), are based on a maximum additional COHb level of 4%. Interpolation of the data was used to derive the corresponding concentration for a 2-hour exposure, namely 210 ppm (742 mg/m^3).

LBW: Human mortality can either be caused by CNS-depression leading to loss of consciousness and respiratory depression, resulting in narcosis, coma, hypoxia and death or by COHb formation leading to a cardiac arrest. Similarly as for AGW values, a PBPK-model was used to estimate the critical endpoint in relation to exposure duration and to derive the respective LBW values from internal dose metrics.
With respect to mortality due to CNS-depression, the 4-h exposure to 11,000 ppm (38,847 mg/m^3) at which no mortality was observed in rats (Haskell Laboratory, 1982) is regarded to be an appropriate PoD. Using the PBPK-model for the rat, a maximum target methylene chloride concentration in rat brain of 3.01 mM was calculated. An interspecies factor of 1 was applied because differences in susceptibility regarding mortality between species are small and a human PBPK-model is used to calculate the external exposure concentrations, thereby discounting the pharmacokinetic differences between rat and human. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Application of an overall UF of 3 results in a maximum target methylene chloride concentration in human brain of 1.0 mM. The human PBPK-model was subsequently used to calculate the DCM concentrations in environmental air for exposure of up to 8 hours that will result in a maximum brain concentration of 1.0 mM. For mortality due to COHb formation, LBW values have to be in compliance with the LBW values for carbon monoxide that are based on a lethality threshold of 40% COHb. Using the default intraspecies of 3 this corresponds to a COHb level of about 15% in adults. The human PBPK-model was used to calculate the concentration-time curves for methylene chloride exposure resulting in a maximum COHb level of 15% for subjects lacking GSST-1 who show a higher formation of COHb.
For exposure durations longer than 4-hours, the formation of COHb is the most important endpoint; the 8-hour LBW value is 2,100 ppm (7,400 mg/m^3). The LBW values for the 10-min, 30-min, 1-hour and 4-hour time periods are based on CNS-depression and are 12,000 ppm (42,000 mg/m^3), 8,500 ppm (30,000 mg/m^3), 6,900 ppm (24,000 mg/m^3) and 4,900 ppm (17,000 mg/m^3), respectively. Interpolation of the data was used to derive the corresponding concentration for a 2-hour exposure, namely 5,400 ppm (19,062 mg/m^3).

Additional toxicological information (including relevant results of a general literature search, if any)

The metabolism of methylene chloride takes place via two routes. For low concentrations the predominant route is oxidation by a saturable oxidative (Mixed Function Oxydase (MFO)) microsomal pathway (by cytochrome P450). Microsomal oxidation of methylene chloride leads to the formation of formyl chloride, which can result in the formation of CO leading to COHb formation or to CO_2 via a reaction with GSH. For higher concentrations, the predominant route is the direct conjugation of methylene chloride via a (first-order) glutathione (GSH) cytosolic pathway (by GSTT1-enzymes) and finally leads to CO_2 formation. The enzymes in the MFO-pathway have a higher affinity for methylene chloride than the GSTT1-enzymes but this pathway is saturable. More carbon monoxide will be formed in non-conjugators (subjects lacking GSTT1) leading to higher COHb levels. The most sensitive subpopulation for the endpoint of COHb formation consists of non-conjugators with severe coronary artery disease.

Acute exposure to methylene chloride may lead to CNS-depression and COHb formation. CNS depression is related to the brain concentration of methylene chloride itself and may occur soon after the onset of exposure. The peak level of COHb may occur hours after the end of exposure, depending on the methylene concentration and exposure duration. COHb formation may lead to cardiac arrest due to a blockade of junctional channels in cardiomyocytes. CNS-depression may lead to loss of consciousness and respiratory depression, resulting in narcosis, coma, hypoxia and finally death.

No human data on developmental or reproductive toxicity after acute exposure were found. No clear teratogenic or adverse developmental effects were observed in rats at exposure levels up to 4,500 ppm (15,885 mg/m^3). A 2-generation study in rats exposed to methylene chloride concentrations of up to 1,500 ppm (5,295 mg/m^3) revealed no exposure-related changes.
Overall, the data indicate that methylene chloride is not genotoxic *in vivo*..

H351: Suspected of causing cancer.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: 2A (probably carcinogenic to humans) Derivation of the carcinogenic risk potency (CRP): 10^{-4} risk level after inhalation: $10^{-4}/4.7 * 10^{-4}$ mg/m^3 = 2.13 x 10^{-1} mg/m^3 [NTP, 1986] CRP = (10^{-4} risk level * average life span in hours)/DRCF = (2.13 x 10^{-1} mg/m^3* 613,200) /2.8 =46,600 mg/m^3	Odour: pungent, sweetish, chloroform like odour No LOA was derived (due to lack of data)

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **710**	*AEGL-1* 710	*ERPG-1* 1,100		*IDLH: 8,100 (30 min)*
AGW level **2,000**	*AEGL-2* 2,000	*ERPG-2* 2,700		
LBW level **24,000**	*AEGL-3* 24,000	*ERPG-3* 14,000		

Stofdocument deel A

CAS-nr: 78-93-3 **Methylethylketon** $CH_3COCH_2CH_3$ **VN-nr: 1193**
GEVI: 33

Synoniemen: MEK, ethylmethylketon, 2-butanon (Engels: methyl ethyl ketone) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	600	600	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	1000	720	570	450	360	260
Levensbedreigende waarden	LBW (mg/m³)	18000*	18000*	9200*	4600	2300	1100

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,333 ppm; 1 ppm = 3,00 mg/m³

Explosiegrens:
LEL = 1,8 Vol% ≈ 54.000 mg/m³
* berekende interventiewaarde hoger dan 10% LEL

Geur: onaangename, scherpe, zoete geur
LOA: 366 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,2

Molecuulmassa: 72,1 g/mol
Zuurgraad: pH 7
LogKow: 0,3
Wateroplosbaarheid: 29 g/100 ml
Verzadigde dampdruk: 105 mbar

Overige informatie

Publieke grenswaarde:
590 mg/m³ (8 uur)
900 mg/m³ (15 min)
(huid)
MAK: 600 mg/m³
TLV-TWA: 600 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: irritatie van ogen, huid en luchtwegen, hoesten

AGW → LBW: hoofdpijn, ernstige irritatie van luchtwegen en ogen, duizeligheid, misselijkheid, sufheid, bewustzijnsdaling, effecten op ongeboren vrucht

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt irriterend op de ogen en de luchtwegen.
- De stof kan inwerken op het centrale zenuwstelsel met als gevolg hoofdpijn, duizeligheid en bewustzijnsdaling.
- Blootstelling kan tot bewusteloosheid leiden.
- Methylethylketon kan embryotoxiciteit veroorzaken

Effecten bij blootstelling aan vloeistof

Huidcontact: droge huid

Oogcontact: roodheid, pijn, branderig gevoel, (reversibele) hoornvliesbeschadiging

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust en onmiddellijk arts raadplegen

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en onmiddellijk arts raadplegen.

***Specifieke behandeling en materialen**: geen.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 78-93-3 **methyl ethyl ketone** $CH_3COCH_2CH_3$ **UN-nr: 1193**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 1 hour value and longer durations not applicable

AGW: Different point of departure, different uncertainty factors, 2 hour value added and time scaling across all time points

LBW: Different point of departure, different uncertainty factors, 2 hour value added and time scaling across all time points

Date: November 2015 | AEGL document: Final, 2011

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	600	600	NA	NA	NA	NA	NOAEL for sensory irritation and CNS effects in humans
AGW	1,000	720	570	450	360	260	Threshold for developmental effects in rats and mice
LBW	18,000*	18,000*	9,200*	4,600	2,300	1,100	Threshold for lethality in rats

* value higher than 10% of LEL

Derivation of the Dutch Intervention Values

VRW: Several clinical studies revealed that exposure to methyl ethyl ketone at variable concentrations ranging from 10 ppm (30 mg/m³) to 380 ppm (1,136 mg/m³) over 4 hours (with five 8-minute peaks to 380 ppm, TWA is 188 ppm) did not result in adverse effects. Also continuous exposure to 100 (300 mg/m³) or 200 ppm (598 mg/m³) for 2 or 4 hours did not result in sensory irritation or CNS effects. Because a steady-state would be approached relatively fast at low concentrations and methyl ethyl ketone is rapidly metabolized the 200 ppm (598 mg/m³) concentration was considered to be appropriate as a NOAEL level for sensory irritation and CNS effects for all VRW durations. However, this would not result in VRW effects below AGW levels at all time points. Therefore, VRW values were not applicable for exposure durations longer than 30 minutes.

AGW: Two developmental toxicity studies in rats and two studies in mice, where animals were exposed to 0, 400, 1,000 or 3,000 ppm (0, 1200, 3,000 or 9,000 mg/m³, respectively) for 7 hr /day during gestation day 6-15, showed a significant increase in fetal malformations (e.g. delayed ossification, skeletal effects and soft tissue anomalies) at 3000 ppm (9000 mg/m³) in both species as compared to controls. It was concluded that 1,000 ppm (3,000 mg/m³) could be considered a NOAEL for developmental effects. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The AGW values were time-scaled from the 7-h POD value using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively.

LBW: The LBWs were based on a 4 hour rat lethality study. The 4 hour LC_{01} of 22,900 mg/m³ calculated using DoseResp was used as point of departure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was performed using the equation $C^n \times t = k$, using the default values of n=1 for all timepoints based on the finding that no mortality was observed after a 30 min exposure at 92,239 ppm (275,795 mg/m³). Because timescaling would lead to a 10 min value (55,000 mg/m³) above the LEL of 54,000 mg/m³, the 10 min value was set equal the 30 min value.

Additional toxicological information (including relevant results of a general literature search, if any)

Methyl ethyl ketone is a hydrophilic solvent which in relatively high concentrations could lead to irritation of the nose and eyes and depression of the central nervous system (CNS). The anesthetic action of methyl ethyl ketone is not well understood, however it may involve interaction with cell membranes or changes in the membrane-bound receptors.

No data on developmental and reprotoxic effects in humans were located. Results in a series of

developmental studies in mice and rats determined that 3,000 ppm (9,000 mg/m^3) was toxic to the fetus, which resulted in a reduction of the fetal body weight and bone abnormalities.

H319: Causes serious eye irritation, H336: May cause drowsiness or dizziness

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived	Odour: unpleasant, sharp, sweet odour Odour threshold: 23.4 mg/m^3 [Devos et al., 1990] LOA = 11.8 * 23 mg/m^3 * 1.33 =366 mg/m^3 (The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT$_{50}$) + 0.5. A correction factor of 1.33 is applied to this value) The LOA lies below the VRW values.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **NA**	*AEGL-1* 586	*ERPG-1* -		*IDLH: 8,900 (30 min)*
AGW level **570**	*AEGL-2* 7,911	*ERPG-2* -		
LBW level **9,200**	*AEGL-3* 11,720	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 60-34-4 | **Methylhydrazine** | **H_2N-NH-CH_3** | **VN-nr: 1244** | **GEVI: 663**

Synoniemen: monomethylhydrazine (Engels: monomethylhydrazine) | ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	39	12	6,0	2,9	1,4	0,67
Levensbedreigende waarden	LBW (mg/m³)	120	37	18	8,7	4,3	2,0

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,522 ppm; 1 ppm = 1,92 mg/m³

Explosiegrens: LEL = 2,5 Vol% ≈ 48.000 mg/m³

Geur: ammoniakachtig, visachtig

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze rokende vloeistof
Brand: zeer brandgevaarlijk
Damp mengt gemakkelijk met lucht, explosiegevaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,03

Molecuulmassa: 46,1 g/mol
Zuurgraad: geen data
LogKow: -1,1
Wateroplosbaarheid: 100 g/100 ml
Verzadigde dampdruk: 48 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 0,019 mg/m³ (huid)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: irritatie van ogen, huid en luchtwegen, hoesten, keelpijn

AGW → LBW: misselijkheid, braken, benauwdheid, duizeligheid, hoofdpijn, stuiptrekkingen, toevallen

Boven LBW: sterfte

LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt irriterend tot bijtend op de ogen, de huid en de luchtwegen.
- Blootstelling aan de stof kan uitwerking hebben op het zenuwstelsel.
- De uitwerking kan vertraagd intreden.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, brandwonden. De stof wordt door de huid opgenomen.
Oogcontact: bijtend, roodheid en pijn, slecht zien.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: 0,46 mg/m³ (herhaalde blootstelling nodig voor carcinogeen effect)

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding, direct spoedeisende medische hulp inzetten

Ontsmetting vloeistof
huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, spoelen met veel water / kleding verwijderen, direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 60-34-4 **Monomethylhydrazine** **H_2N-NH-CH_3** **UN-nr: 1244**

Basis for the Dutch Intervention Values

VRW: Not recommended (in accordance with AEGL)

AGW: AEGL value is adopted, 10 min value added, 2h value added

LBW: AEGL value is adopted, 10 min value added, 2h value added

Date: November 2015 | AEGL document: Final 2000

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	not recommended
AGW	39	12	6.0	2.9	1.4	0.67	One third of LBW
LBW	120	37	18	8.7	4.3	2.0	LC_{01} in squirrel monkeys

Derivation of the Dutch Intervention Values

VRW: A study with healthy volunteers revealed that a 10-min exposure to 90 ppm (173 mg/m³) monomethylhydrazine resulted in irritation of eyes, nose and throat. Although these effects are considered relevant for derivation of VRW-values, the data are not considered appropriate as they are not compatible with the AGW and LBW values that were derived from animal data. The data also suggest that there is little difference between exposure resulting in no response and exposures causing irreversible effects and lethality. The VRW values are therefore not recommended.

AGW: The various studies did not provide adequate data that described irreversible nonlethal effects of acute exposure. Although the occurrence of hemolysis without mortality in rhesus monkeys at an 1-hour exposure to a concentration of 160 ppm (307 mg/m³) would be a relevant effect for AGW, it is inacceptably close to the mean concentration of 170 ppm leading to 66% mortality in rhesus monkeys (1-hour LC_{50} of 162 ppm (311 mg/m³)). Overall, the data indicate that there is a very small window between exposure associated with lethality and exposure causing nonlethal reversible effects. Due to the absence of relevant data, the AGW values are estimated by dividing the LBW values by a factor 3.

LBW: Lethality data (1-hour LC_{50} values) are available for several animal species. The AEGL used the lowest available 1-hour LC_{50} value of 82 ppm (157 mg/m³) obtained from a study in squirrel monkeys as starting point for the AEGL-3. In contrast to the AEGL, LBW values were based on Cxt analysis using the squirrel monkey data in DoseResp. The resulting LC_{01} values were 353, 112, 54, 26, 13, 6.1 mg/m³ Although using the LC_{50} value would lead to similar LBW values, the use of calculated LC_{01} values leads to better substantiated values. A total uncertainty factor of 3 was considered sufficient to account for inter- and intraspecies differences, because squirrel monkeys are considered to be even more sensitive than humans and because a 10 min exposure to 173 mg/m³ only leads to irritation of the eyes, nose and throat in healthy human volunteers (see VRW).

Additional toxicological information (including relevant results of a general literature search, if any)

The exact mechanism of toxicity of monomethylhydrazine is uncertain. Exposure to monomethylhydrazine at sublethal doses shows subjects having tremors and convulsions and show behavioral changes. An alternate mechanism of toxicity is implied by other effects like, renal, hepatic and hemolytic toxicity. A steep concentration-response relationship appeared to be present for monomethylhydrazine.

Data on developmental and reproductive toxicity upon inhalation show that reproductive and developmental effects would be in the range of concentrations that also could cause maternal lethality. A teratogenicity study in rats in which groups of 14-18 pregnant rats were dosed intraperitoneally with 2.5, 5.0 and 10 mg monomethylhydrazine/kg bw/d on gestation day 6-15 revealed increased incidence of resorptions and eye abnormalities. However, findings were not considered definitive and close to levels causing maternal death.

No harmonized hazard sentences.

Carcinogenicity and derivation of the CRP value
IARC classification: not classified Derivation of the carcinogenic risk potency (CRP): 10^{-4} risk level after inhalation: $2.1*10^{-6}$ mg/m^3 [Kinkead et al., 1985] CRP = (10^{-4} risk level * average life span in hours)/DRCF = ($2.1*10^{-6}$ mg/m^3 * 613,200) /2.8 = 0.46 mg/m^3

Odour and derivation of the LOA value
Odour: ammonia-like or fishy odour Odour threshold: 1.92 mg/m^3 – 5.76 mg/m^3

Other standards and guidelines *(1h values in mg/m^3, unless otherwise indicated)*				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH: 38 (30 minutes)*
AGW level **6.0**	*AEGL-2* 1.7	*ERPG-2* -		
LBW level **18**	*AEGL-3* 5.1	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 624-83-9 **Methylisocyanaat** **CH_3-N≡C=O** **VN-nr: 2480**

GEVI: 663

Synoniemen: geen (Engels: methyl isocyanate) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	2,9	0,95	0,48	0,24	0,12	0,060
Levensbedreigende waarden	LBW (mg/m³)	20	6,6	3,3	1,6	0,82	0,41

Datum vaststelling: 20-10-2011

Conversiefactor: 1 mg/m³ = 0,421 ppm; 1 ppm = 2,38 mg/m³

Explosiegrens: LEL = 5,3 vol% ≈ 126.000 mg/m³

Geur: stekend

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,4

Molecuulmassa:	57,1 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	464 mbar

Overige informatie

Publieke grenswaarde: 0,05 mg/m³ (15 min)

MAK: 0,024 mg/m³

TLV-TWA: 0,048 mg/m³

Zeer reactief

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: irritatie aan ogen, neus en keel

AGW → LBW: effecten op de ongeboren vrucht, toenemende mate van irritatie, hoesten, keelpijn, tranenvloed, benauwdheid, CZS effecten, misselijkheid, braken, spierzwakte

Boven LBW: ademnood, hartstilstand, sterfte

LET OP: Mogelijk ligt de irritatiegrens boven het niveau dat systemische effecten veroorzaakt.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Methylisocyanaat werkt sterk irriterend op de slijmvliezen
- Methylisocyanaat kan embryotoxiciteit veroorzaken.
- Secundair aan hypoxie kunnen effecten op het CZS ontstaan.
- Overlijden kan plaatsvinden door het optreden van longoedeem of hartstilstand.
- Methylisocyanaat wordt beschouwd als een sensibiliserende stof.

Effecten bij blootstelling aan vloeistof

Huidcontact: irritatie, roodheid, pijn, brandwonden

Stof kan door de huid opgenomen worden!

Oogcontact: irritatie, roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 624-83-9 **Methyl isocyanate** **CH_3-N≡C=O** **UN-nr: 2480**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with the AEGL

AGW: Based on additional point of departure, different uncertainty factors used, 2h value added

LBW: Based on a different point of departure, 2h value added

Date: 20-10-2011 | AEGL document: Final, 2003

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	- (systemic effects can not be excluded)
AGW	2.9	0.95	0.48	0.24	0.12	0.060	Decreased fetal bodyweight, cardiac arrythmias, fetal death
LBW	20	6.6	3.3	1.6	0.82	0.41	Threshold of animal lethality

Derivation of the Dutch Intervention Values

VRW: The concentrations causing irritation in humans in a number of controlled human studies after several minutes of exposure (1-4 ppm; 2.4-9.5 mg/m³) are similar to, or higher than, the concentrations resulting in embryo and fetal lethality in well conducted animal studies. However as no NOAEL could be established for AGW effects (see below), systemic effects of methyl isocyanate at this exposure level cannot be excluded. Therefore, the results of controlled human exposures were not used in derivation of VRW and VRW values were not recommended.

AGW: The AGW-values were based on 3 animal studies. Mice (n=12-24) were exposed to 0, 2, 6, 9, 15 ppm (0, 4.8, 14, 21, 36 mg/m³) methyl isocyanate for 3 hours on day 8 of gestation. The LOEL for lower fetal body weights in the absence of maternal toxicity was an exposure of mice at 2 ppm (4.8 mg/m³) for 3 hours on day 8 of gestation. In the second animal study rats were exposed to 3, 10, 30 ppm (7.1, 24, 71 mg/m³) methyl isocyanate for 2 hours. The exposure of rats at 3 ppm (7.1 mg/m³) for 2 h was a LOEL for cardiac arrhythmias evaluated 4 months post-exposure. In contrast to the AEGL, the AGW-level was also based on an additional point of departure. In the third animal study (neonatal survival study with mice) pregnant mice were exposed to 0, 1, 3 ppm (0, 2.4, 7.1 mg/m³) methyl isocyanate for 6h/d on day 14-17 of gestation. Although the exposures were repeated on 4 consecutive days, the exposure to the fetus is considered similar to a single exposure because the stage of development and potential susceptibility changes daily throughout gestation and is different on each of the exposure days. In addition, the lower pup survival seen experimentally following repeated maternal exposure is the same end point as fetal and infant death in humans observed following accidental exposure. A significant increase in the total number of dead fetuses at birth was observed in both exposure groups (controls: 0.4%; 1 ppm (2.4 mg/m³): 3.3%; 3 ppm (7.1 mg/m³): 6.4%). The 6-h exposure at 1 ppm (2.4 mg/m³) was used as point of departure to derive AGW.
These three exposure concentration and duration scenarios yield identical AGW values when used for derivation. The experimental concentrations were reduced by a modifying factor of 3 to estimate a threshold for the observed effects. A total uncertainty factor of 10 was applied, including 3 for interspecies variation, because similar results for developmental toxicity have been obtained in both rats and mice, and 3 for intraspecies variation. Time scaling was performed using the equation $C^n \times t = k$, using n=1 (derived from rat LC_{50} values).

Human data relevant to AGW derivation are limited to studies that used very short exposure durations. Among volunteers exposed at 1 ppm (2.4 mg/m³) for 10 min, 7/7 had eye irritation and tears by 4 and 5 min, respectively, and nose and throat irritation were reported by 3/7 after 9 min. Eye irritation and tearing were also reported for individuals exposed at 2 or 4 ppm (4.8 or 9.5 mg/m³) for 1-5 min and at 0.5 ppm (1.2 mg/m³) for 10 min.

LBW: The LBW-values were based on mortality data from a rat study. Rats were exposed by inhalation to various concentrations methyl isocyanate (17.5-541 ppm; 41.7-1285 mg/m³) for 7.5-240 minutes. Point of departure was the 1-hour LC_{50}-value of 41.3 ppm (98 mg/m³). Based on the rat LC_{50} data in this study a n-value of 1 was calculated. The LC_{50}-value was divided by 3 to obtain an estimate of

the threshold for lethality. An uncertainty factor of 3 was used for interspecies variation and an uncertainty factor of 3 was used for intraspecies variation. Time-scaling was performed using $C^n \times t = k$, with the chemical-specific n-value of 1.

Additional toxicological information (including relevant results of a general literature search, if any)

The mechanism of action for the pulmonary, skin, and ocular toxicity is severe irritation to mucous membranes, but the mechanism of action for the systemic effects is unknown. The most frequently reported symptoms among a large population of accidentally exposed humans were burning of the eyes, coughing, respiratory distress from pulmonary congestion, watering of the eyes, nausea, vomiting, muscle weakness, and CNS involvement secondary to hypoxia. Death due to methyl isoscyanate exposure is attributed to pulmonary edema.

An increased rate of self-reported spontaneous abortions as well as a decrease in the number of live births among women pregnant at that time is described after the Bhopal disaster. Developmental and reproductive toxicity has also been shown in rats and mice following inhalation exposure to methyl isocyanate.

H301: Toxic if swallowed; H311: Toxic in contact with skin; H315: Causes skin irritation; H317: May cause an allergic skin reaction; H318: Causes serious eye damage; H330: Fatal if inhaled; H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled; H335: May cause respiratory irritation; H361d: Suspected of damaging the unborn child.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No information was found regarding the carcinogenic potential of methyl isocyanate in humans.

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: pungent

No LOA was derived due to the absence of consistent odour perception. Methyl isocyanate has notoriously poor warning properties.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **NR**	*AEGL-1* NR	*ERPG-1* 0.059		*IDLH:* 7.1 (30 minutes)
AGW level **0.48**	*AEGL-2* 0.16	*ERPG-2* 0.59		
LBW level **3.3**	*AEGL-3* 0.48	*ERPG-3* 3.6		

Stofdocument deel A

CAS-nr: 74-88-4 **Methyljodide** **CH_3-I** **VN-nr: 2644** **GEVI: 66**

Synoniemen: joodmethaan, monojoodmethaan (Engels: methyl iodide) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	96	67	53	53	53	53
Alarmeringsgrenswaarden	AGW (mg/m³)	330	230	183	183	183	183
Levensbedreigende waarden	LBW (mg/m³)	3.000	2.100	1.700	1.300	1.100	530

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,169 ppm; 1 ppm = 5,90 mg/m³

Explosiegrens: LEL=8,5 vol% ≈ 500.000 mg/m³

Geur: zoete etherische geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot gele vloeistof

Brand: moeilijk brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,7

Molecuulmassa:	141,9 g/mol
Zuurgraad:	geen data
LogKow:	1,6
Wateroplosbaarheid:	0,9 g/100 ml (slecht)
Verzadigde dampdruk:	441 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 12 mg/m³ H

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen klachten

VRW → AGW: lichte irritatie van de ogen en neus, zwaktegevoel, duizeligheid, misselijkheid, sufheid

AGW → LBW: irritatie van de ogen, neus en luchtwegen, coördinatie- en spraakstoornissen, slecht zien, lethargie, slaperigheid

Boven LBW: mogelijk na een symptoomvrij interval: opwinding, toevallen, verwardheid, delier, coma en sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt irriterend op de ogen, de huid en de luchtwegen.
- De stof kan inwerken op het centrale zenuwstelsel en de nieren met als gevolg functiestoornissen en nierschade.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn, branderig gevoel, brandwonden. De stof wordt door de huid opgenomen!

Oogcontact: roodheid en pijn, slecht zien

Carcinogeniteit

IARC classificatie: 3

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en onmiddellijk arts raadplegen.

ogen: zie hierboven.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 74-88-4 **Methyl iodide** **CH_3-I** **UN-nr: 2644**

Basis for the Dutch Intervention Values

VRW: Same point of departure as for AEGL, but using different n-value, different time-scaling, 2h value added

AGW: Different point of departure as for AEGL and using different n-value, different time-scaling, 2h value added

LBW: Different point of departure, different n-value, 2h value added

Date: 06-10-2016 AEGL document: proposed, 2009

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	96	67	53	53	53	53	Threshold for neurotoxic effects in rats
AGW	330	230	183	183	183	183	Threshold for convulsions in rats
LBW	3,000	2,100	1,700	1,300	1,100	530	Threshold for lethality in rats

Derivation of the Dutch Intervention Values

VRW: In a study in rats, groups of 12 male and 12 female rats were exposed to 0 ppm, 27 ppm (159 mg/m^3), 93 ppm (549 mg/m^3) and 401 ppm (2,366 mg/m^3) for 6 hours. The results show that exposures up to 27 ppm (159 mg/m^3) for 6 hours can be considered to be the NOAEL for neurotoxicity. The threshold for neurotoxic effects is considered to be protective for respiratory effects. An exposure to 159 mg/m^3 for 6 hours is used as a point of departure for the derivation of the VRW values. Based on a higher blood:air partition coefficient for rats than humans, uptake is higher in rats than humans. Therefore, an interspecies uncertainty factor of 1 is considered sufficient. The default intraspecies uncertainty factor of 3 is considered sufficient to account for intraspecies variability. The VRW was set equal for the time points of 1 hour to 8 hour because CNS-effects are generally concentration-dependent but not time-dependent. The 10 min and 30 min values were set using time-scaling because plasma steady-state levels are not reached until 1 hour. For these time points, time scaling was performed using the equation $C^n \times t = k$, using the default value for n of 3 to extrapolate to shorter exposure durations.

AGW: In a study in rats, groups of 12 male and 12 female rats were exposed to 0 ppm, 27 ppm (159 mg/m^3), 93 ppm (549 mg/m^3) and 401 ppm (2,366 mg/m^3) for 6 hours. At 93 ppm (549 mg/m^3) signs of neurotoxicity were observed which included convulsions, decreased body temperature and decreased motor activity. The neurotoxicity signs were limited to the day of exposure. An exposure to 93 ppm (549 mg/m^3) for 6 hours was considered as a point of departure for derivation of the AGW values. Based on a higher blood:air partition coefficient for rats than humans, uptake is higher in rats than humans.. Therefore, an interspecies uncertainty factor of 1 was considered sufficient. The default intraspecies uncertainty factor of 3 was considered sufficient to account for intraspecies variability. The AGW was set equal for the time points of 1 hour to 8 hour because CNS-effects are generally concentration-dependent but not time-dependent. The 10 min and 30 min values were set using time-scaling because plasma steady-state levels are not reached until 1 hour. For these time points,time scaling was performed using the equation $C^n \times t = k$, using the default value for n of 3 to extrapolate to shorter exposure durations.

LBW: LBW-values were derived based on a rat 4h acute inhalation toxicity study. Rats were exposed for 4 hour to exposure concentrations of 581, 70, 797 and 1198 ppm (corresponding to 3428, 4189, 4702 and 7068 mg/m^3). The 4h LC01 was calculated using Doseresp and was 3165 mg/m^3. This was used as point of departure for deriving the LBW values. Based on a higher blood:air partition coefficient for rats than humans, uptake is higher in rats than humans. Therefore, an interspecies uncertainty factor of 1 was considered sufficient. The default intraspecies uncertainty factor of 3 was considered sufficient to account for intraspecies variability. Time scaling was performed using the equation $C^n \times t = k$, using the default values for n of 1 and 3 to extrapolate to longer and shorter exposure durations, respectively.
The resulting LBW values for 10 min to 1hour durations are supported by results of a second rat

acute inhalation toxicity data using a 1 hour exposure duration.

Additional toxicological information (including relevant results of a general literature search, if any)

The studies that are available identify three main effects that are the result of exposure to methyl iodide, namely nasal lesions (rat), acute neurotoxicity (rat) and fetal loss in rabbits. The nasal lesions are suggested to be the result of glutathione depletion. The transient neurotoxicity in rats is most likely the result of the modification of ion currents in nerve cells and the rabbit fetal resorptions are probably the result of the modulation of the thyroid hormones by iodine. In humans, an acute iodine load can cause a transient decrease in thyroid hormone production and a transient increase in TSH. During pregnancy and lactation, iodine requirements are higher than normal and sufficient iodine for synthesis of thyroid hormone is important for normal brain development in the developing embryo and fetus.

For methyl halides, toxicity increases according to atomic weight, in the order methyl chloride, methyl bromide, and methyl iodide.

Inter-individual variation in the rate of metabolism of methyl halides has been observed in humans. At least two distinct populations of humans with differences in the rate of metabolism of the structurally-similar methyl chloride have been identified. Fast metabolism may lead to the formation of toxic metabolites that can exert their action before they can be eliminated whereas slow metabolizers would be expected to be less susceptible to the toxic effects of methyl halides.

No studies were located regarding reproductive or developmental effects in humans after inhalation of methyl iodide. However, in developmental studies, rabbits, but not rats, were sensitive to the fetotoxic effects of methyl iodide. A developmental toxicity study in rabbits (exposure 6h/day during GD 6-19) showed an increase in fetal losses and post-implantation loss. These effects were observed for exposure concentrations at 26 ppm (153 mg/m^3) and higher, though in presence of maternal toxicity. Based on a comparative metabolism study in rat, rabbit and human, it was shown that methyl iodide was well metabolized in most of the tissue cytosol samples, but not in blood or fetal rabbit kidney. Further, it was shown that the rabbit fetus does not regulate the uptake of iodine and is therefore not a good model for human iodine-induced fetotoxicity.

H351: Suspected of causing cancer, H331: Toxic if inhaled, H301: Toxic if swallowed, H312: Harmful in contact with skin, H315: Causes skin irritation, H335: May cause respiratory irritation

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to its carcinogenicity to humans)

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: sweet, ethereal odour

No LOA was derived (due to a lack of data)

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **53**	*AEGL-1* 130	*ERPG-1* 150		*IDLH: 590 mg/m^3*
AGW level **183**	*AEGL-2* 480	*ERPG-2* 300		
LBW level **1,700**	*AEGL-3* 1,700	*ERPG-3* 740		

Stofdocument deel A

CAS-nr: 74-93-1 **Methylmercaptaan** CH_3SH **VN-nr: 1064** **GEVI: 263**

Synoniemen: mercaptomethaan, methaanthiol, methylsulfhydraat (Engels: Methylmercaptan) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	5,1	4,0	3,4	2,9	2,5	2,1
Alarmeringsgrenswaarden	AGW (mg/m³)	83	57	46	36	29	14
Levensbedreigende waarden	LBW (mg/m³)	250	170	140	110	86	43

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,500 ppm; 1 ppm = 2,00 mg/m³

Explosiegrens: LEL = 3,9 vol% ≈ 78.000 mg/m³

Geur: typerende walgingwekkende geur (rotte koolgeur)

LOA: 0,0038 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos, onder druk tot vloeistof verdicht gas

Brand: zeer brandgevaarlijk

Relatieve dichtheid: 1,7

Molecuulmassa:	48,1 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	2,3 g/100 ml (matig)
Verzadigde dampdruk:	1700 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: 1,0 mg/m³

TLV-TWA: 1,0 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	mogelijk lichte oogirritatie en hoofdpijn, misselijkheid
VRW → AGW:	oogirritatie, tranenvloed, lichte irritatie van de luchtwegen
AGW → LBW:	benauwdheid, longoedeem, ophoesten bloed, hyperventilatie, hoornvliesbeschadiging, fotofobie, misselijkheid en braken, hoofdpijn, duizeligheid, verwarring/opwinding, pijn op borst, bewustzijnsdaling
Boven LBW:	ademstilstand, convulsies, collaps, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Methylmercaptaan blokkeert de ademhalingsketen in de cel. Hierdoor wordt de energiehuishouding verstoord en kan lactaatacidose ontstaan.
- Primaire doelorganen zijn het centrale zenuwstelsel en het cardiovasculaire systeem.
- Methylmercaptaan werkt in lage concentraties irriterend op de ogen en luchtwegen.
- De stof kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Verlamming van de geurzenuw kan optreden bij hoge concentraties, waardoor de geurwaarneming en het daarmee gepaard gaande waarschuwingssignaal achterwege kan blijven.
- Door de snelle activering van sulfide in het lichaam wordt de toxiciteit van methylmercaptaan met name bepaald door de concentraties en minder door de blootstellingsduur.

Effecten bij blootstelling aan vloeistof

Huidcontact: bij bevriezing: roodheid, pijn, wonden

Oogcontact: bij bevriezing: roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, 100% zuurstof, halfzittende houding, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: aan de huid vastgevroren kleding NIET lostrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen..

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas).

Specifieke behandeling en materialen: Bij vergiftiging door deze stof is specifieke eerste hulp noodzakelijk; specifieke antidota (o.a. 100% zuurstof) moeten met gebruiksaanwijzing ter plekke beschikbaar zijn. Voor aanwijzingen over verdere behandeling zo nodig het NVIC (+31(0)30-274 88 88) bellen.

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 74-93-1 **Methyl mercaptan** **CH_3SH** **UN-nr: 1064**

Basis for the Dutch Intervention Values

VRW: In contrast to AEGL values are derived for all time points based on the VRW for H_2S

AGW: AEGL value is adopted, 2h value added and time scaling applied for 10-min value

LBW: AEGL value is adopted, 2h value added and time scaling applied for 10-min value

Date: November 2015 | AEGL document: final 2013

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	5.1	4.0	3.4	2.9	2.5	2.1	Based on VRW for H_2S (headache)
AGW	83	57	46	36	29	14	One-third of LBW-value
LBW	250	170	140	110	86	43	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: The database of methyl mercaptan is insufficient for the derivation of VRW values. Therefore, the AEGL does not recommend AEGL-1 values. However, the comparability of the toxicity profile of methylmercaptan with the less toxic ethylmercaptan and the equally or more toxic hydrogen sulfide suggests that VRW values for methyl mercaptan should lie between 0.33 and 1.0 ppm (0.66 and 2.0 mg/m³, respectively). One molecule of methylmercaptan may form one molecule of H_2S, but it is unknown to what extent this hydrolysis occurs. Since it is not completely clear whether methyl mercaptan is less toxic than hydrogen sulfide, it is proposed to use the same VRW levels on a ppm basis.

The VRW-levels for hydrogen sulfide were based on a human volunteer study. Three of ten asthmatic volunteers exposed to 2 ppm (2.8 mg/m³) H_2S for 30 minutes complained of headache and eight of ten experienced (non-significant) increased airway resistance. Since there were no clinical symptoms of respiratory difficulty and there were no changes in FVC or FEV_1, the VRW was based exclusively upon increased complaints of headache. The values were scaled across time using $C^n \times t = k$, using the empirically-derived chemical specific value of 4.4 (derived from pooled rat lethality data ranging from 10 minutes to 6 hours exposure duration) for n. It was noted that the derivation of the value of n=4.4 is based on data derived from three different studies, which is not in line with the procedures of the Dutch expert panel on probits. However, using the data of a single rat study (Zwart et al., 1990) would result in an n with a very broad confidentiality range (-3.16-25) or would be either 2.8 or 7.8 based on two different mice studies (Zwart et al 1990 or Clanachan 1979.) both based on a very short time range (10 to 30 or 60 minutes, respectively). The third alternative, using the default values for n (n=1, n=3) would lead to unrealistically low AGW-values. Therefore, the n-value of 4.4, as used by AEGL, is adopted for derivation of LBW-values.

AGW: AGW-values were calculated as one-third of the LBW values according to the rationale of AEGL. In the absence of relevant data on methyl mercaptan and because of its steep concentration-response relationship for lethality. Those values are estimated thresholds for the inability to escape. The only observations consistent with the definition of AGW are from the study of SRI International(1996), in which shallow breathing and hypoactivity (an end point relevant to impairment of escape) were noted in mice exposed to methyl mercaptan at 258 ppm (516 mg/m³) for 6 h. However, this concentration is close to the lethality thresholds for mice and rats and, therefore, cannot be used as a basis for AGWs. The lethality data also demonstrate a steep concentration-response relationship for methyl mercaptan. Lethality in rats after a 4-h exposure to methyl mercaptan was 20% (2/10) at 600 ppm (1200 mg/m³) and 100% (10/10) at 700 ppm (1400 mg/m³), and the 4-h LC_{50} and LC_{01} values were 675 ppm (1350 mg/m³) and 430 ppm (860 mg/m³), respectively (Tansy et al. 1981). AEGL-2 values are considered protective because rats exposed to methyl mercaptan at 57 ppm (114 mg/m³) for 7 h/day, 5 days/week for 3 months experienced only decreased body weight and decreased serum albumin (Tansy et al. 1981). Also, workers exposed to methyl mercaptan at concentrations up to 15 ppm (30 mg/m³) experienced only headache and trouble concentrating (Kangas et al. 1984). However, the

workers were also simultaneously exposed to hydrogen sulfide, dimethyl sulfide, and dimethyl disulfide.

LBW: The LC_{01} of 430 ppm (860 mg/m^3) in rats exposed to methyl mercaptan for 4 hours was used to derive the LBW values. The LC_{01} value was calculated from an acute inhalation study using 5 animals/sex/concentration and concentrations of 0, 400, 600, 650, 680, 690, 700 (twice), and 800 ppm (resp. 800, 1,200, 1,300, 1,360, 1,380, 1,400 and 1,600 mg/m^3). An intraspecies uncertainty factor of 3 was applied based on the steepness of the concentration-response relationship in the key study. An interspecies uncertainty factor of 3 was applied, because application of a higher factor would yield values that are inconsistent with the total data base; e.g. the LBW values would range from 15-80 mg/m^3, whereas no effects were observed in rats exposed to 17 ppm (34 mg/m^3) methyl mercaptan for 7 hours/day, 5 days/week, for 3 months and occupational exposures at concentrations up to 30 mg/m^3 (with simultaneous exposure to hydrogen sulfide, dimethyl sulfide, and dimethyl disulfide) resulted in headache and trouble concentrating. Furthermore, the LBW values would be 2 to 4 fold lower than the LBW values for hydrogen sulfide, which has a comparable toxic mechanism, but is more toxic than methyl mercaptan (the lowest 4-hr LC_{50} for H_2S in rats is 444 ppm (630 mg/m^3), whereas the 4-hr LC_{50} for methyl mercaptan in mice is 675 ppm (1350 mg/m^3)). Time scaling was performed using the equation $C^n \times t = k$, with n=1 to extrapolate to longer time points and n=3 to extrapolate to shorter time points. In contrast to the 10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Ethylmercaptan, methylmercaptan and hydrogen sulfide have a comparable mechanism of toxicity, but differ in toxic potency in the following order: hydrogen sulfide > methylmercaptan > ethylmercaptan. Hydrogen sulfide and ethyl and methylmercaptan are both irritants and asphyxiants. In humans at relatively low concentrations (<10 ppm; 14 mg/m^3), minor ocular and respiratory irritation occur, while at higher concentrations (hundreds to thousands of ppm), the central nervous system is affected and paralysis of the respiratory center may lead to rapid death. Liver and kidney damage is also mentioned in literature, but is considered to be secondary to asphyxiation.

No data on developmental and/or reproductive toxicity were located.

H331: Toxic if inhaled

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Genotoxicity data are limited and equivocal and no data on carcinogenicity were located.

Odour and derivation of the LOA value

Odour: typical, revolting odour, comparable to decaying cabbage

ODT: 0.00024 mg/m^3 [AEGL]

LOA = 11.8 * OT_{50} * 1.33 = 0.0038 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **3.4**	*AEGL-1* NR	*ERPG-1* 0.01		*IDLH:* 300 mg/m^3 (30 minutes)
AGW level **46**	*AEGL-2* 43	*ERPG-2* 50		
LBW level **140**	*AEGL-3* 130	*ERPG-3* 200		

Stofdocument deel A

CAS-nr: 80-62-6 **Methylmethacrylaat** **$CH_2=C(CH_3)COOCH_3$** **VN-nr: 1247**

Synoniemen: methacrylzuur, methylester, methylmethacrylaat monomeer, 2-methylpropeenzure methylester (Engels: methyl methacrylate)

GEVI: 339

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	69	69	69	69	69	69
Alarmeringsgrenswaarden	AGW (mg/m³)	920	630	500	400	320	210
Levensbedreigende waarden	LBW (mg/m³)	4.300	3.000	2.400	1.900	1.500	750

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,240 ppm; 1 ppm = 4,16 mg/m³

Explosiegrens: LEL = 1,7 vol% ≈ 71.000 mg/m³
Damp met lucht explosief

Geur: Scherpe, fruitige geur
LOA: 13,7 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze vloeistof
Brand: Zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,09

Molecuulmassa:	100,1 g/mol
Zuurgraad:	geen data
LogKow:	1,4
Wateroplosbaarheid:	1,6 g/100 ml (matig)
Verzadigde dampdruk:	39 mbar

Overige informatie

Publieke grenswaarde:
410mg/m³ (8 uur)
MAK: 210 mg/m³
TLV-TWA: 210 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: irritatie neus, ogen, huid en keel, keelpijn en hoesten, duizeligheid, hoofdpijn

AGW → LBW: irritatie onderste luchtwegen, vertraagde ademhaling, benauwdheid, longoedeem, zwakte, verminderde reflexen, lever-, nier- en thymusschade

Boven LBW: ademnood, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Methylmethacrylaat werkt in lage concentraties irriterend op de huid en de neus door enzymatische omzetting in methacrylzuur.
- Bij blootstelling aan hogere concentraties kan de stof de onderste luchtwegen bereiken, wat kan resulteren in emfyseem, oedeem en klaplong.
- Methylmethacrylaat heeft effecten op het centrale zenuwstelsel, vermoedelijk via remming van de hypocampus en hypothalamus.
- Methylmethacrylaat kan bij zeer hoge concentraties schade veroorzaken aan onder andere lever, urinewegen en thymus.
- Methylmethacrylaat is sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie!

Effecten bij blootstelling aan vloeistof

Huidcontact: Prikkeling, roodheid, jeuk. De stof is ensibiliserend. Na sensibilisatie kan de stof huidallergie aken bij dermaal contact!

Oogcontact: Prikkeling, roodheid, pijn, slecht zien.

Carcinogeniteit

IARC classificatie: 3
CRP: niet afgeleid.

Beknopte medische informatie

Ontsmetting *damp*

algemeen: frisse lucht, rust en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 80-62-6 **Methyl methacrylate** **$CH_2=C(CH_3)COOCH_3$** **UN-nr: 1247**

Basis for the Dutch Intervention Values

VRW: AEGL value was adopted, 2h value added

AGW: AEGL value was adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value was adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 16-12-2010 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	69	69	69	69	69	69	NOEL for slight irritation in humans.
AGW	920	630	500	400	320	210	Threshold for irreversible effects on the olfactory epithelium in rats
LBW	4,300	3,000	2,400	1,900	1,500	750	$BCML_{05}$ for lethality in rats

Derivation of the Dutch Intervention Values

VRW: VRW values are based on medical examinations of 91 workers in poly-methyl methacrylate-sheet-production plants, which revealed no significant acute effects (no cardiovascular changes, no effects on lung function and no effects in the upper respiratory tract) at measured exposure of 25-50 ppm (100-210 mg/m³) for the 8 hour workday. From this study, a no adverse effect concentration for irritation of 50 ppm (210 mg/m³) is derived. An uncertainty factor of 3 is used to extrapolate from workers to the general public including sensitive subpopulations. No time scaling was applied because the point of departure is considered a NOEL for slight irritation.
The approach is supported by the results from animal studies. Reversible degenerative effects on the olfactory mucosa were observed in rats after single exposure to 110 ppm (460 mg/m³) for 6 hours. The severity of injuries is judged above VRW levels necessitating a modifying factor of 2. Due to the lower susceptibility of humans against methyl methacrylate-exposure to the nasal tissue the interspecies uncertainty factor would be reduced to 1. To cover interindividual differences, an intraspecies uncertainty factor of 3 would be chosen. Application of the overall uncertainty/modifying factor of 6 to 110 ppm (460 mg/m³) gives a nearly identical VRW (76 mg/m³) as derived based on human data.

AGW: Irritating effects on the respiratory tract and degeneration, atrophy and necrosis of olfactory epithelium are considered as most relevant endpoints for AGW derivation. The target tissue at lower exposure is the olfactory epithelium and injuries have been observed in various rat studies.
Nasal toxicity of methyl methacrylate was studied in 5 rats exposed to 200 ppm (833 mg/m³) for 6 hours. Degeneration of olfactory epithelium was observed in 3 of the 5 animals. In a second study, rats were exposed to 0 or 200 ppm (833 mg/m³) for 3 or 6 hours. Nasal passages of the 3 hour-exposed rats showed no morphological abnormalities compared with control rats. Exposure for 6 hours led to degeneration/atrophy of the olfactory epithelium. Based on these studies, exposure to 200 ppm (830 mg/m³) for 6 hours is considered as point of departure for the AGW values.
Because several studies suggest that humans are less susceptible than rats regarding effects on the nasal cavity and no major differences in toxicodynamics are expected the interspecies factor is reduced to 1. An uncertainty factor of 3 to account for susceptible populations was chosen. Time scaling was performed using the equation $C^n \times t = k$, using the default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: The $BMCL_{05}$ of 3,613 ppm (15,000 mg/m³) for a 4 hour exposure derived from the analysis of the combined data from two rat lethality studies was used as the point of departure for the LBW values. Although several studies dealing with the toxic effects of methyl methacrylate as well as its metabolism suggest that humans are less susceptible than rats regarding effects on the nasal cavity, this conclusion is probably not valid for other parts of the respiratory tract. Therefore an interspecies factor of 3 was chosen. In addition, an uncertainty factor of 3 to account for susceptible populations was chosen. Time scaling was performed using the equation $C^n \times t = k$, using the default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. In contrast to the

10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Methyl methacrylate is irritant to skin and mucosa of the respiratory tract. The lung is the major site of injury at high concentrations. The absorption and hydrolysis of methyl methacrylate to methacrylic acid by local nasal tissue esterases has been considered as the main reason for olfactory toxicity. The lesions are seen in that part of mucosa with the highest level of carboxylesterase activity. For humans this would be the whole epithelium including sensory cells, basal cells, and sustentacular cells, as well as the submucosal glands. Carboxylesterase activity in nasal tissue is several times higher in rats than in humans and primary located in the olfactory epithelium. At higher exposure (>1,000 ppm, 4,200 mg/m^3) not all the methyl methacrylate will be removed by the upper respiratory tract and methyl methacrylate reaches the lung, resulting in pulmonary effects (dyspnea, emphysema, edema, and collapsed lungs) and CNS effects. It was concluded that the mechanism of toxicity at higher concentration of methyl acrylate and other esters is related to the depletion of non-protein sulfhydryl in various tissues. It was suggested that the reduced appetite reported from human studies is due to effects of methyl methacrylate on the hypothalamus and hippocampus as reduced neuronal firing rates were observed after inhalation exposure. Such correlations seem plausible because of the way that the hypothalamus and the superimposed hippocampus control the vegetative nervous system. Therefore all other observed effects related to the central nervous system (decrease of reflex activity, motor weakness, increased gastrointestinal activity and excretion, effects on respiratory rate and cardiovascular system) possibly result from these neuronal changes. After high dose exposure, systemic lesions are observed in several tissues. Injuries of liver, kidney, urinary passages, thymus, and cardiovascular system are reported for different species.

There is no information concerning potential reproduction or developmental toxicity of methyl methacrylate.

H315: Causes skin irritation; H317: May cause an allergic skin reaction; H355: May cause respiratory irritation

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to carcinogenicity to humans)

No carcinogenic risk potency (CRP) was derived.

No evidence for carcinogenicity is available from animal studies or from human investigations.

Odour and derivation of the LOA value

Odour: acrid, fruity odour

ODT: 0.21 ppm (0.87 mg/m^3) [Nagata, 2003]

LOA = 11.8 * ODT * 1.33 = 13.7 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/ODT) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is below all VRW values

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **69**	*AEGL-1* 71	*ERPG-1* not derived		*IDLH:* 4,200 (30 minutes)
AGW level **500**	*AEGL-2* 500	*ERPG-2* not derived		
LBW level **2,400**	*AEGL-3* 2,400	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr:
163702-07-6
163702-08-7

Methylnonafluoro(iso)butylether

$CF_3(CF_2)_3OCH_3$
$(CF_3)_2CFCF_2OCH_3$

VN-nr: geen
GEVI: geen

Synoniemen: Hydrofluoroether-7100, HFE-7100, 40% methylnonafluorobutylether en 60% methylnonafluoroisobutylether (Engels: methylnonafluoro(iso)butylether)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	170.000	170.000	170.000	170.000	170.000	170.000
Levensbedreigende waarden	LBW (mg/m³)	310.000	310.000	310.000	310.000	310.000	310.000

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,0962 ppm; 1 ppm = 10,4 mg/m³

Explosiegrens: geen gegevens

Geur: lichte ethergeur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: heldere kleurloze vloeistof
Brand: geen gegevens

Relatieve dichtheid van verzadigd damp-lucht mengsel: 8,6

Molecuulmassa:	250 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	0,0012 g/100 ml (zeer slecht)
Verzadigde dampdruk:	270 mbar (25°C)

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: lever- en nierfunctiestoornissen en effecten op de milt, mogelijk zonder merkbare klachten

AGW → LBW: agitatie, tremoren, convulsies, hartritmestoornissen

Boven LBW: sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De inhalatoire toxiciteit is gering.
- De stof veroorzaakt een verhoogde gevoeligheid van het hart voor catecholaminen zoals adrenaline.
- Convulsies kunnen mogelijk veroorzaakt worden door de lipofiliteit van de stof of interacties met neurotransmitters.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid

Oogcontact: roodheid

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep.
ogen: spoelen met water (evt. contactlenzen verwijderen.
inslikken: mond laten spoelen (uitspugen!), rust en zo nodig arts raadplegen.

***Specifieke behandeling en materialen**: geen.*
Neem contact op met het NVIC (tel: +31 (0)30-274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr:
163702-07-6
163702-08-7

Methylnonafluoro-butylether and Methylnonafluoro-isobutylether

$CF_3(CF_2)_3OCH_3$ **$(CF_3)_2CFCF_2OCH_3$** **UN-nr:** None

Basis for the Dutch Intervention Values

VRW: Not recommended in contrast to AEGL.

AGW: AEGL value adopted, 2hr value added, no MF.

LBW: AEGL value adopted, 2hr value added, no MF.

Date: 06-10-2016 | AEGL document: Final, 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	170,000	170,000	170,000	170,000	170,000	170,000	Threshold for impaired ability to escape in animals (tremors, stiff limbs)
LBW	310,000	310,000	310,000	310,000	310,000	310,000	Assumed threshold for animal mortality

Derivation of the Dutch Intervention Values

VRW: VRW values are not recommended, because there are no exposure-response data in humans or animals consistent with VRW-level effects. The lack of VRW-values does not necessarily mean that exposure below AGW-levels is without any effects.

AGW: The exposure of beagles to 48,900 ppm (508,560 mg/m³) in a cardiac sensitization test was chosen as the basis for the AGW. No clinical signs were observed during the first 5-minute exposure to methylnonafluoro-(iso)butylether prior to the challenge dose of epinephrine. In the second 5-minute exposure to methylnonafluoro-(iso)butylether after the challenge, clinical effects were observed, such as agitation. At the next highest exposure, 89,300 ppm (928,720 mg/m³), clinical signs of agitation, tremors, and stiff limbs were observed which might impair the ability to escape. Therefore, the first 5-minute exposure at 48,900 ppm (508,560 mg/m³) was chosen as point of departure. An interspecies uncertainty factor of 1 was applied for several reasons: when considering clinical signs, the dog was shown to be more sensitive than the rat, and the respiration rate of dogs and rodents is greater than that of humans, resulting in greater uptake. The default intraspecies uncertainty factor of 3 was considered sufficient to account for intraspecies differences. The resulting value is 84,760 mg/m³ (rounded: 85,000 mg/m³). Time scaling may not be relevant for halogenated hydrocarbons as blood concentrations of these chemicals rapidly reach equilibrium and do not greatly increase as exposure duration is increased. The use of the same value across all exposure durations is supported by a study in which rats were exposed to concentrations up to 30,000 ppm (312,000 mg/m³) for 6 hours/day, 5 days/week for four weeks. These rats exhibited reversible liver hypertrophy which is attributed to the repeated nature of the exposures.

LBW: The animal data indicate that the threshold for lethality in both the rat and dog lies above 89,300 ppm (928,720 mg/m³) methylnonafluoro-(iso)butylether. In a study of rats, the EC_{50} for convulsions was 214,000 ppm (2,225,600 mg/m³) and 3 of 4 rats died following the 4h exposure. In dogs, during the first 5 min exposure to methylnonafluoro-(iso)butylether prior to the second epinephrine challenge in a cardiac sensitization study, one of two dogs exposed to 89,300 ppm (928,720 mg/m³) exhibited severe clinical signs including agitation, tremors and stiff limbs. Because the data are insufficient for calculating the exact threshold for lethality in either species, the 5-minute exposure of the dog to 89,300 ppm (928,720 mg/m³) was used as the basis for the LBW values. Although the tremors in dogs are rapidly reversible and do not cause lasting effects, they may have a severe effect on populations such as patients with heart disease. An interspecies uncertainty factor of 1 was applied for several reasons: when considering clinical signs, the dog was shown to be more sensitive than the rat, and the respiration rate of dogs and rodents is greater than that of humans, resulting in greater uptake. The default intraspecies uncertainty factor of 3 was considered sufficient

to account for intraspecies differences. Time scaling may not be relevant for halogenated hydrocarbons as blood concentrations of these chemicals rapidly reach equilibrium and do not greatly increase as exposure duration is increased. Therefore, the resulting 154,787 mg/m^3 (rounded: 150,000 mg/m^3) concentration is applicable for all LBW time points.

Additional toxicological information (including relevant results of a general literature search, if any)

Methylnonafluoro(iso)butylether is not considered acutely toxic. No information on the mechanism of toxicity was located. The chemical structure may presume an anesthetic mechanism, however methylnonafluoro(iso)butylether is not an anesthetic but a “nonimmobilizer”. Nonimmobilizers are compounds whose lipophilicity predicts an anesthetic effect but have no such effect, either when given alone or when added to a known anesthetic. Nonimmobilizers may produce clonic convulsions by two interrelated mechanisms: one correlates with lipophilicity (nonpolarity), implying an action in a nonpolar phase, and the second correlates with an action on the neurotransmitter GABA (γ-aminobutyric acid), perhaps by modifying the action of GABA on receptors.

The toxic effects of the substance are all systemic. The substance is taken up by the body until equilibrium has been reached. Initial uptake would be more rapid in rodents than in primates (based on the higher respiratory rate and cardiac output of rodents compared with primates, equilibrium would be reached more rapidly in rodents). Storage in adipose tissue is expected to be minimal based on its poor solubility in biological fluids and the elimination of the heptafluorobutyric acid metabolite within 48 hours of an intravenous dose.

Methylnonafluoro(iso)butylether is not considered reprotoxic or developmental toxic. Studies addressing neurotoxicity and cardiac sensitization and studies with pregnant rats failed to identify significant toxicological effects.

No harmonized H-sentences for human health

Carcinogenicity and derivation of the CRP value

IARC classification: Not classified

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: etherlike odour

No LOA was derived (no data on odour thresholds found).

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **NR**	*AEGL-1* 26,000	*ERPG-1* -		*IDLH: -*
AGW level **170,000**	*AEGL-2* 85,000	*ERPG-2* -		
LBW level **310,000**	*AEGL-3* 160,000	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 681-84-5 **Methylsilicaat** **$(CH_3O)_4Si$** **VN-nr: 2606**

GEVI: 663

Synoniemen: tetramethoxysilaan, tetramethylorthosilicaat, methylorthosilicaat (Engels: tetramethyl silicate)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	31	22	17	14	11	7,1
Levensbedreigende waarden	LBW (mg/m³)	47	33	26	21	16	8,2

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,158 ppm; 1 ppm = 6,33 mg/m³

Explosiegrens: LEL = 0,88 Vol% ≈ 56.000 mg/m³

Geur: lichte esterachtige geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: heldere, kleurloze vloeistof

Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,07

Molecuulmassa: 152,2 g/mol
Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: Reactie
Verzadigde dampdruk: 13 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 6,3 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW: keelpijn en hoesten

AGW → LBW: irritatie van ogen, huid en luchtwegen, branderig gevoel achter het borstbeen, moeizaam ademen, kortademigheid, ademnood

Boven LBW: sterfte

LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt irriterend op de ogen en de luchtwegen
- Blootstelling aan methylsilicaat kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Mogelijk zijn mensen met een verminderde longfunctie gevoeliger voor effecten van de stof
- Methylsilicaat is in het bijzonder schadelijk voor de ogen. Blootstelling aan de dampen of aerosol van de stof kan initieel zonder merkbare irritatie aan de ogen verlopen, maar na een latentietijd van 10-12 uur kan heftige (oog)pijn, roodheid en tranenvloed ontstaan, wat zich verder kan ontwikkelen tot troebeling en laesies van de cornea. In ernstige gevallen kan zelfs blindheid ontstaan.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn

Oogcontact: roodheid, pijn, slecht zien, ernstige brandwonden, mogelijk permanent verlies van gezichtsvermogen

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: spoelen met veel water / kleding verwijderen en onmiddellijk arts raadplegen.
ogen: zie hierboven.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 681-84-5 **Tetramethyl silicate** **$(CH_3O)_4Si$** **UN-nr: 2606**

Basis for the Dutch Intervention Values

VRW: Not recommended (in accordance with AEGL)

AGW: Same point of departure as for AEGL values, but using different uncertainty factors and time scaling applied to the 10 minute value, 2h value added

LBW: Same point of departure as for AEGL values, but using different uncertainty factors and time scaling applied to the 10 minute value, 2h value added

Date: November 2015 | AEGL document: Final, 2013

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	31	22	17	14	11	7.1	No-effect level for irreversible effects in rats
LBW	47	33	26	21	16	8.2	Estimate $BMCL_{05}$ for lethality threshold in rats

Derivation of the Dutch Intervention Values

VRW: The VRW values are not derived. Available human and animal data were insufficient and indicate a steep dose-response curve which would result in VRW values very similar to AGW levels. Therefore VRW values were not recommended. The lack of VRW-values does not necessarily mean that exposure below AGW-levels is without any effects.

AGW: In a repeated exposure study, rats were exposed via inhalation to 0, 1, 5, 10, 15, 30 or 45 ppm for 6h/day, 5 days/week for 28 days. In this study lung lesions, acute inflammation of nasal epithelium and acute keratitis was found minimal at 15 ppm (95 mg/m^3). Therefore, the level of 15 ppm (95 mg/m^3) was regarded the no-effect level for irreversible effects. Although it was acknowledged that this value is rather conservative as it is based on repeated exposure, it was considered acceptable as the point of departure for derivation of the AGW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences.Time-scaling was performed using the equation $C^n \times t = k$, using the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively.

LBW: The LBW values were determined by using mortality data in rats. The $BMCL_{05}$ value of 26 ppm (165 mg/m^3) for 4 hours was considered to be to most conservative value to estimate the threshold for lethality in rats and was used as a point of departure for deriving the LBW values. The variation in effects is not expected to vary much among species. Therefore, an interspecies uncertainty factor of 3 was considered sufficient. A default factor of 3 was used to account for intraspecies variability, which is a deviation from the AEGL-standard which used a factor of 10 to estimate human variability. A total uncertainty factor of 10 was applied. Time-scaling was performed using the equation $C^n \times t = k$, using the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-X value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

The exact mechanism of toxicity of tetramethyl silicate is not known. The substance is a strong ocular irritant. Epithelial tissue is the target tissue for the substance, especially in the eye and respiratory tract. Animal studies show that the substance can cause lung damage, therefore subjects with a compromised lung function would be considered to be more at risk from exposure to the substance.

Data on developmental and reproductive toxicity in humans and in animals are not located.

No harmonized hazard sentences.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: Sweet-fruity, faint ester-like

No LOA was derived (due to inadequate data)

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* N/A		*IDLH: not derived*
AGW level **17**	*AEGL-2* 5.6	*ERPG-2* 63		
LBW level **26**	*AEGL-3* 8.7	*ERPG-3* 127		

Stofdocument deel A

CAS-nr: 1634-04-4 **Methyl-tert-butylether** **$(CH_3)_3COCH_3$** **VN-nr: 2398**

GEVI: 33

Synoniemen: MTBE, tert-butylmethylether, 2-methoxy-2-methylpropaan (Engels: Methyl tertiary-Butyl Ether) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	180	180	180	180	180	180
Alarmeringsgrenswaarden	AGW (mg/m³)	5100	2900	2100	1500	1500	1500
Levensbedreigende waarden	LBW (mg/m³)	48.000**	28.000*	20.000*	14.000*	9800*	6900*

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,273 ppm; 1 ppm = 3,67 mg/m³

Explosiegrens: LEL = 1,6 vol% ≈ 59.000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

** berekende interventiewaarde hoger dan 50% LEL

Geur: typerende, terpeen-achtige geur

LOA: niet afgeleid.

Geurwaarneming mogelijk beneden VRW; gerapporteerde geurdrempels 0,32-0,47 mg/m³.

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,5

Molecuulmassa:	88,2 g/mol
Zuurgraad:	Geen data
LogKow:	1,1
Wateroplosbaarheid:	5,1 g/100 ml (matig)
Verzadigde dampdruk:	268 mbar

Overige informatie

Publieke grenswaarde: 180 mg/m³ (8 uur)

MAK: 180 mg/m³

TLV-TWA: 180 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen klachten

VRW → AGW: keelpijn, hoesten, oogirritatie

AGW → LBW: misselijkheid, hoofdpijn, benauwdheid, ataxie, verminderde coördinatie

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt irriterend op de slijmvliezen van luchtwegen en ogen.
- Bij hoge concentratie kan de stof depressie van het centrale zenuwstelsel veroorzaken.

Effecten bij blootstelling aan vloeistof

Huidcontact: misselijkheid, hoofdpijn

Stof kan door de huid worden opgenomen.

Oogcontact: roodheid, pijn

Carcinogeniteit

IARC classificatie: 3

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust en arts raadplegen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken en minimaal 20 min. spoelen met veel water of douchen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 1634-04-4 **Methyl tertiary-Butyl Ether** **$(CH_3)_3COCH_3$** **UN-nr: 2398**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 16-12-2010 | AEGL document: Interim, 2009

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	180	180	180	180	180	180	No effect level in humans
AGW	5100	2900	2100	1500	1500	1500	Transient CNS depression in rats
LBW	48,000**	28,000*	20,000*	14,000*	9800*	6900*	Calculated $BMCL_{05}$ from rat LC_{50} data

* value higher than 10% of LEL; ** value higher than 50% of LEL

Derivation of the Dutch Intervention Values

VRW: The VRW derivation is based on a study with 10 male volunteers exposed to 5, 25 or 50 ppm (18, 92, 180 mg/m³) for 2 hours during light exercise. At 50 ppm (180 mg/m³), no notable discomfort or irritation was noted. An uncertainty factor of 1 was applied as this was a human study and no effects were noted besides the odour. The VRW value was not scaled across time since no effects were observed at 50 ppm (180 mg/m³) and sensory effects are usually concentration, rather than time, dependent. PBPK models for MTBE have been published. These models, however, were not used to develop intervention values because of limitations in the data available to evaluate the models.
In animals studies, both 400 ppm (1500 mg/m³) as well as 800 ppm (2900 mg/m³ were shown as NOAELs for CNS depression in rats (in a subchronic and an acute animal study respectively). Using the 800 ppm (2900 mg/m³) concentration and dividing by an uncertainty factor of 10 (3 each for inter- and intra-species) results in a value of 80 ppm (290 mg/m³), making the 50 ppm (180 mg/m³) concentration a conservative number.

AGW: The AGW derivation is based on a study with 22 male and 22 female rats exposed to 0, 800, 4000 or 8000 ppm (0, 2900, 15000, 29000 mg/m³) for 6 hours. At 4000 ppm (15,000 mg/m³) rats demonstrated reversible, transient CNS depression [altered gait (ataxia, duckwalk), piloerection, and decreased hind-limb strength (females)]. An interspecies uncertainty factor of 3 was applied. An intraspecies uncertainty factor of 3 was chosen based on MTBE acting as a CNS depressant and based on several papers on anesthesia (AEGL) as well as on the NRC AEGL SOP (NRC, 2001) describing the CNS depression variability in the human population being no greater than 3 fold. Time scaling was performed for extrapolating to the 10 min, 30 minutes, and 1 hour timepoints. The 2-, 4- and 8 hour AGW values were set equal to the 6 hour value for two reasons. Firstly, a steady state of 2 hours was reported in a rat inhalation study with 40 and 400 ppm (150 and 1500 mg/m3). Furthermore PBPK modelling data, while not used in the intervention value derivations, also showed steady state of MTBE being achieved in 2 hours at 500 and 5000 ppm (1800 and 18000 mg/m³) and 4 hours in humans. Both of these data-points thus justify using 2 hours as the point-of-departure and flatlining at 4 and 8 hrs. Time scaling was performed using the equation $C^n \times t = k$, using exposure to 4000 ppm (15,000 mg/m³) for 2 hours as a point of departure and n=2 (derived by ten Berge from a mouse study).

LBW: LBW values were derived from an acute LC_{50} study exposing rats to MTBE vapour for 4 hours. Clinical signs ranging from prostration, hypo-activity, and laboured breathing followed by death were recorded. From these data, a 4-hour $BMCL_{05}$ value was calculated by a log-probit analysis using U.S. EPA Benchmark Dose Software version 1.3.2. The resulting 4-hour- $BMCL_{05}$ of 26,690 ppm (98,000 mg/m³) was used to derive the LBW values. A total uncertainty factor of 10 was applied. Data from a mouse study used by ten Berge to derive the n = 2 value had very similar values when compared to the above data, thus supporting the point-of-departure number. An interspecies uncertainty factor of 3 (based on the similar data in rats and mice) and an intraspecies uncertainty factor of 3 (see AGW derivation) were applied. Time scaling was performed using the equation $C^n \times t = k$ and the n-value of 2 (based on ten Berge).

Additional toxicological information (including relevant results of a general literature search, if any)

Toxicity of MTBE is most evident as transient CNS depression in animals. MTBE is metabolized by oxidative demethylation to tert-butyl alcohol (TBA). However, the underlying mechanisms that initiate cellular alterations by MTBE and its metabolites are unknown.

Little information is available on toxicity of MTBE in children or susceptible populations. Most reported age-dependent susceptibilities on effects of solvents or vapours are less than threefold on the order of magnitude in human population.

No data are available on the developmental and reproductive toxicity of MTBE in humans.

H315: Causes skin irritation.

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to carcinogenicity to humans)

No carcinogenic risk potency (CRP) was derived.

MTBE did not display any genotoxic effects but did result in some carcinogenicity in mice and rats. Mice were observed to have more hepatocellular adenomas in females when exposed to 8000 ppm (29,000 mg/m^3) MTBE via inhalation. Male rats exposed to 3000 and 8000 ppm (11,000 and 29,000 mg/m^3) MTBE by inhalation were also observed to have an increased incidence of renal tubular cell tumors. Finally, rats exposed by oral route to 1000 mg/kg had an increased incidence of testicular tumors in males and leukemias/lymphomas in females.

Odour and derivation of the LOA value

Odour: pungent, terpene-like

No LOA was derived due to the absence of consistent odour perception.

Odour threshold ranging from 0.32-0.47 mg/m^3 are reported, which indicates that the odour may be perceived at exposure levels lower than the VRW values.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level 180	*AEGL-1* 180	*ERPG-1* 180		*IDLH:* not derived
AGW level 2100	*AEGL-2* 2100	*ERPG-2* 3700		
LBW level 20,000	*AEGL-3* 19,000	*ERPG-3* 18,300		

Stofdocument deel A

CAS-nr: 75-79-6 **Methyltrichloorsilaan** CH_3Cl_3Si **VN-nr: 1250**

GEVI: X338

Synoniemen: methylsilicochloroform, trichloormethylsilaan (Engels: methyltrichlorosilane) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	3,7	3,7	3,7	3,7	3,7	3,7
Alarmeringsgrenswaarden	AGW (mg/m³)	230	110	69	43	27	27
Levensbedreigende waarden	LBW (mg/m³)	700	330	210	130	81	81

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,161 ppm; 1 ppm = 6,22 mg/m³

Explosiegrens: LEL = 5,1 vol% ≈ 320.000 mg/m³

Geur: scherpe, bijtende geur

LOA: onvoldoende betrouwbare gegevens

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze, rokende vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,8

Molecuulmassa: 149,5 g/mol

Zuurgraad: geen data

LogKow: geen data

Wateroplosbaarheid: reactie

Verzadigde dampdruk: 190 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW geen informatie

VRW → AGW: irritatie van ogen en luchtwegen, tranenvloed, hoesten, lichte benauwdheid

AGW → LBW: ernstige irritatie van ogen en luchtwegen, pijn op de borst, benauwdheid, longontsteking, longoedeem

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Chloorsilanen reageren zeer snel met water onder vorming van chloorwaterstof (HCl). De acute toxiciteit van methyltrichloorsilaan wordt veroorzaakt door chloorwaterstof.
- Inhalatie van chloorwaterstof veroorzaakt een type I inhalatie intoxicatie.
- Chloorwaterstof veroorzaakt irritatie van de slijmvliezen van ogen en luchtwegen.
- Chloorwaterstof kan bij inhalatie longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, brandwonden

Oogcontact: bijtend, roodheid en pijn, hoornvliesbeschadiging, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: n.v.t.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen, en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**:* geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 75-79-6 **Methyltrichlorosilane** **CH_3Cl_3Si** **UN-nr: 1250**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same rationale as AEGL (analogy with HCl), 2h value added

LBW: Same rationale as AEGL (analogy with HCl), 2h value added

Date: November 2015 | AEGL document: Final, 2012

Proposal for the Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	3.7	3.7	3.7	3.7	3.7	3.7	Based on HCl (Threshold of irritation in humans)
AGW	230	110	69	43	27	27	Based on HCl (one-third of LBW)
LBW	700	330	210	130	81	81	Based on HCl (Threshold of lethality in animals)

Derivation of the Dutch Intervention Values

VRW: Since no appropriate data exist for methyltrichlorosilane, VRW values for hydrogen chloride will be used (on ppm-basis) to derive VRW values for methyltrichlorosilane. The use of hydrogen chloride as a surrogate for methyltrichlorosilane was deemed appropriate since it is believed that the hydrolysis product, HCl, is responsible for the adverse effects. Because three moles of hydrogen chloride are produced for every mole of methyltrichlorosilane, a molar adjustment factor of 3 was applied to the hydrogen chloride VRW values.

Derivation of VRW values for HCl

The hydrogen chloride VRW values were based on a no-adverse-effect-level of 1.8 ppm (2.73 mg/m³) in exercising asthmatics with an exposure duration of 45 min. Because the test subjects were considered a sensitive subpopulation and the endpoint was essentially a no-effect level, no uncertainty factor was applied to account for sensitive human subpopulations. The VRW values were held constant for all specified exposure periods since mild irritant effects represent threshold effects and generally do not vary over time.

AGW: Since no appropriate data exist for methyltrichlorosilane, AGW values for hydrogen chloride will be used (on ppm-basis) to derive AGW values for methyltrichlorosilane. Because three moles of hydrogen chloride are produced for every mole of methyltrichlorosilane, a molar adjustment factor of 3 was applied to the hydrogen chloride AGW-values.

Derivation of AGW values for HCl

The AGW values of HCl for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data. The only study of HCl that addressed effects that meet the definition of an AGW, severe nasal lesions, was a study on hydrogen halides by Stavert et al. (1991). Nevertheless, this study was not considered a suitable basis for derivation of AGW values because 6% of the animals died after exposure to HCl at 1300 ppm (1974 mg/m³), only one concentration was tested and the number of animals tested was inconsistent.

LBW: Since no appropriate data exist for methyltrichlorosilane, LBW values for hydrogen chloride will be used (on ppm-basis) to derive LBW values for methyltrichlorosilane. Because three moles of hydrogen chloride are produced for every mole of methyltrichlorosilane, a molar adjustment factor of 3 was applied to the hydrogen chloride LBW-values.

Derivation of LBW values for HCl

The LBW values were based on a lethality study in rats. The rat study included six exposure durations and various concentrations. Probit analyses using DoseResp was performed and yielded LC_{01} values for the 10 min, 30 min, 1-, 2-,4-, and 8hrs exposure durations of 3370, 1602, 1002, 627, 393 and 246 ppm (5116, 2433, 1522, 952, 596, and 373 mg/m³), respectively, which were used as point of departure for LBW derivation. The default total uncertainty factor of 10 (3x3) was considered

sufficient to account for inter- and intraspecies differences. The probit analyses yielded an n-value of 1.48, which was supported by the n-value of 1.59 calculated by Arts *et al.* (2000) from the C*t study. To maintain consistency with other hydrogen halogenides, the 8 hour value was set equal to the 4 hour value, as performed for the most potent hydrogen halogenide HF.

Additional toxicological information (including relevant results of a general literature search, if any)

No data concerning lethality or nonlethal toxicity in humans from methyltrichlorosilane exposure were located in the available literature.

Chlorosilanes react violently with water to produce hydrogen chloride gas. Data suggest that the acute toxicity of chlorosilanes is due to the hydrogen chloride hydrolysis product; acute toxicity of the chlorosilanes is both qualitatively (based on clinical signs) and quantitatively (based on molar equivalents of hydrogen chloride) similar to that of HCl.

Although toxicity data are limited for individual chlorosilanes, well-conducted 1-hr inhalation toxicity studies in rats are available for a series of chlorosilanes. In general, LC_{50} values for monochlorosilanes were approximately twice the LC_{50} values for dichlorosilanes and three times the LC_{50} values for trichlorosilanes. Clinical signs were consistent with hydrogen chloride exposure and included lacrimation, salivation, dried material around or on the eyes and/or nose, green staining around the nose and mouth, and perineal urine staining. Labored breathing, rales, hypoactivity, closed or partially closed eyes, prostration, corneal opacity or opaqueness, and swollen and/or necrotic paws were also observed. Hemorrhage, congestion and/or consolidation of the lungs, ectasia of the lungs, gaseous distension of the gastrointestinal tract, absence of body fat, obstruction of nostrils, dried and/or firm nares, alopecia around the eyes and discoloration of hair were observed at necropsy

No data concerning developmental/reproductive toxicity in humans or experimental animals from methyltrichlorosilane exposure were located in the available literature.

H315: Causes skin irritation. H319: Causes serious eye irritation. H335: May cause respiratory irritation.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency was derived

No data on the carcinogenicity of methyltrichlorosilane in humans or experimental animals were identified in the available literature.

Odour and derivation of the LOA value

Odour: sharp, acrid odour [AEGL]

No LOA was derived

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **3.7**	*AEGL-1* 3.7	*ERPG-1* 3.1		*IDLH:* not derived
AGW level **69**	*AEGL-2* 45	*ERPG-2* 19		
LBW level **210**	*AEGL-3* 210	*ERPG-3* 93		

Stofdocument deel A

CAS-nr: 78-94-4 **Methylvinylketon** CH_3-CO-CH=CH_2 **VN-nr: 1251**
GEVI: 639

Synoniemen: 1-buteen-3-on, MVK, vinylmethylketon (Engels: methyl vinyl ketone) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,49	0,49	0,49	0,49	0,49	0,49
Alarmeringsgrenswaarden	AGW (mg/m³)	6,4	4,5	3,5	2,8	2,2	1,5
Levensbedreigende waarden	LBW (mg/m³)	13	8,9	7,1	5,6	4,5	2,9

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,343 ppm; 1 ppm = 2,92 mg/m³

Explosiegrens: LEL = 2,1 vol% ≈ 61.000 mg/m³

Geur: Sterk irriterende geur

LOA: niet afgeleid; mogelijk kan de geur op VRW niveau waargenomen worden

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot lichtgele vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,12

Molecuulmassa:	70,1 g/mol
Zuurgraad:	geen data
LogKow:	-0,3
Wateroplosbaarheid:	goed
Verzadigde dampdruk:	100 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: irritatie ogen, neus en keel, hoesten

AGW → LBW: benauwdheid, longoedeem

Boven LBW ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De damp werkt bijtend op ogen en luchtwegen
- Blootstelling aan methylvinylketon kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- De stof heeft een steile concentratie-respons relatie.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, pijn, brandwonden

Oogcontact: bijtend, roodheid, pijn, slecht zien, tranenvloed, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: spoelen met veel water / kleding verwijderen en direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31(0)30-274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 78-94-4 **Methyl vinyl ketone** **CH_3-CO-CH=CH_2** **UN-nr: 1251**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 16-12-2010 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.49	0.49	0.49	0.49	0.49	0.49	No effect level for respiratory tract irritation in animals.
AGW	6.4	4.5	3.5	2.8	2.2	1.5	Respiratory tract irritation in animals
LBW	13	8.9	7.1	5.6	4.5	2.9	Threshold for lethality in animals.

Derivation of the Dutch Intervention Values

VRW: The VRW values are based on a whole-body inhalation exposure study in which rats and mice were exposed to 0, 0.25, 0.5, 1, 2, 4, or 8 ppm (0, 0.73, 1.5, 2.9, 5.8, 12, or 23 mg/m³) methyl vinyl ketone 6 hours/day, 5 days/week for a total of 12 exposures. The selected point of departure for deriving the VRW values was irritation with a no observed adverse effect level (NOAEL) of 0.5 ppm (1.5 mg/m³) based on slight nasal lesions observed in both rats and mice after multiple exposures to 1 ppm (2.9 mg/m³). No interspecies uncertainty factor was considered necessary since similar NOAELs were obtained in multiple species (rat, mice, guinea pigs and rabbits) in two separate studies. An uncertainty factor of 3 was used for sensitive populations (intraspecies). The toxic effects of methyl vinyl ketone are related to contact irritation and responses are not expected to vary substantially among individuals, or to vary with duration of exposure. Therefore, VRW values were held constant across all time periods.

AGW: The AGW values are based on the same study as used for the derivation of the VRW values. In this study the lowest concentration causing nasal cavity necrosis was 2 ppm (5.8 mg/m³) in both rats and mice. This concentration was a NOAEL for lung lesions in rats, which was observed after exposure to 4 ppm (12 mg/m³). The toxic effects of methyl vinyl ketone are related to contact irritation of the respiratory tract. Nasal necrosis was not regarded in determining the point of departure for the AGW values due to the repeated exposure regimen in this study, but irritation during the first exposure was assumed to precede the tissue damage. Therefore, the AGW values are based on respiratory tract irritation at 2 ppm (5.8 mg/m³) that could impair escape for some individuals. A total uncertainty factor of 3 was used according to the same rationale as used for the VRW values. Time scaling was performed using $C^n \times t = k$, with the default values of n = 1 and n = 3 for extrapolations to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-2 value that was set equal to the 30 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: The LBW values are based on 4 ppm (12 mg/m³) as a point of departure for the lethal effects of methyl vinyl ketone in experimental animals. A single 6-hour exposure to 8 ppm (23 mg/m³) resulted in 100% mortality in rats, and 2/5 male mice died after ten exposures to the same concentration. There were no deaths in rats or mice exposed to 4 ppm (12 mg/m³) for 12 days. Another study showed 20% mortality in rats after 8 days of exposure to 3.9 ppm (11.4 mg/m³; all concentrations nominal), but no mortality after 10 days exposure to 2.1 ppm (6.1 mg/m³). In this same study there were no deaths in guinea pigs after 9 days exposure at either 3.9 or 7.8 ppm (11.4 or 22.7 mg/m³), no deaths in rabbits at 7.8 ppm, (22.7 mg/m³) though 1/3 rabbits died after 9 days exposure to 3.9 ppm (11.4 mg/m³). These data suggest that 4 ppm (12 mg/m³) is a reliable point of departure for deriving LBW values. A total uncertainty factor of 3 (intraspecies) was used because responses will not vary substantially among individuals, and do not appear to vary substantially among species since the dose-response relationship was similar in rats, rabbits, guinea pigs, and mice. Time scaling was performed using $C^n \times t = k$, with the default values of n = 1 and n = 3 for extrapolations to longer and shorter exposure durations, respectively. In contrast to

the 10 minute AEGL-3 value that was set equal to the 30 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Methyl vinyl ketone is a direct acting irritant on mucous membranes and is noted as a severe irritant to skin, eyes, and the respiratory system. Non lethal inhalation animal studies indicate that methyl vinyl ketone is an irritant and that the upper respiratory tract is the target for toxicity.

No information concerning potential human reproductive toxicity was found.

No harmonized H-statements for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No information concerning potential carcinogenicity was located.

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: pungent

No LOA was derived due to lack of reliable information.

Ruth (1986) reports an odour threshold of 0.57 mg/m^3, which implies that the odour of methyl vinyl ketone may be perceived at concentrations around VRW levels.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **0.49**	*AEGL-1* 0.50	*ERPG-1* not derived		*IDLH:* not derived
AGW level **3.5**	*AEGL-2* 3.5	*ERPG-2* not derived		
LBW level **7.1**	*AEGL-3* 7.0	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 64-18-6 **Mierenzuur** CH_2O_2 **VN-nr: 1779**

GEVI: 83

Synoniemen: E236, methaanzuur, waterstof carbonzuur (Engels: formic acid) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	40	27	22	17	14	9,0
Alarmeringsgrenswaarden	AGW (mg/m³)	160	110	87	69	55	36
Levensbedreigende waarden	LBW (mg/m³)	1900	1300	1100	840	660	330

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,523 ppm; 1 ppm = 1,913 mg/m³

Explosiegrens: 10 vol% ≈190.000 mg/m³

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot lichtgele hygroscopische rokende vloeistof
Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,02

Molecuulmassa: 46,0 g/mol
Zuurgraad: pH bij 1 g/100 mL = 2,2
LogKow: ca. -2
Wateroplosbaarheid: volledig
Verzadigde dampdruk: 43 mbar

Overige informatie

Publieke grenswaarde: 5 mg/m³ (15 min TGG)
MAK: 9,5 mg/m³
TLV-TWA: 9,4 mg/m³ (STEL 19 mg/m³)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte irritatie van neus en ogen
VRW → AGW: irritatie van slijmvliezen, pijn achter het borstbeen,
AGW → LBW: bijtend, keelpijn en hoest, tranen, branderig gevoel, dyspneu
Boven LBW: larynx- en glottisoedeem, longoedeem, ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Mierenzuur werkt irriterend tot bijtend op de ogen, de huid en de luchtwegen.
- Blootstelling aan mierenzuur kan longontsteking, longoedeem en een astmatische reactie veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- In ernstige gevallen kans op verstikking door zwellingen in de keel.
- Personen met astma en allergische rhinitis zijn mogelijk gevoeliger voor de effecten van mierenzuur.

Effecten bij blootstelling aan vloeistof

Huidcontact: *bijtend*, roodheid en pijn, brandwonden.
Oogcontact: *bijtend*, tranenvloed, roodheid en pijn, slecht zien.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding, direct spoedeisende medische hulp inzetten

Ontsmetting vloeistof
huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, spoelen met veel water / kleding verwijderen, direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 64-18-6 **Formic acid** **CH_2O_2** **UN-nr: 1779**

Basis for the Dutch Intervention Values

VRW: Based on information as described in ERPG-document, different values are derived, other time-points added

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added.

LBW: Based on additional information to that described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017 ERPG 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	40	27	22	17	14	9.0	Slight nasal irritation in rats
AGW	160	110	87	69	55	36	Threshold for moderate nasal irritation in rats
LBW	1900	1300	1100	840	660	330	Acute lethality in rats

Derivation of the Dutch Intervention Values

VRW: In the absence of suitable single exposure experiments in animals or humans, the VRW levels were based on results of subacute inhalation toxicity studies with formic acid. Rats and mice (5/sex/concentration) were exposed for 6 hours/day, 5 days/wk for two weeks to analytically determined concentrations of 31, 62.5, 125, 250, or 500 ppm, corresponding to 59.3, 120, 239, 478 and 957 mg/m³. Effects observed were consistent with respiratory irritants. No effects were seen in rats and mice exposed to 59.3 mg/m³. The severity ranged from minimal at 120 mg/m³ to moderate at 957 mg/m³. Mice were similarly affected, but with somewhat greater severity. Comparable effects were observed in a 13 wk toxicity study in mice and rats. It is noted that formic acid is considered to be a stronger irritant than acetic acid. This is confirmed by the VRW proposals for acetic acid based on human data. The concentration of 120 mg/m³, still showing minimal effects, was used as point of departure for derivation of the VRW values. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter time points respectively.

AGW: In the absence of suitable single exposure experiments, the AGW levels were based on results of the same subacute inhalation toxicity studies as used for VRW. At 239 mg/m³ the respiratory irritation effects observed were still scaled as mild (except for squamous metaplasia in nose of females) and still moderate at 957 mg/m³ in the surviving animals. The concentration of 478 mg/m³ was considered the threshold for moderate respiratory irritation and therefore considered suitable as point of departure for derivation of the AGW. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter time points respectively.

LBW: Several acute inhalation toxicity studies have been performed in rats and mice. In three studies rats were exposed to a saturated concentration of formic acid for 3-116 minutes. The theoretical maximum concentration was 41400 to 46100 ppm (corresponding to 79215-88210 mg/m³). The majority of the rats died after exposure durations of between less than 3 minutes and 10 minutes. The results are not suitable for use as point of departure for the LBW as no LC_{01} or LC_{50} could be calculated. In another study rats and mice were exposed for 15 minute to unknown concentrations of formic acid. Original data were not available. Reported 15-min LC_{50}'s were 15,200 mg/m³ (8,070 ppm) and 6,200 mg/m³ (3,300 ppm) for rats and mice, respectively. The key study for acute inhalation toxicity as described in the publicly available REACH registration dossier on ECHAs website is more suitable for use as PoD for derivation of LBW values. The original publication was not available and though the reported LC_{50} value of 3900 ppm (7400 mg/m³) was included in the ERPG document in a summarising table, the original data were not. In this study Sprague-Dawley

rats, 10 per sex/concentration, were exposed to analytical concentrations of 3380, 7290, 8370, 11100, 14700 mg/m^3 for 4 hours. The mortality data were used to calculate a 4-hour LC_{01} value of 6630 mg/m^3 and an LC_{50} of 7868 mg/m^3. This value is supported by the 15-minute LC_{50} values in rats and mice. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter time points respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Additional study used for LBW: In the publically available REACH registration dossier on ECHAs website an additional (key) acute inhalation study was described. Although the study was referenced with a reported LC_{50} of 3900 ppm in the ERPG document, the original raw data and description of the study were not included in the ERPG document. According to the summary of the registrant (*https://echa.europa.eu/registration-dossier/-/registered-dossier/15127/7/3/3*) the study was performed according to OECD TG 403. In this study Sprague-Dawley rats, 10 per sex/concentration, were exposed, whole body, to analytical vapour concentrations of 3380, 7290, 8370, 11100, 14700 mg/m^3 for 4 hours. Mortality rates for males and females were 0/10, 2/10, 8/10, 10/10, 10/10 and 0/10, 1/10, 8/10, 10/10, 10/10, respectively. Clinical signs included closed lids, snout wiping, discharge from nose and eye, corrosion of nose and eyes, salivation, corneal opacity, loss of pain reflex, dyspnea, respiration sounds, flatulence, apathy, hunched posture, unsteady gait in all dose groups. Symptoms persisted until termination at 14 days after treatment, except for the animals at 3380 mg/m^3, which were free of symptoms. Body weights were dose dependently depressed. Gross pathology of the dead animals showed hyperemic heart dilatation, inflated lung. There were no pathological findings in the sacrificed animals.

Formic acid induces irritation of the conjunctival mucosa, oropharynx, trachea, and principal bronchi. Formic acid can also induce eye and skin burns, pharyngeal edema, and chronic bronchitis.

Susceptible populations include individuals with chronic respiratory, skin or eye disease, asthmatics and individuals with seasonal allergic rhinitis.

Inhalation of formic acid does not lead to developmental or reproductive effects in animals.

H314 (causes severe skin burns and eye damage)

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: pungent

AIHA compiled data demonstrate a wide range of 1.6 – 340 ppm (3.1-651 mg/m^3), but concluded the data were not acceptable (AIHA 1989).

No **LOA** was derived (due to absence of suitable reviewed data).

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [61]

VRW level **22**	*AEGL-1* -	*ERPG-1* 5.6		*IDLH:* 57 mg/m^3 (30 minutes)
AGW level **87**	*AEGL-2* -	*ERPG-2* 47		
LBW level **1100**	*AEGL-3* -	*ERPG-3* 470		

[61] Note that the AEGL and ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL and ERPG, respectively.

Stofdocument deel A

CAS-nr: 79-11-8

Monochloorazijnzuur

$CH_2ClCOOH$

VN-nr: 1751
GEVI: 68

Synoniemen: chloorazijnzuur, MCA (Eng.: monochloroacetic acid)

***Status*: geen**

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,40	0,40	0,40	0,40	0,40	0,40
Alarmeringsgrenswaarden	AGW (mg/m³)	120	85	67	53	42	21
Levensbedreigende waarden	LBW (mg/m³)	370	250	200	160	130	63

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ =0,254 ppm; 1 ppm = 3,93 mg/m³

Explosiegrens: LEL = 8 vol% ≈ 314.500 mg/m³

Geur: Stekende geur
LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: witte hygroscopische kristallen of wit poeder
Brand: Brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,0

Molecuulmassa: 94,5 g/mol
Zuurgraad: Geen data

LogKow: -0,2
Wateroplosbaarheid: volledig
Verzadigde dampdruk: 0,22 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 1 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: irritatie van ogen, neus en luchtwegen, hoest, keelpijn, apathie, kortademigheid

AGW → LBW: pijn op de borst, benauwdheid, lethargie, hypotensie

Boven LBW: metabole acidose, bewustzijnsdaling tot coma, longoedeem, ademstilstand, hemolyse, shock

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Blootstelling aan monochloorazijnzuur vindt voornamelijk plaats via stofdeeltjes.
- Monochloorazijnzuur werkt bijtend op de ogen, de huid en ademhalingsorganen.
- Blootstelling aan monochloorazijnzuur kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- De systemische toxiciteit is gebaseerd op remming van (onder meer) de glycolyse, waardoor effecten op het hart, centraal zenuwstelsel en spieren optreden. Door ophoping van melkzuur en citroenzuur in het lichaam kan metabole acidose ontstaan.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, pijn, ernstige brandwonden. Monochloorazijnzuur wordt via de huid opgenomen

Oogcontact: roodheid, pijn, slecht zien.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: n.v.t.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding, specifieke behandeling en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en direct spoedeisende medische hulp inzetten. Na spoelen van de huid deze neutraliseren met een 5%-oplossing van natriumcarbonaat in water.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen:

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 79-11-8 **Monochloroacetic acid** **$CH_2ClCOOH$** **UN-nr: 1751**

Basis for the Dutch Intervention Values

VRW: New values derived instead of NR

AGW: Different point of departure than AEGL, 2h value added.

LBW: Different rationale than AEGL (NR for all time points), values derived for all time points

Date: November 2015	AEGL document, final 2009

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.40	0.40	0.40	0.40	0.40	0.40	Respiratory and skin irritation in humans
AGW	120	85	67	53	42	21	One-third of LBW
LBW	370	250	200	160	130	63	Absence of lethality

Derivation of the Dutch Intervention Values

VRW: A recent report describing the health effects of workers exposed to monochloroacetic acid was considered an adequate basis for deriving the VRW. No respiratory tract, skin and mucous membrane irritation and effects on lung function parameters in workers were noticed that were potentially exposed to monochloroacetic acid concentrations between <0.5 mg/m^3 (0.13 ppm) for 3 hours and 1.2 mg/m^3 (0.31 ppm) for 7 hours. The 7-hour 1.2 mg/m^3 exposure was used as point of departure. A total uncertainty factor of 3 was applied to account for intraspecies variability. The derived VRW was held constant across time, since irritation effects generally do not vary greatly over time.
The VRW is supported by experimental data from rats and guinea pigs showing only very slight effects (lower oxygen uptake, lower rectal temperature and lower chlorine concentrations in the urine) following a 4-month exposure to 5.8 mg/m^3. A 4-month exposure to 20.8 mg/m^3 induced kidney effects and inflammatory alterations of respiratory organs.

AGW: For the derivation of AGW values a study in rats was used. Exposure of rats to 66 ppm (260 mg/m^3) for 1 hour resulted in eye squint and in some lethargy, which might be interpreted as an effect on the central nervous system. There is some uncertainty as to the exposure because of the large discrepancy between the nominal exposure concentration of 964 ppm (3,798 mg/m^3) and the analytically measured exposure concentration of 66 ppm (260 mg/m^3). Considering the uncertainties regarding the used exposure concentrations observed in this single inhalation that is suitable as basis for the AGW, 1/3 of the LBW was used to derive AGWs.

LBW: An acute (4-hour) inhalation toxicity study in rats was performed by TNO in 2007 with MCA vapour and nebulised MCA solutions (50 or 500 g/L). These data were not available in the AEGL TSD. The nominal concentrations were 1385 and 3241 mg/m^3 with actual concentrations of 512 and 1268 mg/m^3, respectively. At the highest concentration no lethality was observed. The effects observed at this level were slightly decreased breathing (all animals) and slight (reversible) growth retardation. In the absence of any lethality data this highest concentration tested was used as point of departure for derivation of the LBWs. Time scaling was performed using $C^n * t = k$, with the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. No additional modifying factor was applied.

Additional toxicological information (including relevant results of a general literature search, if any)

Monochloroacetic acid is an acid (pKa 2.85) and therefore can cause eye and skin irritation upon contact with a diluted monochloroacetic acid solution and skin corrosion and conjunctival burns upon contact with more concentrated solutions. The systemic toxicity of monochloroacetic acid is caused by inhibition of enzymes of the glycolytic pathway and the tricarboxylic acid cycle. This metabolic blockage damages organs with a high energy-demand, such as heart, CNS and muscles, and leads to metabolic acidosis due to the accumulation of lactic acid and citric acid in the body.
An acute inhalation toxicity study (OECD 403 compliant) in rats was identified during the review phase. The study by Arts et al, 2007 (TNO study report, publication date 29-11-2007) exposed 5 animals per/sex/group (nose only) for 4 hours The nominal concentrations were 209 (pilot I), 1388 (pilot II), 1385 and 3241 mg/m^3 (concentrations A and B in main experiment) with actual concentrations of 102, 588, 512 and 1268 mg/m^3, respectively.

No studies evaluating developmental or reproductive toxic effects after inhalation exposure were located in the literature (search up to 2015).

H301: Toxic if swallowed; H311: Toxic in contact with skin; H314: Causes severe skin burns and eye damage; H331: Toxic if inhaled.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified. No carcinogenic risk potency (CRP) was derived.	Odour: Pungent odour. No LOA was derived. It is unknown whether odour awareness is accompanied by toxic effects.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **0.4**	*AEGL-1* NR	*ERPG-1* -		*IDLH:* not established
AGW level **67**	*AEGL-2* 26	*ERPG-2* -		
LBW level **200**	*AEGL-3* NR	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 108-90-7 **Monochloorbenzeen** C_6H_5Cl **VN-nr: 1134**

GEVI: 30

Synoniemen: chloorbenzeen, fenylchloride, MCB (Engels: chlorobenzene) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	47	47	47	47	47	47
Alarmeringsgrenswaarden	AGW (mg/m³)	2.000	1.400	700	700	700	700
Levensbedreigende waarden	LBW (mg/m³)	5.400	3.700	1.900	1.900	1.900	1.900

Datum vaststelling: november 2015

Conversiefactor: 1 mg/m³ = 0,214 ppm; 1 ppm =4,68 mg/m³

Explosiegrens: LEL = 1,3 Vol% ≈ 61.000 mg/m³

Geur: amandelachtige geur

LOA: 14,8 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,03

Molecuulmassa:	112,6 g/mol
Zuurgraad:	pH 7
LogKow:	3,0
Wateroplosbaarheid:	0,02 g/100 ml
Verzadigde dampdruk:	12 mbar

Overige informatie

Publieke grenswaarde:
23 mg/m³ (TGG 8 uur)
70 mg/m³ (TGG 15 min)
MAK: 46,8 mg/m³
TLV-TWA: 46,8 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: irritatie van ogen, neus en luchtwegen, sufheid, hoofdpijn, keelpijn en hoesten

AGW → LBW: misselijkheid, coördinatiestoornissen, bewusteloosheid

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt irriterend op de huid en de slijmvliezen.
- De stof kan inwerken op het centrale zenuwstelsel, de lever, de nieren en de longen.
- Blootstelling aan hoge concentraties kan tot bewusteloosheid leiden.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn, droge huid, jeuk

Oogcontact: prikkeling, roodheid en pijn

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, en onmiddellijk arts raadplegen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: Let op: aspiratiegevaar! Mond laten spoelen (uitspugen!), GEEN braken opwekken, en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen*.

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 108-90-7 **Chlorobenzene** C_6H_5Cl **UN-nr: 1134**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: November 2015 | AEGL document: Final, 2012

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	47	47	47	47	47	47	No irritant or CNS effects in humans
AGW	2,000	1,400	700	700	700	700	Threshold for narcosis in rats and guinea pigs
LBW	5,400	3,700	1,900	1,900	1,900	1,900	Threshold for mortality in rats and guinea pigs

Derivation of the Dutch Intervention Values

VRW: Studies showed that volunteers exposed to chlorobenzene at 60 ppm (292 mg/m³), for 3h in the morning and 4h in the afternoon, experience slight CNS depression and irritation. These effects were not experienced by subjects that were exposed concentrations of 10 ppm (46.8 mg/m³) for 8 hours.
The effects observed at 60 ppm (292 mg/m³) are considered above VRW level. The concentration of 10 ppm for 8 hours was therefore chosen as point of departure for derivation of the VRW values. An intraspecies factor of 1 was applied because the chosen point of departure was already considered conservative. Considering the fact that there is no information available about the time dependency of the effects, the value of 10 ppm (46.8 mg/m³) was considered appropriate for all time points.

AGW: Studies show that the threshold for AGW effects lies between 2,990 ppm (13,572 mg/m³), showing slight ocular and nasal irritation, and 5,980 ppm (27,986 mg/m³), showing narcosis, in rats and guinea pigs. Behavioral and neurophysiological effects were found in in rats and mice at concentrations below 2,990 ppm (13,993 mg/m³), but these effects were not considered relevant for derivation of AGW-levels. The concentration of 2,990 ppm (13,572 mg/m³ for 30 min was therefore chosen as point of departure for derivation of the AGW values. An interspecies uncertainty factor of 3 was applied because the critical effect is CNS depression and data were found comparable for rats and guinea pigs. The concentration of chlorobenzene in the brain is suggested to be directly related to the inhalation rate. Rodents have a higher inhalation rate which would suggest that humans would require a higher level of exposure. Information from studies with anesthetic gases shows that intraspecies variability in CNS depression is generally not greater than a factor 2 or 3. Therefore an intraspecies uncertainty factor of 3 was used. A total uncertainty factor of 10 was applied. Using a higher factor would result in values incompatible with human data found in other studies. Time-scaling was performed using the equation $C^n \times t=k$, using the default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. The 1-h and 10 min values were time-scaled from the 30-min AGW value. The 2, 4 and 8-hour AGW values were set equal to the 1-h value for time-scaling with n = 1, as studies show that a steady state of chlorobenzene concentration in blood is reached within 1 hour and the substance is rapidly excreted.

LBW: Several animal studies relevant to deriving LBW-values were available, but most studies lacked adequate details. The established 6-h LC_{50} of 2,965 ppm for chlorobenzene in male Sprague-Dawley rats conflicted with another rat lethality study reporting that no deaths occurred in male Long Evans rats exposed at 1,000-2,400 ppm for 8 h/day for 5 days. Other animal data suggest that no mortality occurred in rats and guinea pigs after exposure to 7,970 ppm (37,300 mg/m³) for 30 minutes. These data were used as point of departure for derivation of the LBW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was performed using the equation $C^n \times t = k$, using the default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. The 1-h and 10 min values were time-scaled from the 30-min LBW value. The 2, 4 and 8-hour LBW values were set equal to the

1-h value for time-scaling. Using n=1 would result in values incompatible with human data found in other studies. Furthermore, studies show that a steady state of chlorobenzene concentration in blood is reached within 1 hour and the substance is rapidly excreted.

Additional toxicological information (including relevant results of a general literature search, if any)

Exposure to chlorobenzene results in contact irritation and CNS depression. Repeated exposure also results in toxicity to several organs including the liver, kidneys, and white blood cells. The mechanism of action of chlorobenzene is unknown. Observed effects are also found in other volatile organic compounds.

Studies have shown that chlorobenzene does not affect fertility in rats at concentrations up to those that induce maternal toxicity.

H332: Harmful if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: aromatic, almond-like odour

Odour threshold: 0.98 mg/m^3 [Ruth, 1986]

LOA = 11.8 * 0.94 * 1.33 = 14.8 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: $I = 2.33 * \log (C/OT_{50}) + 0.5$. A correction factor of 1.33 is applied to this value)

The LOA lies below the VRW values.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **47**	*AEGL-1* 47	*ERPG-1* 140		*IDLH: 4,680 (30 min)*
AGW level **700**	*AEGL-2* 705	*ERPG-2* 2,340		
LBW level **1,900**	*AEGL-3* 1,880	*ERPG-3* 4,680		

Stofdocument deel A

CAS-nr: 12058-85-4 **Natriumfosfide** **Na_3P** **VN-nr: 1432**

GEVI: geen

Synoniemen: trinatriumfosfide (Engels: sodium phosphide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	50	17	8,3	4,2	2,1	1,0
Levensbedreigende waarden	LBW (mg/m³)	90	30	15	7,5	3,7	1,9

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,241 ppm; 1 ppm = 4,157 mg/m³

Explosiegrens: geen data
Kans op explosie door reactie met water of zuren.

Geur: typerende geur (geur als bij fosfine)
LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: rode kristallen
Brand: Niet brandbaar. Echter, bij contact met vocht kans op brand en explosie.

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa: 99,94 g/mol

Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: reactie
Verzadigde dampdruk: geen data

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling
(gebaseerd op vrijkomen fosfine)

*Onder **AGW***: irritatie aan ogen, huid, neus en luchtwegen, hoofdpijn, misselijkheid, braken, zwakte, paresthesie, duizeligheid, tremor

AGW → LBW: benauwdheid, longoedeem, bewustzijnsdaling, hartritmestoornissen, nier- en leverfunctiestoornissen

Boven LBW: convulsies, cardiovasculaire collaps, myocardinfarct, ademnood, coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Natriumfosfide kan bij contact met vocht uit de lucht of luchtwegen omgezet worden in fosfine. De toxiciteit van natriumfosfide wordt bepaald door de vorming van fosfine.
- Fosfine verstoort door effecten op de celademhaling de zuurstofopname en energievoorziening van de cel.
- Fosfine werkt irriterend op de ogen, huid en luchtwegen.
- Blootstelling aan natriumfosfide kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Kinderen zijn mogelijk gevoeliger voor toxiciteit door fosfine.

Effecten bij blootstelling aan vloeistof
Huidcontact: roodheid
Oogcontact: roodheid, pijn

Carcinogeniteit
IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
ogen: spoelen met water (evt. contactlenzen verwijderen).

Ontsmetting vaste stof
huid: verontreinigde kleding uittrekken, afspoelen met water.
ogen: spoelen met water (evt. contactlenzen verwijderen).
inslikken: mond laten spoelen (uitspugen!), rust, GEEN mond-op-mondbeademing, actieve kool (carbomix) toedienen, en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*
Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 12058-85-4 **Sodium phosphide** **Na_3P** **UN-nr: 1432**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 16-10-2018 | AEGL document: Final 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	(insufficient data)
AGW	50	17	8.3	4.2	2.1	1.0	Irritation nasal mucosa rats (phosphine)
LBW	90	30	15	7.5	3.7	1.9	Lethality rats (phosphine)

Derivation of the Dutch Intervention Values

VRW: No data are available for sodium phosphide. As toxicity of sodium phosphide is due to phosphine, which is formed due to reaction of sodium phosphide with moisture, data on phosphine could be used to derive intervention values. However, no appropriate data were available for derivation of VRW values for phosphine. Therefore VRW values are not recommended. This does not imply that exposure below AGW is without adverse effects.

AGW: Since no appropriate data exist for sodium phosphide, AGW values for phosphine will be used (on ppm-basis) to derive AGW values for sodium phosphide. The use of phosphine as a surrogate for sodium phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because one mole of phosphine is produced for every mole of sodium phosphide, no molar adjustment factor was needed.

Derivation of AGW values for phosphine

The phosphine AGW values were based on red mucoid nasal discharge in rats exposed to 10 ppm (14 mg/m³) phosphine for 6 hours, corresponding to 41.6 mg/m³ sodium phosphide. Since this endpoint is less severe than effects defined by AGW, the resulting values should be protective. The default uncertainty factor of 3 was applied to account for interspecies variability. An uncertainty factor of 10 was applied to account for intraspecies variability since the human data suggest that children may be more sensitive than adults when exposed to presumably similar phosphine concentrations. For example, in two reports, exposed children died, but exposed adults survived. Time scaling was performed using the equation $C^n \times t = k$, and an n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine).

LBW: Since no appropriate data exist for sodium phosphide, LBW values for phosphine will be used (on ppm-basis) to derive LBW values for sodium phosphide. The use of phosphine as a surrogate for sodium phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because one mole of phosphine is produced for every mole of sodium phosphide, no molar adjustment factor was needed.

Derivation of LBW values for phosphine

The highest concentration yielding no deaths in rats (18 ppm = 25 mg/m³) for 6 hours was used as point of departure for the calculation of the LBW values, corresponding to 74.8 mg/m³ sodium phosphide. The default uncertainty factor of 3 for interspecies and an intraspecies factor of 10 were applied for reasons provided above. Time scaling was performed using the equation $C^n \times t = k$ and a chemical specific n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine). These values are considered protective since workers were repeatedly exposed for “brief” periods of time to phosphine concentrations up to 35 ppm (49 mg/m³) with no life-threatening effects and workers exposed to >50 ppm (>70 mg/m³) for 2-5 minutes experienced only odour.

Additional toxicological information (including relevant results of a general literature search, if any)

When sodium phosphide reacts with moisture, phosphine gas will be formed. Phosphine is considered to induce acute toxic effects following oral and inhalation exposure. Children are thought to be more vulnerable to phosphine exposure. Common clinical signs after exposure to phosphine are headache, vomiting, coughing, shortness of breath, paresthesia, weakness, tremors and jaundice. Pulmonary congestion, pleural effusion, and congestive heart failure may be observed upon post-mortem examination.

In vitro, phosphine reacts with cytochrome c and cytochrome c oxidase, thereby inhibiting mitochondrial oxygen uptake. In vitro studies have also shown that phosphine can react with the heme moiety of hemoglobin in the presence of oxygen. Cell death and loss of cell membrane integrity accounted for the increased liver enzymes, bronchiolytic effects, cloudy swelling of renal tubular epithelia, and hemorrhagic myocardial lesions.

No reproductive or developmental data were found.

No harmonised H sentences available.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not evaluated. No carcinogenic risk potency (CRP) was derived. No data concerning carcinogenicity of sodium phosphide are available. Fumigation workers exposed long-term to phosphine have a higher incidence of both stable and less stable chromosomal aberrations. Molecular analysis of these lesions suggests that the breakpoints are near proto-oncogenes involved in non-Hodgkin's lymphoma, possibly contributing to the increased incidence of lymphomas in pesticide workers.	Odour: no information. Pure phosphine is odourless at concentrations up to 200 ppm. Technical-grade phosphine has a garlic-like odour (may be due to impurities). For phosphine, no LOA was derived due to lack of reliable data. Ruth (1986) reported an odour range of 0.028-3.6 mg/m^3 for phosphine.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [62]

VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH:* not derived
AGW level **8.3**	*AEGL-2* 8.2	*ERPG-2* -		
LBW level **15**	*AEGL-3* 15	*ERPG-3* -		

[62] Note that the AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL.

Stofdocument deel A

CAS-nr: 13463-39-3 **Nikkelcarbonyl** **Ni(CO)4** **VN-nr: 1259** **GEVI: 663**

Synoniemen: Nikkeltetracarbonyl, tetracarbonylnikkel (Engels: Nickel carbonyl) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	1,1	0,75	0,38	0,19	0,19	0,19
Levensbedreigende waarden	LBW (mg/m³)	3,2	2,2	1,1	0,56	0,56	0,56

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,141 ppm; 1 ppm = 7,09 mg/m³

Explosiegrens: LEL = 2 vol% ≈ 142.000 mg/m³

Geur: Zwakke geur, muf

LOA: 55,6 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze vloeistof

Brand: zeer brandgevaarlijk; zelfontbranding bij 60°C.

Relatieve dichtheid van verzadigd damp-lucht mengsel: 3,1

Molecuulmassa: 170,8 g/mol

Zuurgraad: Geen data

LogKow: Geen data

Wateroplosbaarheid: 0,02 g/100 ml (niet oplosbaar)

Verzadigde dampdruk: 428 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-ceiling: 0,12 mg/m³ als Ni

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: het (vertraagd) optreden van effecten is niet uitgesloten: hoofdpijn, hoesten, braken, duizeligheid.

AGW → LBW: effect op de ongeboren vrucht, pijn op de borst, ademnood, hyperglycemie, leverfunctiestoornissen, longontsteking

Boven LBW: longoedeem, hersenbloeding, bewusteloosheid, convulsies, sterfte.

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Na initiële milde symptomen en een asymptomatische periode, kunnen ernstige symptomen als gevolg van blootstelling aan nikkelcarbonyl vertraagd optreden (1-5 dagen).
- Blootstelling aan nikkelcarbonyl kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Nikkelcarbonyl wordt beschouwd als een reprotoxische stof.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn

Oogcontact: roodheid en pijn

Carcinogeniteit

IARC classificatie: 1 (Nikkelhoudende stoffen)
Nikkelcarbonyl niet separaat geclassificeerd.
Epidemiologische gegevens duiden niet op carcinogeniteit bij mensen (werkers).
CRP: niet afgeleid.

Beknopte medische informatie

Ontsmetting damp
Algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting Vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!) en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en Materialen geen
Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 13463-39-3 **Nickel Carbonyl** **Ni(CO)4** **UN-nr: 1259**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL.

AGW: Different point of departure than AEGL, 2hr value added.

LBW: AEGL value adopted, 2hr value added.

Date: November 2015 | AEGL document, final 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	1.1	0.75	0.38	0.19	0.19	0.19	One-third of LBW
LBW	3.2	2.2	1.1	0.56	0.56	0.56	Animal lethality

Derivation of the Dutch Intervention Values

VRW: VRW values are not recommended. Available data indicate that severe toxicity (i.e., lethality) may occur days after exposures that are initially suggestive of little or no toxicity. Therefore, VRW values are not recommended for nickel carbonyl.

AGW: The overall data set for nickel carbonyl is deficient regarding non-lethal effects of nickel carbonyl inhalation. In contrast to the AEGL, AGW-values were derived by using one-third of the LBW-values. This is supported by mouse data: Upon a 30-minute inhalation exposures to nickel carbonyl at 2.17 ppm (15.4 mg/m³), pulmonary damage was observed though not resulting in irreversible adverse effects.

LBW: A lethality threshold (LC_{01}) of 3.17 ppm (22.5 mg/m³) for 30 minutes was estimated from a mouse study. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Lethality data from the most sensitive species was used for development of the LBW. Because the available LC_{50} values vary approximately 8-fold, the total uncertainty adjustment of 10 is weighted towards the uncertainty in individual sensitivity to nickel carbonyl exposure. Time scaling was performed using $C^n * t = k$, with the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively. The 4- and 8-hour LBW values were flatlined to 0.56 mg/m3, given the TLV-ceiling level of 0.12 mg/m³ (as Ni).

Additional toxicological information (including relevant results of a general literature search, if any)

The primary target of nickel carbonyl-induced acute toxicity appears to be the lungs, although extrapulmonary involvement has also been reported. Human case studies have shown that a latency period often occurs between initial signs of toxicity and subsequent serious effects that may progress to death. Significant signs and symptoms of toxicity are known to occur in the absence of recognizable odour.

Both Type I and Type II alveolar cells were affected by nickel carbonyl, although the former were reportedly the primary target. It has also been shown that pulmonary edema and chemical pneumonitis are characteristic of severe nickel carbonyl poisoning.

Nickel carbonyl is considered to be a developmental toxicant. An increased incidence in offspring malformations and a decrease in live pups were observed in the rat at exposures of 160 to 300 mg/m³ for 15 minutes on gestation day 7. A decrease in live pups was observed in the rat at exposures of 80 mg/m³ for 15 minutes (AEGL document). Although the dams displayed toxic effects, the severe reprotoxic effects are considered relevant.

H330: Fatal if inhaled; H351: Suspected of causing cancer; H360D: May damage the unborn child;

Carcinogenicity and derivation of the CRP value

IARC classification: 1, however based on the category approach, where nickel compounds are classified category 1. Epidemiology data up until now did not show a relation between nickel carbonyl exposure and increased cancer incidence (AEGL document).

Odour and derivation of the LOA value

Odour: Weak odour.

OT_{50}: 3.5 mg/m3 [AIHA as cited in AEGL document]
LOA = 11.8 * OT_{50} * 1.33 = 55.6 mg/m3

No carcinogenic risk potency (CRP) was derived.	The LOA was based on the lowest noticeable odour level reported by AIHA, which was 0.5 ppm (3.5 mg/m3). It is noted that this level could not be validated. The LOA is far above the derived LBW levels and does not warn against toxic effects.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* Not derived		*IDLH:* 14 (30-min, as nickel)
AGW level **0.38**	*AEGL-2* 0.26	*ERPG-2* Not derived		
LBW level **1.1**	*AEGL-3* 1.1	*ERPG-3* Not derived		

Stofdocument deel A

CAS-nr: 8014-95-7 **Oleum** **SO_3 in H_2SO_4** **VN-nr: 1831**

GEVI: X886

Synoniemen: rokend zwavelzuur (Engels: Oleum) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,20	0,20	0,20	0,20	0,20	0,20
Alarmeringsgrenswaarden	AGW (mg/m³)	25	18	15	13	10	8,7
Levensbedreigende waarden	LBW (mg/m³)	270	200	160	140	110	93
Datum vaststelling: 13-05-2009				Conversie is niet van toepassing			

Explosiegrens: geen data

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos tot bruine hygroscopische, viskeuze en aan de lucht rokende oplossing

Brand: Niet brandbaar, bevordert brand van andere stoffen

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,01 -1,3 (hangt af van gedeelte vrij SO_3 (20% tot 65%)

Molecuulmassa:	98,1 g/mol (H_2SO_4) 80,1 g/mol (SO_3)
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid	reactie
Verzadigde dampdruk:	2,7 - 4,8 - 172 mbar (20-30-65% gedeelte vrij SO_3)

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 1 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: lichte irritatie ogen en luchtwegen, hoesten

AGW → LBW: benauwdheid, longoedeem

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Toxiciteit van oleum wordt voornamelijk bepaald door de aanwezigheid van en vorming (na contact met vocht) van zwavelzuur.
- Zwavelzuur is irriterend en corrosief.
- Primaire effecten zijn irritatie en schade aan de luchtwegen
- Zwavelzuur kan longoedeem veroorzaken waarbij de verschijnselen vertraagd kunnen optreden.
- Astmapatiënten zijn gevoeliger voor de effecten van zwavelzuur.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, pijn, ernstige brandwonden

Oogcontact: bijtend, roodheid, pijn, slecht zien.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
Zwavelzuur in sterke anorganische mist wordt beschouwd als carcinogeen (groep 1)(IARC monograph 54, 1992).

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding, specifieke behandeling en direct spoedeisende medische hulp inzetten.

ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof

huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen, arts raadplegen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**:* geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 8014-95-7 **Oleum** **SO_3 in H_2SO_4** **UN-nr: 1831**

Basis for the Dutch Intervention Values

VRW: AEGL value of sulfuric acid adopted, 2hr value added. In accordance with AEGL.

AGW: Same point of departure as for AEGL, but using time-scaling to derive values for other time points.

LBW: AEGL value of sulfuric acid adopted, 2hr value added. In accordance with AEGL.

Date: 13-05-2009 | AEGL document: interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.20	0.20	0.20	0.20	0.20	0.20	Nondisabling irritation in humans
AGW	25	18	15	13	10	8.7	Absence of AGW effects
LBW	270	200	160	140	110	93	Threshold of animal lethality

Derivation of the Dutch Intervention Values

VRW: VRW values are based on sulfuric acid, which is present and can be formed after contact of oleum with moist, because the ambient exposure will be to sulfuric acid mist after accidents.
The results of various studies clearly indicate that the first signs of respiratory irritation that can be characterized as notable discomfort occur at concentrations higher than 0.2 mg/m³ in humans. It is therefore concluded that the concentration of 0.2 mg/m³ can be used as the point of departure for VRW. Since the test subjects included exercising asthmatics, the most sensitive subpopulation, an intraspecies uncertainty factor of 1 is considered sufficient. There are no good data to establish a time-concentration effect (there are no data beyond 120 minutes where concentrations higher than 0.39 mg/m³ were tested). Considering the data up to 120 minutes of exposure and the type of effect (local irritation) the value of 0.2 mg/m³ was flat-lined across the 10- and 30-minute, and the 1-, 2-, 4-, and 8-hour exposure time points. This approach was considered appropriate because mild irritant effects generally do not vary greatly with time, and is in line with the derivation of VRW values for other respiratory irritants.

AGW: AGW values are based on sulfuric acid, which is present and can be formed after contact of oleum with moist, because the ambient exposure will be to sulfuric acid mist (containing aerosols) after accidents.
Occupational studies indicate that no irreversible or other serious health effects or an impaired ability to escape are to be expected from single exposures to concentrations of up to 35 mg/m³. The concentration of 26.0 mg/m³ (8-hour exposure) was used as the point of departure for AGW. Under these exposure conditions workers were perfectly able to complete their work shift. An intraspecies uncertainty factor of 3 is needed to account for sensitive subpopulations. This results in an 8-hour AGW value of 8.7 mg/m³. This AGW level is considered to be rather conservative because no irreversible or disabling effects were observed following acute exposure to sulfuric acid in any of the relevant human volunteer studies. Time scaling was performed, with n=3.7 (see LBW). This approach is in contrast with the AEGL approach, which flat-lined the level of 8.7 mg/m³ across time.

LBW: LBW values are based on sulfuric acid, which is present and can be formed after contact of oleum with moist, because the ambient exposure will be to sulfuric acid mist after accidents.
The calculated LC_{01} values (796, 592, 491, 338, 280 mg/m³ for 10 min, 30 min, 1-, 4-, and 8 hrs, respectively) for mice were used as a point of departure for the LBW. The probit method was used to derive the LC_{01} for the various exposure durations, because it allows to determine the combined effect of both concentration and time with all data included in the analysis simultaneously. Based on these data, the n-value appears to be 3.7. Using this n-value the 2 hr LBW was derived. No uncertainty factor is applied for the extrapolation from animals to humans, considering that (1) monkeys did not die and showed no serious effects up to 502 mg/m³ for an unknown exposure duration per day for 7 days, and (2) occupational concentrations up to 35 mg/m³ were tolerated during work shifts without significant acute health effects. An uncertainty factor of 3 is applied to account for variation in sensitivity among humans.

Additional toxicological information (including relevant results of a general literature search, if any)

Sulfuric acid mist may appear rapidly after oleum release into the ambient air and thus adverse health effects are expected to result from sulfuric acid exposure. Effects will occur rapidly, consisting of irritation and corrosive effects on the lungs primarily. May cause lung edema possibly resulting in death. Asthmatics may have an enhanced risk to health effects.

No data are available on reprotoxic or developmental toxic effects of oleum.

H314: Cause severe skin burns and eye damage; H335: May cause respiratory irritation; H330: Fatal if inhaled; H335: May cause respiratory irritation; H318: May cause serious eye damage

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: Oleum is not classified Strong-inorganic-acid mists containing sulfuric acid are carcinogenic to humans (group 1) (IARC monograph 54, 1992). No carcinogenic risk potency was derived due to lack of data.	Pungent odour. No LOA was derived due to lack of data.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **0.20**	*AEGL-1* 0.20	*ERPG-1* 2		*IDLH:*15 (30 min)
AGW level **15**	*AEGL-2* 8.7	*ERPG-2* 10		
LBW level **160**	*AEGL-3* 160	*ERPG-3* 30		

Stofdocument deel A

CAS-nr: 20816-12-0 **Osmiumtetroxide** **OsO_4** **VN-nr: 2471**

GEVI: 66

Synoniemen: osmiumtetroxide, osmiumzuur, osmiumzuuranhydride, osmiumoxide (Engels: osmium tetroxide)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	0,14	0,096	0,074	0,059	0,030	0,015
Levensbedreigende waarden	LBW (mg/m³)	77	53	42	34	27	21

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,0946 ppm; 1 ppm = 10,6 mg/m³

Explosiegrens: geen data

Kans op explosie bij contact met waterstofperoxide en zoutzuur.

Geur: sterke, onaangename, chloor-achtige geur

LOA: niet afgeleid; geurwaarneming mogelijk beneden AGW; gerapporteerde geurdrempels 0,02 mg/m³.

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot gele kristallen of poeder.
Brand: niet brandbaar, doch bevordert brand van andere stoffen

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,08

Molecuulmassa:	254,2 g/mol
Zuurgraad:	Geen data
LogKow:	0,9
Wateroplosbaarheid:	6,4 g/100 ml (matig)
Verzadigde dampdruk:	10 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: 0,002 mg/m³ (als osmium)

TLV-TWA: 0,002 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***:	irriterende effecten niet uitgesloten
AGW → LBW:	tranenvloed, pijn en irritatie ogen, verlies van gezichtsvermogen, hoofdpijn, keelpijn, hoesten, benauwdheid
Boven LBW:	ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Osmiumtetroxide werkt irriterend en bijtend op de ogen en luchtwegen.
- De irriterende effecten van osmiumtetroxide kunnen tot 12 uur na blootstelling aanhouden.
- Personen met verminderde longfunctie zijn mogelijk gevoeliger voor de effecten van osmiumtetroxide.
- Sterfte door blootstelling aan osmiumtetroxide kan mogelijk toegeschreven worden aan het optreden van ernstige weefselschade in de luchtwegen.

Effecten bij blootstelling aan vloeistof

Huidcontact: droge huid, jeuk, pijn.
Stof kan door de huid worden opgenomen

Oogcontact: bijtend, roodheid en pijn, slecht zien, corneabeschadiging

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, spoelen met veel water / kleding verwijderen[1)], en onmiddellijk arts raadplegen..

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 20816-12-0 **Osmium Tetroxide** OsO_4 **UN-nr: 2471**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 16-12-2010 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended due to insufficient data
AGW	0.14	0.094	0.074	0.059	0.030	0.015	Severe eye irritation in occupational exposed humans
LBW	77	53	42	34	27	21	No-effect level for lethality in animals

Absence of VRW values does not imply that exposure to concentrations less than the AGW values is without effect.

Derivation of the Dutch Intervention Values

VRW: Data consistent with VRW effects are not available and, therefore, VRW values for osmium tetroxide toxicity are not recommended.

AGW: AGW levels were based on the analysis of seven case reports of workers exposed to osmium tetroxide in the refining of osmiridium. Exposures to 133-640 μg osmium/m³ (equivalent to 177-853 μg osmium tetroxide/m³) produced intense and sudden smarting of the eyes associated with lacrimation and occasionally orbital headache, occasional gritty feeling in the eyes, conjunctival injection, and a halo effect around bright objects. The irritation effects of osmium tetroxide may persist for up to 12 hours. Most of the aforementioned symptoms subsided within 24 hours. Clinical data (blood pressure, hematology indices, urinalysis) were not indicative of systemic involvement. Although the report suggested a total exposure time of 6 hours, monitoring intervals were 2 hours. Because it was likely that osmium tetroxide-mediated ocular irritation would occur within the first 2-hour monitoring interval, a 2-hour exposure to 177 μg/m³ osmium tetroxide was considered an appropriate point-of-departure for AGW derivation. This was the lower limit of the exposure concentration range producing reversible ocular irritation, headache and visual disturbances. Because human occupational exposure data were used, the interspecies uncertainty factor was 1. Although most individuals would likely respond similarly to the direct-contact action of osmium tetroxide, those with compromised respiratory function (e.g., asthmatics and those with other COPD disorders) are considered especially susceptible and, therefore, an uncertainty factor of 3 for intraspecies variability was considered appropriate. Time extrapolation was performed using $C^n \times t = k$, where the defaults n = 3 and n = 1 are applied for extrapolations to shorter and longer durations, respectively. In contrast to the 10 minute AEGL-2 value that was set equal to the 30 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: LBW levels were based on a study with rats (5 male rats/group) exposed to 21, 210, 420 mg/m³ osmium tetroxide for 8 hours. The no effect level for lethality (210 mg/m³ during 8 hours) was selected as point of departure for the derivation of LBW values. At the next highest concentration, 420 mg/m³ during 8 hours, 5 out of 5 rats died. Exposure to 420 mg/m³ for 4 hours was lethal to 3 out of 5 rats. Lethality data for rats and mice were similar. Because osmium tetroxide is a direct-contact irritant its effects are probably similar across species although dosimetry may vary. Therefore, a factor of 3 is considered sufficient to account for species variability. Although most individuals would likely respond similarly to the direct-contact action of osmium tetroxide, those with compromised respiratory function (e.g., asthmatics and those with COPD) are considered especially susceptible and, therefore, an uncertainty factor of 3 for intraspecies variability is considered appropriate. Time extrapolation was performed using $C^n \times t = k$, where the default n = 3 is applied for extrapolations to shorter durations. In contrast to the 10 minute AEGL-3 value that was set equal to the 30 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Osmium tetroxide is reportedly very irritating to the eyes, and has a sudden vigorous irritant effect on the mucosal surfaces of the nose, pharynx, and bronchi. No quantitative exposure data are available regarding lethal effects of osmium tetroxide in humans. Nonlethal exposure is characterized by extreme irritation of the eyes and respiratory tract like that caused by bromine or chlorine. Ocular effects include sudden smarting of the eyes associated with lacrimation and occasionally orbital headache, occasional gritty feeling in the eyes, conjunctival injection, and a halo effect around bright objects. The irritation effects of osmium tetroxide reportedly may persist for up to 12 hours.

The oxidizing potential of osmium tetroxide is likely the basis for its action on biological tissues. Lethality resulting from osmium tetroxide exposure is ultimately a function of tissue damage leading to pulmonary edema. No definitive mechanistic studies are available.

Upon inhalation, osmium tetroxide is assumedly reduced to osmium metal based upon the dark discoloration of tissue upon contact with it.

Limited lethality data in rats, mice, and rabbits suggest little species variability. For both rats and mice, signs of toxicity were similar.

No developmental/reproductive toxicity data were found regarding inhalation exposure to osmium tetroxide.

H300: Fatal if swallowed; H310:Fatal in contact with skin; H314: Cause severe skin burns and eye damage; H330: Fatal if inhaled

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

No data were found regarding the carcinogenic potential of osmium tetroxide.

Odour and derivation of the LOA value

Odour: powerful and disagreeable chlorine-like

No LOA was derived due to lack of reliable data.

An odour threshold of 0.02 mg/m^3 [AEGL, 2008] has been reported, which implies that the odour of osmium tetroxide may be perceived at concentrations below AGW levels.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **NR**	*AEGL-1* NR	*ERPG-1* Not derived		*IDLH*: 1 (30 minutes)
AGW level **0.074**	*AEGL-2* 0.089	*ERPG-2* Not derived		
LBW level **42**	*AEGL-3* 42	*ERPG-3* Not derived		

Stofdocument deel A

CAS-nr: 56-38-2 **Parathion** **$C_{10}H_{14}NO_5PS$** **VN-nr: 3278 n.o.s.**
GEVI: 66

Synoniemen: DNTP, O-O-diethyl-O-p-nitrofenylthiofosfaat (Engels: parathion) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	8,3	5,8	4,6	3,6	2,9	1,4
Levensbedreigende waarden	LBW (mg/m³)	11	7,5	6,0	4,7	3,8	1,9

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,083 ppm; 1 ppm = 12,1 mg/m³

Explosiegrens: geen data

Geur: knoflook-achtige geur

LOA: 7,47 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: Lichtgele tot donkerbruine vloeistof
Brand: brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,0

Molecuulmassa:	291,3 g/mol
Zuurgraad:	geen data
LogKow:	3,8
Wateroplosbaarheid:	0,01 g/100 ml (zeer slecht)
Verzadigde dampdruk:	4.0 * 10^{-3} mbar (24 °C)

Overige informatie

Publieke grenswaarde:
niet afgeleid
MAK: 0,1 mg/m³ H
TLV-TWA: 0,05 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW: lichte oog- en huidirritatie, misselijkheid, hoofdpijn, miosis, duizeligheid.
AGW → LBW: diarree, braken, incontinentie, speekselvloed, ademnood, tremoren, longoedeem, bradycardie
Boven LBW: spierzwakte, convulsies, coma, bronchospasme, bronchorroe, bradycardie, ademstilstand, sterfte
LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt licht irriterend op de ogen en de huid.
- De stof kan inwerken op het centrale zenuwstelsel (als cholinesteraseremmer) met als gevolg hoofdpijn, duizeligheid en bewusteloosheid.
- Blootstelling aan parathion kan longoedeem en chemische pneumonitis veroorzaken.
- De verschijnselen van cholinesteraseremming en van longschade kunnen vertraagd optreden. Ze worden versterkt door lichamelijke inspanning kunnen tot vele dagen aanhouden.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, pijn
De stof wordt door de huid opgenomen!
Oogcontact: roodheid, pijn

Carcinogeniteit

IARC classificatie: 2B
CRP: niet afgeleid, onvoldoende gegevens

Beknopte medische informatie

Ontsmetting damp
algemeen: hulpverleners: persoonlijke bescherming (o.a. handschoenen); frisse lucht, rust halfzittende houding, GEEN mond-op-mondbeademing en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: hulpverleners: persoonlijke bescherming, verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen).
inslikken: hulpverleners: persoonlijke bescherming, mond laten spoelen (uitspugen!), specifieke behandeling en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: atropine moet ter plekke aanwezig zijn. Hulpverleners: let op persoonlijke bescherming! Toedienen van oximen en/of zuurstof kan overwogen worden.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 56-38-2 **Parathion** **$C_{10}H_{14}NO_5PS$** **UN-nr: 3278 n.o.s.**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: Same POD as for AEGL-2, different uncertainty factors, 2h value added.

LBW: Same POD as for AEGL-3, different uncertainty factors, 2h value added.

Date: 06-10-2016 | Document AEGL: Interim, 2009

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	8.3	5.8	4.6	3.6	2.9	1.4	Threshold for muscle tremors in rats.
LBW	11	7.5	6.0	4.7	3.8	1.9	Threshold for lethality in rats.

Derivation of the Dutch Intervention Values

VRW: VRW values are not recommended, because there are no exposure-response data in humans or animals consistent with VRW-level effects. The lack of VRW-values does not necessarily mean that exposure below AGW-levels is without any effects.

AGW: For derivation of the AGW values the incidence data for parathion-induced muscle tremors from a rat study were used for analysis using Benchmark Dose software. Rats (34/concentration level) were exposed (whole body) to 31, 35, 50, 71, 97, 100.6, 118.5, or 230.5 mg parathion/m^3 for 4 hours. A BMC_{01} of 28.9 mg/m^3 and a $BMCL_{05}$ of 32.3 mg/m^3 were derived using the Benchmark Dose software. The AGW values are based upon the 4-hour BMC_{01} level as being the lower point of departure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The intraspecies factor of 3 was considered sufficiently protective for the variability between species for organophosphates. Time scaling was performed using the equation $C^n \times t = k$ to derive exposure duration-specific values, using the default value n=3 for extrapolation from 4 hours to shorter exposure durations and the default value of n=1 for extrapolation from 4 hours to 8 hours.

LBW: For derivation of the LBW values the lethality data from the same rat study that was used for derivation of the AGW values was used for analysis using Benchmark Dose software. Rats (34/concentration level) were exposed (whole body) to 31, 35, 50, 71, 97, 100.6, 118.5, or 230.5 mg parathion/m^3 for 4 hours. A $BMCL_{05}$ of 37.5 mg/m^3 and a BMC_{01} of 41.1 mg/m^3 were derived using the Benchmark Dose software. The LBW values are based upon the $BMCL_{05}$ level as an estimate for the threshold for lethality observed in a rat study, resulting $BMCL_{05}$ estimate exposure of 37.5 mg/m^3 for 4 hours which was used as the point of departure for derivation of the LBW values.
The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The intraspecies factor of 3 was considered sufficiently protective for the variability between species for organophosphates. Time scaling was performed using the equation $C^n \times t = k$ to derive exposure duration-specific values, using the default value n=3 for extrapolation from 4 hours to shorter exposure durations and the default value of n=1 for extrapolation from 4 hours to 8 hours.

Additional toxicological information (including relevant results of a general literature search, if any)

The absorption of parathion by the respiratory tract is rapid and complete. Parathion will be rapidly metabolized in the liver to the more toxic paraoxon metabolite. Studies showed that parathion is a potent inhibitor of cholinesterase resulting in an excess of acetylcholine resulting at neuronal synapses and myoneural junctions. The oxon phosphorylates cholinesterase by phosphorylating the serine hydroxyl group of the esteratic subsite of the enzyme which in turn prevents the enzyme from deactivating acetylcholine. The overall result is an enhancement of cholinergic-mediated function (DUMBELS (muscarinic effects: Diarrhea, Urination,Miosis, Bronchorrea, Bronchospasm, Bradycardia, Emesis, Lachrymation, Salivation, Secretions, Sweating).

There is no information available on developmental or reproductive toxicity and genotoxicity of parathion.

H300: Fatal if swallowed, H311: Toxic in contact with skin, H330: Fatal if inhaled, H372: Causes damage to organs through prolonged or repeated exposure

Carcinogenicity and derivation of the CRP value
IARC classification: 2B (possibly carcinogenic to humans) No carcinogenic risk potency (CRP) could be derived due to inadequate data.

Odour and derivation of the LOA value
Odour: garlic-like odour ODT: 0.4760 mg/m^3 [Ruth, 1986] LOA = 11.8 * ODT * 1.33 = 7.47 mg/m^3 (The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/ODT) + 0.5. A correction factor of 1.33 is applied to this value) The LOA lies below the 10 min AGW and the 10 and 30 min LBW values.

Other standards and guidelines *(1h values in mg/m^3, unless otherwise indicated)*				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH: 10 mg/m^3 (30 min)*
AGW level 4.6	*AEGL-2* 1.5	*ERPG-2* -		
LBW level 6.0	*AEGL-3* 2.0	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 19624-22-7 **Pentaboraan** B_5H_9 **VN-nr: 1380**

GEVI: geen

Synoniemen: nonahydropentaboraan, pentaboornonahydride (Engels: pentaborane) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	1,2	0,59	0,37	0,23	0,14	0,089
Levensbedreigende waarden	LBW (mg/m³)	4,5	2,1	1,3	0,83	0,52	0,32

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,382 ppm; 1 ppm = 2,62 mg/m³

Explosiegrens: LEL = 0,42 vol% ≈ 11.000 mg/m³

Geur: stekend

LOA: 39,2 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: zelfontbranding bij 35˚C

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,26

Molecuulmassa: 63,1 g/mol
Zuurgraad: Geen data
LogKow: Geen data
Wateroplosbaarheid: ontleedt
Verzadigde dampdruk: 220 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: 0,013 mg/m³

TLV-TWA: 0,013 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: (vertraagde) effecten kunnen niet worden uitgesloten

AGW → LBW: hoofdpijn, misselijkheid, braken, duizeligheid, verminderd beoordelings- en reactievermogen

Boven LBW: tremoren, convulsies, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Pentaboraan heeft een effect op het CZS. Het exacte mechanisme hiervan is niet bekend, maar de CZS effecten zouden veroorzaakt kunnen worden door verlaging van serotonine en norepinefrine niveaus in de hersenen.
- De CZS-effecten kunnen direct of zelfs vertraagd optreden.
- De stof werkt irriterend of zelfs corrosief op de huid en ogen.
- Pentaboraan heeft steile concentratie-respons relatie.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn, brandwonden

Oogcontact: roodheid en pijn, slecht zien (centraal zenuwstelsel-visusklachten), hoornvliesbeschadiging

Carcinogeniteit

IARC classificatie: niet geclassificeerd.

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 19624-22-7 **Pentaborane** B_5H_9 **UN-nr: 1380**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL-1.

AGW: Same point of departure as for AEGL values but using different n-values, 2h value added.

LBW: Same point of departure as for AEGL values but using different n-values, 2h value added.

Date: November 2015 | AEGL document: Final, 2015

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended.
AGW	1.2	0.59	0.37	0.23	0.14	0.089	CNS effects in dogs
LBW	4.5	2.1	1.3	0.83	0.52	0.32	Threshold for animal (mice) mortality

Derivation of the Dutch Intervention Values

VRW: The derivation of VRW values is not recommended, because no studies were found with an endpoint within the scope of VRW type effects.

AGW: The point of departure for the AGW was a single 60-minute exposure to 1.4 ppm (3.7 mg/m³), of an exposure study of 5 successive days in beagle dogs, which caused no neurological signs or conditioned avoidance response (CAR) impairment. Dogs similarly exposed a second time (the following day) began to exhibit central nervous system (CNS) effects including decreased activity, miosis, and CAR delays, and additional exposures caused irritability and aggressiveness. At a higher exposure concentration of 3.0 ppm (7.9 mg/m³) in another study in dogs also no toxic signs were observed, but CAR impairment was not examined. Furthermore, at 4.5 ppm (11.8 mg/m³) convulsions were reported. Therefore, the point of departure was set at 1.4 ppm (3.7 mg/m³) for a 60 minute exposure. A total uncertainty factor (UF) of 10 was applied. This included an interspecies uncertainty factor of 3 because pentaborane caused similar effects (CNS toxicity) in four species of animals and humans, and LC_{50} values varied less than 3-fold among species. An intraspecies uncertainty factor of 3 was applied because the homogenous response among species and the steep dose-response for lethality indicate that there would be little variability among humans. Concentration was scaled across time using the relationship $C^n \times t = k$ with a value of n=1.47, based on mice-lethality data (this in contrast to the AEGL-2, for which an n-value of 1.3 based on rat data was used). The dog LC_{50} data (other study) yielded an n=1.0, but this was not used because the exposure duration was only 2-15 minutes. Using a value of n based on a mice study was considered appropriate because neurotoxicity was the primary toxic effect in both species, and they were similarly sensitive to pentaborane exposure.

LBW Acute lethality data were available from studies of monkeys, rats, mice, and dogs. The studies portrayed a consistent picture of pentaborane intoxication, which was manifested as tremors, weakness, ataxia, aggressiveness, and convulsions. LC_{50} values were comparable for monkeys, rats, and dogs, but were consistently lower for mice; however, the values in mice were generally less than 2-fold lower than other tested species. In general, there was less than a 3-fold difference in the LC_{50} values in rats, mice, dogs, and monkeys for a given exposure duration indicating very little species differences. The lowest LC_{50} values found in mice were used for derivation of the LBWs. Benchmark dose software (EPA Version 1.3.2 and 2.4.0) was used to calculate LC_{50}, $BMCL_{05}$, and BMC_{01} values. The respective values for the 60-min study were 7.75, 5.08, and 6.04 ppm, and for the 4-h study were 3.5, 2.2, and 2.6 ppm. The $BMCL_{05}$ of 5.08 ppm was selected as an estimate of the threshold for lethality. Concentrations were scaled across time using the equation $C^n \times t = k$ with a value of n=1.47, based on mice-lethality data (this in contrast to the AEGL-3, for which an n-value of 1.3 based on rat data was used). A total uncertainty factor of 10 was applied. An interspecies uncertainty factor of 3 was used because pentaborane caused similar effects (CNS toxicity) in humans and four species of laboratory animals, and LC_{50} values varied less than 3-fold among species. An intraspecies uncertainty factor of 3 was applied because the homogeneous response among species and the steep concentration-response curve for lethality indicate that there would be

little variability among humans.
The 60-min $BMCL_{05}$ of 5.08 ppm was selected as the point-of-departure for the LBW values because it yielded slightly lower LBW values in comparison with LBW values calculated on the basis of the 4-h $BMCL_{05}$. The LBW values for pentaborane are supported by the LC_{50} values of Weir et al. (1961, 1964) for rats exposed for 60 min, which would have yielded slightly higher LBW values. The lethality data from studies of monkeys exposed for 2 min and dogs exposed for 2-15 min (Weeks et al. 1964) also would have yielded similar LBW values, but were not used because of the short exposure durations.

Additional toxicological information (including relevant results of a general literature search, if any)

The mechanism of pentaborane toxicity is unknown, but may involve decreased brain serotonin and norepinephrine levels. Pentaborane is a potent reducer capable of reacting with ammonia, organic amines, and unsaturated hydrocarbons. The mechanism of toxicity appears to be similar among species, as the CNS was consistently the primary target organ. Symptoms in humans have included dizziness, drowsiness, headache, hiccups, impaired judgment, incoordination, muscle spasms, and convulsions, and in animals included tremors, salivation, miosis (constriction of pupils), lethargy, aggressiveness, and convulsions.
May cause severe chemical burns upon contact with the liquid of high vapour concentrations.

No developmental or reproductive toxicity animal studies were found, although reprotoxic effects were noted in a subchronic animal study. It is noted that pentaborane hydrolysis product boric acid has been shown to induce reprotoxic and developmental toxic effects after repeated inhalation exposure.

No risk phrases were found.

Carcinogenicity and derivation of the CRP value

IARC classification: Not classified.

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: pungent

OT_{50}: 2.5 mg/m^3 [AEGL]
LOA = 11.8 * OT_{50} * 1.33 = 39.2 mg/m^3

(The concentration Level leading to distinct Odour Awareness (l=3) is calculated using the formula: l = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is above the LBW, which is in agreement with the safety statement on the material data sheet, which states that severe effects may occur before odour detection.

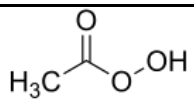
***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **NR**	*AEGL-1* NR	*ERPG-1* Not derived		*IDLH: 2.6 (30 min)*
AGW level **0.37**	*AEGL-2* 0.37	*ERPG-2* Not derived		
LBW level **1.3**	*AEGL-3* 1.3	*ERPG-3* Not derived		

Stofdocument deel A

CAS-nr: 79-21-0
$C_2H_4O_3$

Perazijnzuur



VN-nr: 3105
GEVI: geen

Synoniemen: acetylhydroperoxide, peroxyazijnzuur (Engels: peracetic acid)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,52	0,52	0,52	0,52	0,52	0,52
Alarmeringsgrenswaarden	AGW (mg/m³)	3,8	2,6	2,1	2,1	2,1	2,1
Levensbedreigende waarden	LBW (mg/m³)	40	28	22	17	14	6,9

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,316 ppm; 1 ppm = 3,165 mg/m³

Explosiegrens: niet bepaald

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze oplossing
Brand: brandgevaarlijk, bij vele reacties kans op brand en explosie

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,0-1,1

Molecuulmassa: 76,1 g/mol

Zuurgraad: pH 1,96 bij 40 g/100 ml

LogKow: geen data

Wateroplosbaarheid: volledig

Verzadigde dampdruk: 27 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid
TLV-STEL: 1,24 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte neusirritatie

VRW → AGW: hoesten, niezen, tranende ogen, pijn achter borstbeen

AGW → LBW: keelpijn en hoesten, rode ogen, tranen, branderig gevoel, kortademigheid

Boven LBW: ademnood, bloed ophoesten, longoedeem, ernstige bloeddrukdaling, bewusteloosheid , sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Perazijnzuur werkt irriterend tot bijtend op de ogen, de huid en de luchtwegen.
- Blootstelling aan perazijnzuur kan longontsteking, longoedeem en een astmatische reactie veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Mensen met COPD en bronchiale hyperreactiviteit kunnen extra gevoelig zijn.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, brandwonden
Oogcontact: bijtend, roodheid en pijn, slecht zien, blindheid

Carcinogeniteit

IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en onmiddellijk spoedeisende hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, aan de huid verkleefde kleiding niet lostrekken, minimaal 20 minuten douchen of spoelen met water, zo nodig arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), (oog)arts raadplegen, blijven spoelen of druppelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

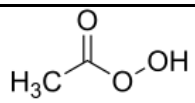
***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 79-21-0
$C_2H_4O_3$

Peracetic acid



UN-nr: 3105

Basis for the Dutch Intervention Values

VRW: AEGL value adopted, 2h value added

AGW: Different point of departure as for AEGL values,, 2h value added

LBW: Different point of departure as for AEGL values, using different value for n, 2h value added

Date: 16-10-2018 | AEGL final, 2010

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.52	0.52	0.52	0.52	0.52	0.52	Threshold for irritation of upper respiratory tract in humans
AGW	3.8	2.6	2.1	2.1	2.1	2.1	Mild irritation of upper respiratory tract in humans
LBW	40	28	22	17	14	6.9	Threshold for lethality in rats

Derivation of the Dutch Intervention Values

VRW: The VRW is based on data from human volunteer studies (unknown number of participants). Humans exposed to peracetic acid at ≤1.56 mg/m³ for up to 45 min experienced no clear discomfort. Others reported that 1.56 mg peracetic acid/m³ is not immediately irritating; this concentration is used as point of departure. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was not applied as mild irritation is considered to be concentration-dependent rather than concentration x time-dependent. The VRW values are supported by the fact that exposure to 0.40-0.53 mg/m³ for up to 3 hours was tolerable and considered not unpleasant.

AGW: The AGW is based on data from a human volunteer study (unknown number of participants). Exposure to peracetic acid at 6.23 mg/m³ for up to 1 h caused extreme discomfort and unbearable irritation, but exposure to 6.23 mg/m³ for 2 min was considered tolerable. A slightly lower concentration of 4.67 mg/m³ caused discomfort or slight discomfort of nasal and eye membranes for exposure durations up to 20 min. The effects at 6.23 peracetic acid mg/m³ appear to be more serious than those described by the definition of the AGW and could hinder the ability to escape. Although irritation to the upper respiratory tract was extreme, no effects occurred in the lower respiratory tract even at concentrations as high as 15.6 mg/m³. Moreover, peracetic acid is freely soluble in water and should be effectively scrubbed in the nasal passages at the concentrations considered for deriving AGW values. The effects at 4.67 mg/m³ are slightly less severe than those defined by AGW, therefore the higher exposure level of 6.23 mg/m³ for up to 1 h was used as PoD for the AGW The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. The human data indicate a time dependency for this effect between 2 minutes and 1 hour. Therefore time scaling was applied to 10 and 30 min with a default n value of 3. Time scaling to longer exposure durations would result in AGW values in conflict with human data (see VRW). Therefore, the 2-, 4- and 8-hour values were set equal to the 1-hour AGW of 2.1 mg/m³.

LBW: The LBW is based on an acute lethality study in rats. Rats (5/sex/conc) were exposed for 4 hours nose-only to an aerosol derived from a peracetic acid formulation (containing 5% peracetic acid, 10% acetic acid, 19% hydrogen peroxide, ~1% surfactant and water). Peracetic acid concentrations of 87, 163, 185 and 267 mg/m³ resulted in lethality ratios of 0/5, 0/5, 2/5 and 4/5 in males and 0/5, 0/5, 2/5 and 5/5 in females, respectively. Doseresp was applied and the calculated 4-hour LC_{50} and LC_{01} values were 207 and 138 mg/m³, respectively. The 4-hour LC_{01} value of 138 mg/m³ was used as point of departure for deriving the LBW values. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter time points, respectively.
A second rat lethality study is available with exposure durations of 15, 30 and 60 minutes. Doseresp

analysis of this dataset did not result in a reliable output. It is however noted that starting from the highest concentration without lethality in this study, similar LBW values for the shorter exposure durations would have been obtained.

Additional toxicological information (including relevant results of a general literature search, if any)

Peracetic acid is a corrosive chemical; it causes irritation to the skin, eyes and mucous membranes of the respiratory tract.

Two constituents in peracetic acid are acetic acid and hydrogen peroxide, and these may have contributed to the observed effects of peracetic acid. Also aerosols and vapours will contain these constituents in addition to peracetic acid. It appears however that acetic acid and hydrogen peroxide are considerably less toxic than peracetic acid. The lowest lethal concentration for a 4-h exposure of rats to acetic acid (39 216 mg/m^3) is about 30 times greater than the LC_{50} (1283 mg/m^3) calculated from the acetic acid concentrations reported in for the study used as PoD for LBW values. Likewise, the LC_{50} for hydrogen peroxide reported for rats (1972 mg/m^3) is almost 3 times greater than the LC_{50} (684 mg/m^3) calculated from these data. Therefore, the concentration of acetic acid appears too low to have caused the deaths among the rats exposed to peracetic acid. The concentration of hydrogen peroxide may have contributed slightly to the overall mortality.

Information on reproductive toxicity is not available for peracetic acid.

H302: Harmful if swallowed, H312: Harmful in contact with skin, H332: harmful if inhaled, H314: Causes severe skin burns and eye damage

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not evaluated No carcinogenic risk potency (CRP) was derived	Odour: pungent No LOA was derived

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [63]

VRW level **0.52**	*AEGL-1* 0.52	*ERPG-1* -		*IDLH:* -
AGW level **2.1**	*AEGL-2* 1.6	*ERPG-2* -		
LBW level **22**	*AEGL-3* 15	*ERPG-3* -		

[63] Note that the AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL.

Stofdocument deel A

CAS-nr: 127-18-4 **Perchloorethyleen** $CCl_2=CCl_2$ **VN-nr: 1897**

GEVI: 60

Synoniemen: tetrachloorethyleen, per, ethyleentetrachloride (Engels: tetrachloroethylene) ***Status*: A-stof**

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	240	240	240	240	240	240
Alarmeringsgrenswaarde	AGW (mg/m³)	1.700	1.700	1.700	1.200	790	540
Levensbedreigende	LBW (mg/m³)	35.000	19.000	13.000	8.600	5.800	3.900

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,145 ppm; 1 ppm = 6,90 mg/m³

Explosiegrens: LEL = n.v.t.

Geur: oplosmiddelachtige / etherische geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,09

Molecuulmassa: 165,8 g/mol

Zuurgraad: geen data

LogKow: 3,4

Wateroplosbaarheid: Niet

Verzadigde dampdruk: 18,9 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 172 mg/m³

Vluchtig

Vloeistof wordt makkelijk door intacte huid opgenomen

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: irritatie ogen, huid en luchtwegen, hoesten, misselijkheid, hoofdpijn, duizeligheid, verminderde coördinatie

AGW → LBW: benauwdheid, misselijkheid, bewustzijnsdaling

Boven LBW: ademnood, verstoring van het hartritme, longoedeem, ademstilstand, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Perchloorethyleen werkt irriterend op de ogen, huid en luchtwegen.
- Perchloorethyleen heeft een depressieve werking op het CZS en de ademhaling.
- Effecten op de lever en nier na blootstelling aan perchloorethyleen zijn beschreven.
- Blootstelling aan perchloorethyleen kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: irritatie, roodheid, pijn

Oogcontact: irritatie, roodheid, pijn, tranen

Carcinogeniteit

IARC classificatie: 2A

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen, arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 127-18-4 **Tetrachloroethylene** **$CCl_2=CCl_2$** **UN-nr: 1897**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same point of departure as AEGL values, but different value for n

LBW: Different point of departure and different value for n than AEGL values

Date: 24-09-2009 | AEGL document: Interim, 2009

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	240	240	240	240	240	240	Mild eye irritation in humans
AGW	1,700	1,700	1,700	1,200	790	540	No-effect level for ataxia in rats
LBW	35,000	19,000	13,000	8,600	5,800	3,900	Calculated treshold (LC_{01}) for lethality in animals (mice).

Derivation of the Dutch Intervention Values

VRW: The VRW derivation is based on the exposure of 6 volunteers to 106 ppm (730 mg/m³) for 1 hour. At this level, an apparent non-objectionable odour and eye irritation were noted, and one subject experienced a slight fullness in the head. An interspecies uncertainty factor was not applicable. An intraspecies uncertainty factor of 3 was applied because mucous membrane irritation is caused by a direct effect of the chemical and the response is not expected to vary greatly among individuals. Because irritation is considered a threshold effect which should not vary over time, the VRW value was not scaled across time, but the same value was applied to all times.

AGW: The AGW values are based upon the no-effect level for ataxia after first exposure in rats following exposure to 1,150 ppm (7,900 mg/m³) tetrachloroethylene for 4 hours/day, 5 days/week for 2 weeks (the time period of 4 hours) was used for the derivation. Exposure to the next higher concentration of 2,300 ppm (16,000 mg/m³) resulted in reversible ataxia. A total uncertainty factor of 10 is applied. An interspecies uncertainty factor of 3 is applied based on the similarity of effects manifested in rodents compared to humans produced by agents that are CNS depressants. An intraspecies uncertainty factor of 3 is applied based on total range of sensitivity (2-3 fold) between several different groups (newborns, pregnant women and the elderly) for anaesthetic gases. Many organic vapours, particularly those which are strongly lipophilic, produce an anaesthetic effect in exposed humans. On the basis of this knowledge, it is reasonable to assume that the same 2-3 fold difference in sensitivity among individuals would apply for tetrachloroethylene.
Time scaling was performed using the equation $C^n \times t = k$ and an n-value of 1.8 (based on probit analysis of rat mortality data). The 10- and 30-minute AGW values were set equal to the 1-hour value of 250 ppm (1,700 mg/m³) because a human study demonstrated an exposure to 600 ppm (4,100 mg/m³) for 10 minutes caused significant effects (eye and nose irritation, dizziness, tightness and numbing about the mouth, some loss of inhibitions, and motor coordination required great effort). After applying an uncertainty factor of 3 (for intraspecies variation), the AGW values based upon this study are consistent with the 1- hour AGW value of 250 ppm (1,700 mg/m³).

LBW: In contrast to the AEGL, the LBW derivation is not based on one-third of the 4-hour mouse LC_{50} value of 5,200 ppm (36,000 mg/m³), resulting in a point of departure of 1,733 ppm (12,000 mg/m³), but on a probit analysis using DoseResp with rat lethality data. This study of Rowe *et al.* tested multiple concentrations and time points. Probit analysis yielded LC_{01} values for the 10-, 30min, 1-, 2-, 4- and 8hr exposure durations of 15390, 8231, 5546, 3736, 2517 and 1696 ppm (106,000, 57,000, 38,000, 26,000, 17,000, 12,000 mg/m³) and an n-value of 1.8 for time scaling. An interspecies uncertainty factor of 1 was applied based on similar exposure effects in humans compared with animals, and pharmacokinetic data indicating an interspecies uncertainty factor for toxicokinetic differences of less than 1 when using rat data to derive exposure values for humans. An intraspecies uncertainty factor of 3 is applied based on the previously described argument that the sensitivity for volatile anaesthetics should not vary more than a factor of 2-3-fold. Use of a total uncertainty factor of 10 (3x3) would be too low, because the LBW values are supported by a human study in which the effects noted were milder than those defined by the LBW definition. In this study, humans exposed to 934 ppm (6,400 mg/m³) for 95 minutes experienced

tightness of the frontal sinuses, increased hand perspiration, nostril irritation, congestion of Eustachian tubes, lassitude, slight mental fogginess, stinging eyes, exhilaration, and/or the tip of the nose and lips anesthetized. An animal study in which rats exposed to 2,300 ppm (16,000 mg/m^3) for 4 hours/day, 5 days/week for two weeks exhibited overt ataxia only following the first 4 hour exposure.

Additional toxicological information (including relevant results of a general literature search, if any)

Tetrachloroethylene has low acute inhalation toxicity. The liver, kidneys, blood and central nervous system (CNS) are the target organs for systemic effects. In humans the initial uptake of tetrachloroethylene following inhalation is rapid, with rates levelling off after a few hours of exposure. The available data suggest that a high proportion is absorbed in humans, but actual percentages have not been reported. Based on the effects of various volatile anaesthetics maximal sensitivity is expected in newborns (particularly prematures), pregnant women, and the elderly. The total variation, however, is not more than 2-3 fold. The least sensitive are older infants, toddlers and children compared to normal adults.

A few epidemiological studies have reported reproductive or developmental abnormalities due to exposure to tetrachloroethylene in drinking water. The results of several studies consistently indicated that occupationally exposed women might suffer higher rates of spontaneous abortion. A retrospective time-to-pregnancy study among Finnish women indicated a reduced ability to reproduce among 20 women exposed to tetrachloroethylene (concentration was not clear) 1-4 days a week or daily by inhalation. The relevance of these effects after single exposures is uncertain.

From the available data, it may be concluded that skin absorption may contribute significantly to the systemic effects of tetrachloroethylene.

H351: Suspected of causing cancer.

Carcinogenicity and derivation of the CRP value

IARC classification: 2A (probably carcinogenic to humans)

No carcinogenic risk potency (CRP) was derived

IARC concluded that there is evidence for consistently positive associations between exposure to tetrachloroethylene and the risks for oesophageal and cervical cancer and non-Hodgkin lymphoma. These associations appear unlikely to be due to chance, although confounding factors cannot be excluded and the total numbers in the cohort studies combined are relatively small.

Odour and derivation of the LOA value

Odour: solvent like, ethereal

No LOA was derived due to the absence of consistent odour perception.

Odour threshold ranging from 2 - 71 ppm (14 – 490 mg/m^3)

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **240**	*AEGL-1* 240	*ERPG-1* 690		*IDLH:* 1035 (30 minutes)
AGW level **1,700**	*AEGL-2* 1,600	*ERPG-2* 1,380		
LBW level **13,000**	*AEGL-3* 8,300	*ERPG-3* 6,900		

Stofdocument deel A

CAS-nr: 594-42-3 **Perchloormethylmercaptaan** Cl_3CSCl **VN-nr: 1670**
GEVI: 66

Synoniemen: trichloormethaansulfenylchloride, trichloormethylsulfenylchloride, trichloormethaanthiol (Engels: perchloromethylmercaptan)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,10	0,10	0,10	0,10	0,10	0,10
Alarmeringsgrenswaarden	AGW (mg/m³)	4,2	2,9	2,3	1,2	0,58	0,29
Levensbedreigende waarden	LBW (mg/m³)	13	8,8	7,0	3,5	1,7	0,87

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,129 ppm; 1 ppm = 7,75 mg/m³

Explosiegrens: geen data

Geur: stekende geur, walgingwekkend, ondraagbaar

LOA: 0,12 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: gele olieachtige vloeistof
Brand: niet brandbaar, bij vele reacties kans op brand en explosie

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,01

Molecuulmassa: 185,9 g/mol
Zuurgraad: Geen data
LogKow: Geen data
Wateroplosbaarheid: Niet oplosbaar
Verzadigde dampdruk: 2,4 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 0,77 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen gegevens

VRW → AGW: lichte irritatie ogen en luchtwegen

AGW → LBW: sterke irritatie ogen en luchtwegen, hoesten, pijnlijke ademhaling, benauwdheid, longoedeem

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Perchloormethylmercaptaan veroorzaakt sterke oog, huid- en luchtwegirritatie.
- Longoedeem kan optreden bij hoge concentraties. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, brandwonden

Oogcontact: bijtend, roodheid en pijn, slecht zien, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: kleding uittrekken (NIET lostrekken), direct spoelen met veel water (minimaal 20 min.), dan pas eventueel aan de huid vastgeplakte kleding verwijderen en verder spoelen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 594-42-3 **Perchloromethyl mercaptan** **Cl_3CSCl** **UN-nr: 1670**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 24-09-2009 | AEGL document: Final, 2011

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.10	0.10	0.10	0.10	0.10	0.10	Mild nasal and pulmonary irritation in animals
AGW	4.2	2.9	2.3	1.2	0.58	0.29	LBW divided by 3
LBW	13	8.8	7.0	3.5	1.7	0.87	Threshold of animal lethality

Derivation of the Dutch Intervention Values

VRW: The VRW is based on mild nasal epithelial changes noted at 0.13 ppm (1.0 mg/m³) in a 2-week repeated dose study in rats and is considered a NOAEL for notable irritation. This concentration is also a NOAEL for pulmonary irritation. A total uncertainty factor of 10 was applied. An interspecies factor of 3 was applied because minor irritation is not expected to vary greatly among species. An intraspecies uncertainty factor of 3 was applied because irritation is not expected to vary greatly among individuals, and the steep dose-response curve may be an indication of little variation within a population (no deaths were observed in rats exposed to 9 ppm (70 mg/m³) but 7/10 died at 18 ppm (140 mg/m³)). No modifying factor was applied because the minor epithelial changes were noted in a repeat-exposure study. The derived value was set equal at all VRW time-points because the endpoint is a no-effect level for mild irritation.

AGW: Insufficient data were available to derive AGW values. Therefore, the AGW values are derived by dividing the LBW values by 3. The divisor of 3 is reasonable based on the steepness of the steep dose-response curve for lethality: no rats died following exposure to 9 ppm (70 mg/m³) for 1 hour, but 7/10 died at 18 ppm (140 mg/m³).

LBW: As starting point for the derivation of the LBW the threshold of rat lethality of 9 ppm (70 mg/m³) for 1 hour was taken. All exposed animals exhibited eye and mucosa irritation within five minutes after exposure, and dyspnea, gasping, and “acute depression” were also observed. Necropsy revealed inflamed mouth and nasal mucosa. A total uncertainty factor of 10 was applied. An interspecies uncertainty factor of 3 was applied on the basis that the mechanism of toxicity appears to be that of a direct irritant, and is therefore not expected to differ significantly among species. An intraspecies uncertainty factor of 3 was applied because the effects of exposure appear to be related to a direct irritant effect, and irritant effects are not expected to vary greatly among individuals. The intraspecies uncertainty factor of 3 is also supported by the steep dose-response curve, which may be an indication of little variation within a population. LBW values are scaled using $C^n * t = k$, using defaults n = 1 or 3 for extrapolation to longer and shorter exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Perchloromethyl mercaptan is a strong irritant to eyes, skin and the respiratory tract (mucosa). Because the substance is insoluble in water it can reach the deeper areas of the lungs. The substance might damage liver and kidneys. It may have adverse effects on the central nervous system causing unconsciousness and death. May have delayed toxicological effects.

No developmental/reproductive toxicity data on perchloromethyl mercaptan were found in the available literature.

No harmonized H-statements for human health.

Carcinogenicity and derivation of the CRP value

Odour and derivation of the LOA value

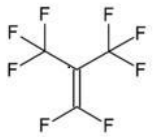
IARC classification: not classified No carcinogenic risk potency (CRP) was derived	Odour: Unbearable acrid odour. OT_{50}: 0.0075 mg/m^3 [ACGIH] LOA = 11.8 * OT_{50} * 1.33 = 0.12 mg/m^3 (The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value) The ACGIH-TLV documented an odour detection threshold of 0.0075 mg/m^3. This value was used to derive the LOA. The LOA is just above the VRW and below the AGW.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*				
VRW level **0.10**	*AEGL-1* 0.10	*ERPG-1* Not derived		*IDLH:* 77 (30 min)
AGW level **2.3**	*AEGL-2* 2.3	*ERPG-2* Not derived		
LBW level **7.0**	*AEGL-3* 7.0	*ERPG-3* Not derived		

Stofdocument deel A

CAS-nr: 382-21-8
C_4F_8

Perfluorisobutyleen



VN-nr: 3162
GEVI: 26

Synoniemen: perfluorisobuteen, PFIB, 1-propene, 1,1,3,3,3-pentafluoro-2-(trifluoromethyl) (Engels: perfluoroisobutylene)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	5,7	1,8	0,93	0,47	0,23	0,12
Levensbedreigende waarden	LBW (mg/m³)	17	5,5	2,8	1,4	0,69	0,35

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,120 ppm; 1 ppm = 8,321 mg/m³

Explosiegrens: geen data

Geur: geurloos
LOA: -

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos (vloeibaar gemaakt) gas
Brand:-

Relatieve dichtheid van gas-lucht mengsel: 6,3

Molecuulmassa:	200,03 g/mol
Zuurgraad:	geen data
LogKow:	3,03
Wateroplosbaarheid:	0,011 g/100 ml
Verzadigde dampdruk:	2320 mbar (bij 25 ºC)

Overige informatie

Publieke grenswaarde: 0,082 mg/m³
MAK: niet afgeleid
TLV-TWA: niet afgeleid
TLV-STEL: 0,083 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW: keelpijn en hoesten

AGW → LBW: pijn op de borst, angst/onrust, kortademigheid, tachycardie, toenemende cyanose

Boven LBW: bloed ophoesten, ademnood, verstikking, circulatoire collaps

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- PFIB kan de permeabiliteit van capillaire bloedvaten verhogen, met bloedingen in alle blootgestelde organen als gevolg. Daarbij zijn de longen het meest gevoelige orgaan voor dit effect.
- Lagere concentraties kunnen na een symptoomvrij interval van 4 – 24 u aanleiding geven tot effecten die snel verergeren (tot circulatoire collaps).
- Hogere concentraties kunnen vrij snel tot een ernstig, hemorragisch longoedeem leiden; sterfte treedt meestal binnen 2 uur na blootstelling op.

Effecten bij blootstelling aan vloeistof

Huidcontact: bevriezingsletsel (gas: geringe irritatie)

Oogcontact:bevriezingsletsel (gas: geringe irritatie)

Carcinogeniteit

IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht (indien mogelijk zuurstof), GEEN mond-op-mondbeademing, vermijd inspanning (rust), half-zittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: kleding uittrekken (NIET lostrekken), direct spoelen met veel water (minimaal 20 min.), dan pas eventueel aan de huid vastgeplakte kleding verwijderen en verder spoelen, direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

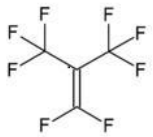
Specifieke behandeling en materialen*:* hulpverleners denk aan *persoonlijke (adem)bescherming.*
Neem contact op met het NVIC (tel: 030 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 382-21-8
C_4F_8

Perfluoroisobutylene

UN-nr: 3162



Basis for the Dutch Intervention Values

VRW: Not recommended due to insufficient data, in accordance with the AEGL

AGW: Same rationale as for AEGL (one-third of LBW), 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 16-10-2018	AEGL, interim (2010)

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	(insufficient data)
AGW	5.7	1.8	0.93	0.47	0.23	0.12	1/3 LBW
LBW	17	5.5	2.8	1.4	0.69	0.35	Threshold of lethality in rats

Derivation of the Dutch Intervention Values

VRW: No appropriate human or animal data are available for derivation of VRW for perfluoroisubytulene (PFIB). Therefore VRW values are not recommended. This does not imply that exposure below AGW is without adverse effects.

AGW: In the absence of appropriate chemical-specific data, the LBW values are divided by 3 to derive AGW values for PFIB. This approach is justified by the steep concentration-response curve observed in several animal studies. No rats died when exposed to 0.25 ppm (2.08 mg/m³) PFIB for 4 hours; whereas 100% lethality (6/6) was noted at 0.5 ppm (4.16 mg/m³) for 4 hours. No mortality was noted in rats, mice, 1 guinea pig, and rabbits exposed to approximately 0.70 ppm (5.82 mg/m³) PFIB for 2 hours; whereas, 10/10 rats, 10/10 mice, 4/5 guinea pigs, and 3/3 rabbits died when exposed to 1.5 ppm (12.48 mg/m³) for two hours.

LBW: The LBW is based on a study in which male rats (6/conc) were exposed for 4 hours to concentrations of 0.25, 0.5 or 1.0 ppm (2.08, 4.16 and 8.32 mg/m³, respectively). No mortality occurred in rats when exposed to 2.08 mg/m³ PFIB for 4-hours, whereas all rats died (6/6) at 4.16 mg/m³ for 4 hours. Clinical signs were noted at 2.08 mg/m³ and included face washing, hyperemia, sneezing, hypernea, dyspnea, and decreased responsiveness. The highest non-lethal concentration of 2.08 mg/m³ was used as PoD for deriving LBWs.
In a C x t acute lethality study, rats (10/concentration) were exposed to different concentrations of PFIB, ranging from 10 ppm to 832 ppm for various exposure durations ranging from 0.25 to 10 minutes, e.g. 1 minute to 100, 102, 106, 130, 158 and 832 ppm (832, 849, 882, 1082, 1315 and 6923 mg/m³, respectively). Although an extrapolation from a 10 minute POD to an exposure duration of 8 hours is not considered reliable, using the C x t study as basis for derivation for the LBW would lead to similar values and can be considered as supportive.
The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. The interspecies UF of 1 is used instead of the default value of 3, because lethality data available for several animal species suggest little interspecies variability; the LC_{50} values for given exposure durations are essentially equivalent. Time scaling was applied using the equation $C^n \times t = k$ with the chemical specific value of n=1 (based on analysis of available LC_{50} data) when extrapolating to longer and shorter time points.

Additional toxicological information (including relevant results of a general literature search, if any)

PFIB may exert its toxic effect by depletion of intracellular nucleophiles, including amines, thiols and alcohols. PFIB-induced tissue damage appears to result from rapid interaction with cells that are either in, or in close proximity to, the respiratory airways. PFIB is a hydrophobic gas that induces a permeability-type edema.

Frequently it is stated that PFIB is10× more toxic than phosgene, however it is not clear what the basis for this statement is. The intervention values for PFIB are primarily based on substance-specific data.

Information on reproductive toxicity is not available for PFIB.

Health effects may be delayed.

No harmonised H-statements for human health.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not evaluated No carcinogenic risk potency (CRP) was derived	No LOA was derived.

Other standards and guidelines *(1h values in mg/m³, unless otherwise indicated)* [64]

VRW level **NR**	*AEGL-1* -	*ERPG-1* -		*IDLH: -*
AGW level **0.93**	*AEGL-2* 0.90	*ERPG-2* 0.83		
LBW level **2.8**	*AEGL-3* 2.7	*ERPG-3* 2.5		

[64] Note that the AEGL values as presented here (in mg/m³) are derived using the conversion factors of the AEGL. The ERPG values are derived using the conversion factor as described in part A.

Stofdocument deel A

CAS-nr: 110-89-4 **Piperidine** CH_2-$(CH_2)_4$-NH, cycl **VN-nr: 2401** **GEVI: 883**

Synoniemen: Azacyclohexaan, cyclopentimine, hexahydropyridine (Eng.: Piperidine) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	18	18	18	18	18	18
Alarmeringsgrenswaarden	AGW (mg/m³)	120	81	64	51	41	27
Levensbedreigende waarden	LBW (mg/m³)	460	320	250	200	160	80

Datum vaststelling: 28-11-2008

Conversiefactor: 1 mg/m³ = 0,282 ppm; 1 ppm = 3,54 mg/m³

Explosiegrens: LEL=1,3 vol% ≈ 46 000 mg/m³

Geur: peper of amine-achtige stekende geur

LOA: 21 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze hygroscopische vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,07

Molecuulmassa:	85,2 g/mol
Zuurgraad:	pH 12,6 (100 g/L, 20 °C)
LogKow:	0,8
Wateroplosbaarheid:	volledig
Verzadigde dampdruk:	34 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: neusirritatie, keelpijn, hoesten

AGW → LBW: oog- en luchtwegirritatie, duizeligheid, versnelde ademhaling, ademnood, verhoging bloeddruk, contractie gladde- en skeletspieren.

Boven LBW: convulsies, verminderde coördinatie, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Piperidine is corrosief voor de huid en zal irritatie van de ogen en luchtwegen veroorzaken.
- Piperidine stimuleert en blokkeert ganglia, chemoreceptoren en neuromusculaire synapsen. Hierdoor kan een diversiteit aan reacties ontstaan op verschillende niveaus in het lichaam.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, pijn, blaren, brandwonden

Oogcontact: bijtend, tranenvloed, roodheid en pijn, hoornvliesbeschadiging, ernstige brandwonden.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
Ontsmetting vloeistof
huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en arts raadplegen. Stof wordt door de huid opgenomen
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.
Vanwege brandgevaar verontreinigde kleding uitspoelen met veel water
Specifieke behandeling en materialen: geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 110-89-4 **Piperidine** **CH_2-$(CH_2)_4$-NH, cycl** **UN-nr: 2401**

Basis for the Dutch Intervention Values

VRW: Deviation from AEGL values: no time-scaling was performed but data were flatlined across the different time points and 2hr value was added

AGW: Same point of departure as for AEGL values but using different value for n; 2hr value added

LBW: Same point of departure as for AEGL values but using different value for n; 2hr value added

Date: 28-11-2008 | AEGL document: Final, 2013

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	18	18	18	18	18	18	Nasal irritation
AGW	120	81	64	51	41	27	Nasal irritation without eye closure or salivation
LBW	460	320	250	200	160	80	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: Although human data were available (a human irritation threshold for inhalation exposure to piperidine of 26 ppm (92 mg/m³) was reported), these data were not used as these were from secondary literature and are not to be verified.
The VRW values are based on the lowest concentration of 50 ppm (177 mg/m³) causing nasal irritation in rats after a 6-hour exposure. Uncertainty factors of 3 for interspecies differences and 3 for intraspecies variability were applied to this level. This total factor of 10 was considered appropriate because the effect was mediated by direct contact of piperidine with the nasal epithelium without involvement of other regions of the respiratory tract and the cell composition of the nasal mucosa is similar among species and among individuals within the population, although the cell distribution and nasal morphology differ among species. In addition, the linear correlation coefficients for the concentration versus time for LC_{50} values for three species are similar, not varying more than 30%. No time scaling was performed because irritancy is generally a threshold effect and prolonged exposure is not likely to result in a greatly enhanced effect.

AGW: The AGW values were based on exposure of rats to piperidine at 100 ppm (354 mg/m³) for 6 hours, which caused nasal irritation without salivation or evidence of eye irritation. The rationale for selecting uncertainty factors were the same as described for the derivation of the VRW values (inter=3, intra=3, total=10). Time scaling was performed using $C^n \times t = k$, with the default values of n =1 and n = 3 for extrapolations to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-2 value that was set equal to the 30 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: The LBW values were based on the LC_{01} calculated from a 4-hour acute inhalation study in rats. The LC_{01} of 448 ppm (1588 mg/m³) for the 4-hr exposure is below the lowest concentration that caused one death among 20 rats and above the highest concentration that caused no deaths or clinical signs indicative of death. Therefore, the LC_{01} appears to be a good estimate of the threshold for lethality. The rationale for selecting uncertainty factors were the same as described for the derivation of the VRW values (inter=3, intra=3, total=10). Time scaling was performed using $C^n \times t = k$, with the default values of n =1 and n = 3 for extrapolations to longer and shorter exposure durations, respectively. Applying an uncertainty factor of 10 for either intra or interspecies sensitivity would yield a LBW-values lower than the irritation threshold of 26 ppm (92 mg/m³).

Additional toxicological information (including relevant results of a general literature search, if any)

Piperidine is severely corrosive to skin, producing third degree burns in human after less than 3 minutes. Because of its corrosive properties, piperidine is expected to cause irritation to the eyes and respiratory tract. Piperidine stimulates and blocks actions on the gangli, chemoreceptors, and neuromuscular junctions. This causes a diverse number of effects/reactions on several levels in the body: respiratory stimulation, raised blood pressure, stimulation of smooth and skeletal muscle. It interacts with cholinergic receptor sites

mimicking effects of acetylcholine. Piperidine also affects CNS responses related to emotional behaviour, physiological processes of sleep and extrapyramidal motor function (ataxia, head turning, and nystagmus).

Available data indicate that piperidine is not toxic for reproduction or development.

H311: Toxic in contact with skin; H314: Causes severe skin burns and eye damage; H331: Toxic if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Piperidine has not demonstrated carcinogenic activity in experimental animals.

Odour and derivation of the LOA value

Pungent pepper, amine-like odour

OT_{50}: 0.367 mg/m^3 (1.3 mg/m^3)
LOA = 11.8 * OT_{50} * 1.33 = 21 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies at or below the VRW-10 min, 30 min, and VRW-1 hr and below all time points of the AGW and LBW values.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **18**	*AEGL-1* 23	*ERPG-1* -		*IDLH: not established*
AGW level **64**	*AEGL-2* 120	*ERPG-2* -		
LBW level **250**	*AEGL-3* 390	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 74-98-6 **Propaan** CH_3-CH_2-CH_3 **VN-nr: 1978**

GEVI: 23

Synoniemen: dimethylmethaan; (Engels: n-Propane) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	18.000*	13.000*	13.000*	13.000*	13.000*	13.000*
Alarmeringsgrenswaarden	AGW (mg/m³)	31.000**	31.000**	31.000**	31.000**	31.000**	31.000**
Levensbedreigende waarden	LBW (mg/m³)	61.000***	61.000***	61.000***	61.000***	61.000***	61.000***

Datum vaststelling: 13-05-2009

Conversiefactor: 1 mg/m³ = 0,546 ppm; 1 ppm = 1,83 mg/m³

Explosiegrens: : LEL=1,7 vol% ≈ 31.000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

** berekende interventiewaarde hoger dan 50% LEL

*** berekende interventiewaarde hoger dan LEL

Geur: reukloos

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos en reukloos onderdruk tot vloeistof verdicht gas.

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,6

Molecuulmassa: 44 g/mol
Zuurgraad: Geen data
LogKow: Geen data
Wateroplosbaarheid: niet
Verzadigde dampdruk: 9000 mbar

Overige informatie

Publieke grenswaarde: Niet afgeleid
MAK: 1800 mg/m³
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: duizeligheid, misselijkheid, slaperigheid

AGW → LBW: verminderde ademhaling, bewustzijnsdaling, hypothermie, hartritmestoornissen

Boven LBW: ademstilstand, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Propaan veroorzaakt asfyxie door verdringing van zuurstof in de lucht. Primaire doelorganen zijn de hersenen en het hart.
- De stof veroorzaakt een verhoogde gevoeligheid van het hart voor catecholaminen, zoals adrenaline.
- Risico op letsel en sterfte door explosie bestaan al beneden de concentratie waarbij letsel en sterfte door toxiciteit optreden.
- Propaan heeft een steile concentratierespons curve.

Effecten bij blootstelling aan vloeistof

Huidcontact: *bij bevriezing*: roodheid, pijn, blaren.

Oogcontact: roodheid, pijn, slecht zien.

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, en arts raadplegen.

Ontsmetting vloeistof

huid: *bij bevriezing*: aan de huid vastgevroren kleding NIET lostrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.

ogen: *bij bevriezing*: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Specifieke behandeling en materialen*: geen*.

Neem contact op met het NVIC (+31(0)30-274 88 88) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 74-98-6 **n-Propane** **CH_3-CH_2-CH_3** **UN-nr: 1978**

Basis for the Dutch Intervention Values

VRW: Same point of departure as AEGL, different time-scaling applied, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 13-05-2009 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	18,000*	13,000*	13,000*	13,000*	13,000*	13,000*	NOAEL for CNS effects in human volunteers.
AGW	31,000**	31,000**	31,000**	31,000**	31,000**	31,000**	NOAEL for cardiac sensitization in dogs.
LBW	61,000 ***	61,000 ***	61,000 ***	61,000 ***	61,000 ***	61,000 ***	Threshold for mortality due to cardiac sensitization in dogs

* value higher than 10% of LEL; ** value higher than 50% of LEL ; *** value higher than LEL

Derivation of the Dutch Intervention Values

VRW: The VRW derivation is based on observations in a study with volunteers on the warning properties of short exposures to propane. No effects were noted during a 10-min exposure to 10,000 ppm (18,000 mg/m³) but distinct vertigo was reported by volunteers when exposed to 100,000 ppm (180,000 mg/m³) for 2 min. An intraspecies uncertainty factor of 1 is considered adequate because the concentration-response curve for CNS effects appears to be very steep and thus the interindividual variability will be relatively small. Further, 10,000 ppm (18,000 mg/m³) appears to be a conservative starting point considering the effects reported at 100,000 ppm (180,000 mg/m³). The anesthetic potency for propane is estimated to be lower than for butane. The VRW values for propane should therefore not be lower than those for butane, which are based on the same study. For reasons of consistency the VRW values for propane are derived in a similar way as for butane. In contrast to the AEGL, time extrapolation was performed from 10 min to 30 using the equation $C^n * t = k$, using a factor of n=3 because available data on butane suggest a relatively high value for n. The effects of CNS depressing substances are assumed to be solely concentration dependent after reaching steady-state. Data on propane and butane indicate that steady-state will be reached within 30 min of exposure. Therefore the 30 min VRW value was adopted for the 1h, 2h, 4h and 8h time points. It is noted that all calculated VRW values are higher than 10% of the lower explosive limit.

AGW: The AGW derivation is based on cardiac sensitization. In a well-performed cardiac sensitization test beagle dogs were exposed to a propane concentration of 50,000 ppm (90,000 mg/m³), 100,000 (180,000 mg/m³), or 200,000 ppm (370,000 mg/m³). No cardiac sensitization occurred in 6 dogs exposed to 50,000 ppm (90,000 mg/m³) whereas at 100,000 ppm (180,000 mg/m³) 2 out of 12 dogs showed cardiac sensitization. These findings were supported by a second study using the same protocol in which an EC_{50} of 180,000 ppm (330,000 mg/m³) was reported. The endpoint of cardiac sensitization as studied in beagle dogs is relevant to human exposures as humans exposed to high concentrations of several substances may develop cardiac arrhythmia. The no-effect concentration of 50,000 ppm (90,000 mg/m³) was chosen as point of departure for the AGW values. Because the dog appears to be a good model for the human heart, an interspecies uncertainty factor of 1 was applied. Because this is a conservative test, an intraspecies uncertainty factor of 3 was applied to protect sensitive individuals. Because the information available indicates that cardiac sensitization is a concentration-related threshold effect and concentrations that do not produce a positive response in the short-term test will also not produce the effect when exposures are continued for longer periods no time-scaling was performed. It is noted that the calculated AGW values are higher than 50% of the lower explosive limit.

LBW: The same study as for AGW is used as starting point for the LBW. Although a marked cardiac response occurred in 2 out of 12 beagle dogs exposed to 100,000 ppm (180,000 mg/m³) in the cardiac sensitization test no deaths were found, whereas 1 case of ventricular fibrillation and cardiac arrest was found at an exposure concentration of 200,000 ppm (370,000 mg/m³). The concentration of 100,000 ppm (180,000 mg/m³) was used as point of departure for the LBW values. For reasons stated above an overall uncertainty factor of 3 was applied and no time-scaling was performed. It is noted that the calculated LBW values are higher than 100% of the lower explosive limit.

Additional toxicological information (including relevant results of a general literature search, if any)
The data on propane are very limited. Most data, especially the animal data, point to cardiac sensitization as an important effect. However, as with other alkanes CNS-depressing effects are also to be expected. The available data are not sufficient to determine, which of the two effects will occur at lower concentrations. Fatal cases of propane intoxication (abuse, suicide attempts, autoerotic cases) have been reported. Death occurred as a result of asphyxia; organs that were most often seriously affected in these cases are the brain and the heart. Studies on reproductive toxicity were not found. No harmonized H-statements for human health.

Carcinogenicity and derivation of the CRP value
IARC classification: not classified
No carcinogenic risk potency (CRP) was derived.
Carcinogenicity studies were not found.

Odour and derivation of the LOA value
Odour: odourless.
No LOA was derived.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***				
VRW level **13,000**	*AEGL-1* 10,000	*ERPG-1* not derived		*IDLH:* 3800 (30 minutes)
AGW level **31,000**	*AEGL-2* 31,000	*ERPG-2* not derived		
LBW level **61,000**	*AEGL-3* 60,000	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 123-38-6 **Propionaldehyde** C_2H_5COH **VN-nr: 1275**

GEVI: 33

Synoniemen: methylacetaldehyde, propanal, propylaldehyde (Engels: propionaldehyde) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	110	110	110	110	110	110
Alarmeringsgrenswaarden	AGW (mg/m³)	1200	810	640	510	400	260
Levensbedreigende waarden	LBW (mg/m³)	3700	2600	2000	1600	1300	640

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,414 ppm; 1 ppm = 2,42 mg/m³

Explosiegrens: LEL = 2,3 vol% ~ 56.000 mg/m³

Geur: zoete, esterachtige geur, ook beschreven als maltachtig en verstikkend

LOA: 1,5 mg/m³; De LOA ligt ver onder de VRW

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,3

Molecuulmassa:	58,1 g/mol
Zuurgraad:	geen data
LogKow:	0,8
Wateroplosbaarheid:	28 g/100 ml (goed)
Verzadigde dampdruk:	343 mbar

Overige informatie

Publieke grenswaarde:
Niet afgeleid
MAK: niet afgeleid
TLV-TWA: 48 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte irritatie slijmvliezen

VRW → AGW: irritatie van ogen, neus en luchtwegen

AGW → LBW: tranenvloed, verhoogde hartslag, hypertensie, benauwdheid, longoedeem

Boven LBW: ophoesten van bloed, ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Propionaldehyde werkt irriterend op de slijmvliezen van ogen en luchtwegen.
- De stof kan, in (zeer) hoge concentraties, longontsteking en longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Propionaldehyde kan bij zeer hoge concentraties mogelijke depressie van het CZS veroorzaken.

Effecten bij blootstelling aan vloeistof

Huidcontact: prikkeling, roodheid en pijn, branderig gevoel.

Oogcontact: bijtend, roodheid en pijn, slecht zien.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid.

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
Ontsmetting vloeistof
huid: eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen, arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: mond laten spoelen (uitspugen!) en direct spoedeisende medische hulp inzetten.
Specifieke behandeling en materialen:
Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 123-38-6 **Propionaldehyde** **C_2H_5COH** **UN-nr: 1275**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 24-09-2009 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	110	110	110	110	110	110	Mild irritation
AGW	1200	810	640	510	400	260	Irritation
LBW	3700	2600	2000	1600	1300	640	Analogy acetaldehyde: threshold lethality

Derivation of the Dutch Intervention Values

VRW: In a study in human volunteers a concentration of 134 ppm (324 mg/m³) propionaldehyde induced only mild irritation of the mucosal surface after a 30 minutes exposure (n=12). This level of severity is considered to be sub-VRW, and a valuable starting point for VRW derivation. Because the effect is direct irritation, differences between individuals are expected to be small. Therefore an intraspecies factor of 3 is applied to account for differences between humans. Because VRW is based on irritation, the VRW values are set equal for all time points. These values are based on the same study and (when expressed in ppm) equal to those proposed for the comparable substance acetaldehyde.

AGW: The value of 1,453 ppm (3511 mg/m³) for 6 hours a day from a well-performed combined repeated dose toxicity study (OECD 422 study) in rats was used as a starting point for AGW. This concentration induced increases in hemoglobin levels, hematocrit and monocyte concentration, absolute thymic region weight and relative kidney weight in males but not females. Microscopic examination indicated an exposure-related effect on the olfactory epithelium of the nasal cavity. At the low and intermediate concentrations tested (151 and 745 ppm; 365 and 1800 mg/m³), vacuolization of the nasal epithelium was seen in males and females. Some atrophy was seen in the mid concentration females and the low concentration males. Rhinitis was seen in high and intermediate concentration males and in the intermediate concentration females. The main effects observed in this study on the nasal epithelium can be attributed to repeated exposure and are not expected to occur after a single day exposure of 6 hours.
A total uncertainty factor of 10 is applied, consisting of an interspecies factor of 3 and an intraspecies factor of 3. A higher factor would reduce the AGW to levels that were tolerated without any serious effects in the human volunteer study with propionaldehyde. In addition, the resulting AGW values would than be inconsistent with the values for acetaldehyde. Default time-scaling $C^n \times t = k$ was performed with default values of n=1 for extrapolation to longer time periods and n=3 for extrapolation to shorter time periods. In contrast to the 10 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value. The AGW values for propionaldehyde are in the same range as the values for acetaldehyde.

LBW: The available acute exposure data on propionaldehyde are qualitatively insufficient and do not provide an adequate basis to derive LBW values from. Based on the rat data with repeated exposures a level without mortality would be at least 2,500 ppm (6,000 mg/m³) for 6 hours. Qualitative much better data are available for the closely-related substance acetaldehyde. The toxicity of both compounds is in quantitative terms similar, and it is expected that propionaldehyde will be equal or (more probably) less toxic than acetaldehyde. Therefore the LBW values for acetaldehyde were adopted for propionaldehyde. The resulting LBW levels are in compliance with the toxicity profile expected for propionaldehyde (including the limited available data).
The LBW values for acetaldehyde are based on a $BMDL_{05}$ of 5,295 ppm for lethality after 4 hours exposure derived from an acute and a subacute inhalation toxicity study in rats. A total uncertainty factor of 10 was applied, consisting of a factor of 3 for interspecies extrapolation and a factor of 3 for sensitive human subpopulations. Time scaling was performed using $C^n \times t = k$ with default values n=1 for extrapolation to longer time periods and n=3 for extrapolation to shorter time periods. In contrast to the 10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Except for limited data on irritation only, data on the toxicity of propionaldehyde to humans are not available. The available study suggests that exposure to 134 ppm (324 mg/m^3) for 30 minutes is only mildly irritating to the mucosal surfaces.

Only limited information is available on the toxicity of propionaldehyde in animals. Airway irritation was found after exposure during approximately 50 days. Minimal effects on the nasal olfactory epithelium were seen after repeated exposure to 150 ppm (360 mg/m^3) increasing to atrophy and squamous metaplasia after exposure to 1,500 ppm (3600 mg/m^3). CNS depression was seen within minutes after exposure of mice to 5,230 ppm (13,000 mg/m^3), and was also observed in rats and other species. Mortality in mice and rabbits was seen after several hours of exposure to 2868 mg/m^3 as aerosol in one very briefly reported study. No mortality was observed in guinea pigs during exposure but 3/20 died on subsequent days after exposure. In rats, mortality was found after short exposure to the saturated vapor (approximately 333,000 ppm or 800,000 mg/m^3).

Propionaldehyde does not affect the fertility and embryotoxicity in the limited study on developmental and reproductive toxicity.

Based on comparisons of biochemical reactivity, cardiovascular and liver effects, kinetics and metabolism and respiratory tract effects from acute exposures between propionaldehyde and acetaldehyde, it was concluded that ”direct extrapolation of effects of acute exposures from acetaldehyde to propionaldehyde appears justified”.

H315: Causes skin irritation; H319: Causes serious eye irritation; H335: May cause respiratory irritation

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived

A carcinogenicity study with propionaldehyde is not available

Odour and derivation of the LOA value

Odour: the odour has been descried as sweet and ester like, malty, and suffocating

OT_{50}: 0.0039 mg/m^3; K_w=1.01 [AEGL]
LOA = $10^{(2.48)}$* OT_{50} * 1.33 = 1.5 mg/m^3

(The concentration Level leading to distinct Oduor Awareness (I=3) is calculated using the formula: $I = K_w * \log (C/OT_{50}) + 0.5$. A correction factor of 1.33 is applied to this value)

The LOA is far below the VRW value

Other standards and guidelines *(1h values in mg/m^3, unless otherwise indicated)*

VRW level **110**	*AEGL-1* 110	*ERPG-1* not derived		*IDLH:* not derived
AGW level **640**	*AEGL-2* 630	*ERPG-2* not derived		
LBW level **2000**	*AEGL-3* 2000	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 107-12-0 **Propionitril** **CH_3-CH_2-CN** **VN-nr: 2404**
GEVI: 336

Synoniemen: propaannitril, cyanoethaan, ethylcyanide (Engels: Propionitrile) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	110	79	62	50	39	26
Levensbedreigende waarden	LBW (mg/m³)	460	320	250	200	160	79

Datum vaststelling: November 2015 — Conversiefactor: 1 mg/m³ = 0,436 ppm; 1 ppm = 2,29 mg/m³

Explosiegrens: LEL = 3,1 vol% ≈ 71.000 mg/m³

Geur: Aangename, zoete ethergeur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,04

Molecuulmassa:	55,08 g/mol
Zuurgraad:	Geen data
LogKow:	0,2
Wateroplosbaarheid:	10 g/100 ml (goed)
Verzadigde dampdruk:	52 mbar

Overige informatie

Publieke grenswaarde:
Niet afgeleid
MAK: Niet afgeleid
TLV-TWA: 14 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: irritatie ogen en bovenste luchtwegen, hoofdpijn

AGW → LBW: hoesten, glottisoedeem, benauwdheid, pijn op de borst, misselijkheid, braken, duizeligheid, krachtsverlies, verwardheid, foetale sterfte

Boven LBW: convulsies, ademnood, ademstilstand, coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Propionitril wordt omgezet tot o.a. cyanide.
- Cyanide blokkeert de ademhalingsketen in de cel. Hierdoor wordt de energiehuishouding verstoord en kan lactaatacidose ontstaan.
- Primaire systemische doelorganen zijn het centrale zenuwstelsel en het cardiovasculaire systeem.
- Propionitril veroorzaakt irritatie van de bovenste luchtwegen.
- Verschijnselen kunnen vertraagd optreden.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, ademnood, blauwe lippen of nagels, duizeligheid, hoofdpijn, zwaktegevoel, krampen.

Oogcontact: roodheid, pijn, slecht zien.

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: 100% zuurstof, direct spoedeisende medische hulp inzetten, specifieke behandeling. GEEN mond-op-mondbeademing!

Ontsmetting vloeistof

huid: eerst: zie *Ontsmetting damp - algemeen*, verder: verontreinigde kleding uittrekken, overmaat stof met PEG 400 opdeppen, spoelen en wassen met water en zeep.

ogen: eerst: zie *Ontsmetting damp - algemeen*, verder: uitspoelen met water (evt. contactlenzen verwijderen).

inslikken: eerst: zie *Ontsmetting damp - algemeen*, verder: mond laten spoelen (uitspugen!), GEEN braken opwekken.

***Specifieke behandeling en materialen**:* De benodigde middelen (specifieke antidota zoals 100% zuurstof en o.a. hydroxocobalamine, en natriumthiosulfaat) moeten met gebruiksaanwijzing ter plekke beschikbaar zijn.

Voor aanwijzingen over verdere behandeling zo nodig het NVIC (tel: +31(0)30 –274 8888) bellen.

Stofdocument deel B

CAS-nr: 107-12-0 **Propionitrile** **CH_3-CH_2-CN** **UN-nr: 2404**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: Different point of departure than AEGL, 2hr value added

LBW: Different point of departure than AEGL, 2hr value added

Date: November 2015 | AEGL document: Final, 2014

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Insufficient data
AGW	110	79	62	50	39	26	No-effect-level level for fetal toxicity from a developmental toxicity study in rats
LBW	460	320	250	200	160	79	Threshold for lethality in rats

Derivation of the Dutch Intervention Values

VRW: Data were insufficient for the derivation of VRW values for propionitrile. Absence of VRW values does not imply that exposure below the AGW value is without adverse effects.

AGW: The no-effect level fetal mortality in pregnant rats exposed to acetonitrile at 150 ppm (458 mg/m^3) for 6 h/day on gestational days 6-20 was used as the point of departure for deriving AGW values. Although the study involved repeated exposures, fetal death is considered relevant for AGW derivation, as fetal death can also occur during a narrow developmental window and does not necessarily require repeated exposures. This is in contrast to maternal death, which also occurred but which is not considered an acute effect, but a result of repeated exposure. Therefore, the observation of increased fetal death was considered an appropriate end point for deriving AGW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. For time-scaling $C^n \times t = k$ was used, using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively.
In contrast to the 10 minute AEGL-2 value that, time scaling was also applied for the 10 minute AGW value. The AGW derivation deviates from the AEGL-2 derivation, where the effects in a developmental toxicity study were used for derivation of the AEGL-3 and divided by 3 for the AEGL-2 values.

LBW: The LBW was based on the highest concentration (690 ppm = 1580 mg/m^3) causing no mortality in rats exposed to propionitrile for 4 hours. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. For time-scaling $C^n \times t = k$ was used, using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.
This approach deviates from the AEGL-3 derivation, where effects in a developmental study were used for derivation of the AEGL-3 values.

Additional toxicological information (including relevant results of a general literature search, if any)

Aliphatic nitriles like proprionitrile are readily absorbed from the lung and gastrointestinal tract, resulting in systemic toxicity. Most of the systemic toxicity of these nitriles is mediated through hepatic and extrahepatic cytochrome P450 catalyzed oxidation of the carbon alpha to the cyano group producing a cyanohydrin and an aldehyde. The metabolically-liberated cyanide is then conjugated with thiosulfate to form thiocyanate and is excreted in the urine. The toxicity of proprionitrile is due to the metabolic liberation of cyanide and signs and symptoms are similar to those observed after cyanide exposure.

Data concerning human exposure to propionitrile are limited to two case reports. A total of three men were occupationally exposed, presented with signs consistent with cyanide poisoning, and recovered after treatment.

No reports regarding developmental/reproductive toxicity of proprionitril in humans were available. In experimental animals no reproductive or developmental toxicity was noted in the absence of maternal toxicity.

No R-sentences.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived. No reports regarding carcinogenicity were available.	Odour: pleasant, ethereal, sweetish odour No LOA was derived due to lack of data.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH:* not derived
AGW level **62**	*AEGL-2* 6.9	*ERPG-2* -		
LBW level **250**	*AEGL-3* 21	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 6423-43-4 **Propyleenglycoldinitraat** $C_3H_6N_2O_6$ **VN-nr: geen** **GEVI: geen**

Synoniemen: isopropyleennitraat, 1,2-propyleenglycoldinitraat, PGDN (Engels: 1,2-propanediol dinitrate) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	6,9	2,3	1,2	0,58	0,35	0,17
Alarmeringsgrenswaarden	AGW (mg/m³)	42	14	6,9	3,5	1,7	0,86
Levensbedreigende waarden	LBW (mg/m³)	160	110	88	70	55	36

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,145 ppm; 1 ppm = 6,91 mg/m³

Explosiegrens: De stof kan detoneren.

Geur: onaangename geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: brandbare vloeistof (ontleedt bij 121 °C)

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1

Molecuulmassa: 166,1 g/mol
Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: 0,13 g/100 ml
Verzadigde dampdruk: 0,093 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: 0,34 mg/m³

TLV-TWA:

0,35 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: lichte hoofdpijn, lichte evenwichtsstoornissen

AGW → LBW: oog irritatie, hoofdpijn, duizeligheid, misselijkheid, matige tot ernstige evenwichtsstoornissen, toename bloeddruk

Boven LBW: braken, bleek zien, blauwe lippen en nagels, convulsies, bewusteloosheid, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof is licht irriterend voor de ogen.
- De stof kan inwerken op het centrale zenuwstelsel met als gevolg hoofdpijn, duizeligheid, evenwichtsstoornis en bewustzijnsdaling.
- De stof kan uitwerking hebben op het bloed en de bloedsomloop en resulteren in bloeddrukstijgingen en de vorming van methemoglobine.

Effecten bij blootstelling aan vloeistof

Huidcontact: De stof wordt door de huid opgenomen! hoofdpijn, duizeligheid, evenwichtsstoornissen, misselijkheid, sufheid, , convulsies, bewusteloosheid.

Oogcontact: Roodheid en pijn

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, en direct spoedeisende medische hulp inzetten

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en onmiddellijk arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen).
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 6423-43-4 **1,2-propanediol dinitrate** $C_3H_6N_2O_6$ **UN-nr: none**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: November 2015 | AEGL Document: Final, 2002

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	6.9	2.3	1.2	0.58	0.35	0.17	Threshold for mild headaches in humans
AGW	42	14	6.9	3.5	1.7	0.86	Threshold for severe headaches and loss of equilibrium in humans
LBW	160	110	88	70	55	36	Threshold for lethality in monkeys

Derivation of the Dutch Intervention Values

VRW: In a study with human volunteers mild headaches were reported in 1/3 subjects after a 6-hour exposure at 0.1 ppm (0.691 mg/m³), in 2/3 subjects after a 2-hour exposure at 0.2 ppm (1.382 mg/m³), and in 1/3 subjects after a 1-hour exposure at 0.5 ppm (3.46 mg/m³). Severe headaches occurred after an 8-hour exposure at 0.2 ppm (1.4 mg/m³, in 6 of 12 exposures) and at 0.35 ppm (2.4 mg/m³) and at 0.5 ppm (3.5 mg/m³) after a 2-hour exposure (1/3 subjects). Mild headache is an example of mild discomfort and the threshold concentration at which subjects first developed a mild headache was considered as point of departure for for derivation of the VRW-levels. The concentration of 0.5 ppm (3.5 mg/m³) was used as point of departure for derivation of the 10-min, 30-min, 1-hour and 2-hour VRW values. The concentration of 0.1 ppm (0.69 mg/m³) was used as point of departure for derivation of the 4-hour and 8-hour VRW values. The default intraspecies uncertainty factor of 3 was considered sufficient. A total uncertainty factor of 3 was applied. Time-scaling was performed using the equation C^n x t=k, using n=1, based on data that show that the relationship between exposure concentration and duration for the endpoints mild and severe headache is approximately linear for 1,2-propanediol dinitrate.

AGW: A study in human volunteers showed that subjects experienced throbbing headaches and became incapacitated after exposure to 1.5 ppm (10.4 mg/m³) for approximately 3 hours. A concentration of 0.5 ppm (3.5 mg/m³) for approximately 6 hours resulted in severe headaches and slight loss of equilibrium which was considered to be the threshold for inability to escape and used as the point of departure for derivation of the AGW values. The default intraspecies uncertainty factor of 3 was considered sufficient. A total uncertainty factor of 3 was applied. Time-scaling was performed using the equation C^n x t=k, using n=1, based on data that show that the relationship between exposure concentration and duration for the endpoints mild and severe headache is approximately linear for 1,2-propanediol dinitrate.

LBW: Two animal studies conducted with high exposure concentrations are considered to be suitable for deriving the LBW values. No death or signs of toxicity were observed in rats exposed to 189 ppm (1306 mg/m³) 1,2-propanediol dinitrate (mist) for 4 hours. A study in monkeys showed severe signs of CNS depression and cardiovascular effects but no deaths at a concentration of 70 ppm (484 mg/m³) for 6-hours. The concentration of 70 ppm (484 mg/m³) was considered to be the threshold for lethality and the point of departure for derivation of the LBW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. In the absence of a substance specific n-value for lethality time-scaling was performed using the equation C^n x t=k, using the default values of n=1 and n=3 for extrapolation to longer and shorter durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

1,2-propanediol dinitrate is rapidly and completely metabolized and eliminated in the urine as inorganic nitrate within 24-hours after exposure. 1,2-propanediol dinitrate has effects on both the cardiovascular and central nervous systems. Exposure to the substance results in vasodilation of cerebral blood vessels and fall in blood

pressure, with headache as the main syptom. Exposure to high levels of 1,2-propanediol dinitrate can increase the levels of methemoglobin and blood nitrate levels, which decreases the ability to bind oxygen. Furthermore, the substance acts as a central nervous system depressant in humans. The mechanism of central nervous system depression induced by 1,2-propanediol dinitrate is poorly understood but may be comparable to volatile anesthetics.

Data on developmental and reproductive toxicity in animals did not indicate reproductive and developmental effects at concentrations below levels that induce maternal toxicity.

No harmonized hazard sentences were found.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived.	Odour: unpleasant odour Odour threshold: 1.38 mg/m^3 [Stewart et al., 1974] No LOA was derived due to a lack of data.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **1.2**	*AEGL-1* 1.1	*ERPG-1* -		*IDLH: -*
AGW level **6.9**	*AEGL-2* 6.8	*ERPG-2* -		
LBW level **88**	*AEGL-3* 93	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 75-55-8

Propyleenimine

CH3(CH2CH2(-N-)H, cycl

VN-nr: 1921
GEVI: 336

Synoniemen: 2-methylaziridine, methylethyleenimine, 1,2-propyleenimine (Engels: propyleneimine)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	99	40	22	12	7,0	3,9
Levensbedreigende waarden	LBW (mg/m³)	300	120	67	37	21	12

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,420 ppm; 1 ppm = 2,38 mg/m³

Explosiegrens: niet bekend, damp met lucht vormt een explosief mengsel

Geur: ammoniakachtige geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze olieachtige rokende vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,2

Molecuulmassa: 57,1 g/mol
Zuurgraad: geen data
LogKow: geen data

Wateroplosbaarheid: volledig

Verzadigde dampdruk: 220 mbar

Overige informatie

Publieke grenswaarde: 0,63 µg/m³ (TGG 8 uur)
MAK: niet afgeleid
TLV-TWA: 4,76 mg/m³
H

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW: keelpijn en hoesten, branderig gevoel, misselijkheid

AGW → LBW: hoofdpijn, duizeligheid, piepende ademhaling, kortademigheid, ademnood

Boven LBW: sterfte

LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De damp van de stof werk sterk irriterend tot bijtend op de luchtwegen.
- De stof werkt sterk irriterend tot bijtend op de ogen en de huid.
- Blootstelling aan propyleenimine kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- De stof kan ook inwerken op het centrale zenuwstelsel en de nieren.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, branderig gevoel, blaren, brandwonden. De stof wordt door de huid opgenomen.

Oogcontact: bijtend, roodheid en pijn, slecht zien, hoornvliesbeschadiging, ernstige brandwonden. De stof wordt door de huid opgenomen.

Carcinogeniteit

IARC classificatie: 2B
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
inademing: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en direct spoedeisende medische hulp inzetten.
ogen: zie hierboven.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 75-55-8 **Propyleneimine** **CH3(CH2CH2(-N-)H, cycl** **UN-nr: 1921**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: Different point of departure, , 2h value added

LBW: Same point of departure as for AEGL values but using different factor for n, 2h value added

Date: November 2015 | AEGL document: Final, 2010

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Insufficient data
AGW	99	40	22	12	7.0	3.9	I/3 of LBW values
LBW	300	120	67	37	21	12	Lethality threshold in rats and guinea pigs

Derivation of the Dutch Intervention Values

VRW: The VRW values were not derived for propyleneimine. There are no exposure-response data in humans or animals available consistent with VRW-level effects.

AGW: There are no exposure-response data available concerning nonlethal effects of propyleneimine. In the absence of relevant data the AEGL has derived the AEGL-2 values by using exposure-response data of ethyleneimine in a relative potency approach. In contrast to the AEGL the AGW values were based on 1/3 of the LBW values.

LBW: Two acute inhalation studies were available for evaluating the toxicity of propyleneimine. One study showed that 5 out of 6 rats died after an exposure for 240 minutes to 500 ppm (1,190 mg/m³). No deaths in rats were found after an exposure for 120 minutes to 500 ppm (1,190 mg/m³). Another study showed that 1 out of 6 guinea pigs died after an exposure to 500 ppm (1,190 mg/m³) for 60 minutes. The study also showed that no deaths occurred after an exposure to 500 ppm (1,190 mg/m³) for 30 minutes. The lowest available threshold for lethality of 500 ppm (1,190 mg/m³) for 30 minutes found in guinea pigs was used as lethality threshold and point of departure for derivation of the LBW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences In contrast to AEGL, time-scaling was performed using the equation $C^n \times t = k$ with n = 1.2 based on rat lethality data (ethyleneimine) of Carpenter, 1948. This n-value was selected to be in line with the Dutch Probit for propyleneimine, for which the rat data of Carpenter (1948) on ethyleneimine were used to derive a value for n for propyleneimine.

Additional toxicological information (including relevant results of a general literature search, if any)

There are no data available on the mechanism of toxicity of propyleneimine. The similarity to ethyleneimine, however, suggests that propyleneimine is likely to be a reactive alkylating agent, with signs of toxicity being delayed until after exposure is terminated depending on the exposure concentration. Toxicity due to exposure to ethylenimine is generally delayed and includes irritation to contact organs (skin, eyes, oral cavity, and upper and lower respiratory tract), systemic toxicity, and death depending upon the concentration. At extremely high concentrations, however, irritation to contact organs may occur during or soon after exposure. The time course of irritation caused by ethylenimine is different from that caused by primary irritants such as ammonia, which causes an immediate response upon exposure regardless of concentration.

Data on developmental and reproductive toxicity are too limited to draw conclusions. For ethyleneimine no data were located on developmental/reproductive toxicity.

H330: Fatal if inhaled, H310: Fatal in contact with skin, H300: Fatal if swallowed, H318: Causes serious eye damage, H350: May cause cancer

Carcinogenicity and derivation of the CRP value

Odour and derivation of the LOA value

IARC classification: 2B (possibly carcinogenic to humans) No carcinogenic risk potency (CRP) was derived.	Odour: ammonia-like odour No LOA was derived (due to lack of data)

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)***				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH: 1,190 (30 minutes)*
AGW level **22**	*AEGL-2* 28	*ERPG-2* -		
LBW level **67**	*AEGL-3* 54	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 75-56-9 **Propyleenoxide** **$CH_3CH(-O-)CH_2$, cyclisch** **VN-nr: 1280**
GEVI: 33

Synoniemen: 1,2-epoxypropaan, methyloxiraan, propeenoxide (Eng.: propylene oxide) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	180	180	180	180	180	180
Alarmeringsgrenswaarden	AGW (mg/m³)	2600	1400	910	600	400	270
Levensbedreigende waarden	LBW (mg/m³)	6100*	3200	2100	1400	930	620

Datum vaststelling: 28-11-2008

Conversiefactor: 1 mg/m³ = 0,413 ppm; 1 ppm = 2,417 mg/m³

Explosiegrens: LEL = 1,9 vol% ≈ 46 000 mg/m³
* berekende interventiewaarde hoger dan 10% LEL

Geur: typerende geur (zoet en alcoholachtige geur)
LOA: 51 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: zeer vluchtige kleurloze vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,6

Molecuulmassa: 58,1 g/mol
Zuurgraad: Geen data
LogKow: 0,3 (berekend)
Wateroplosbaarheid: 41 g/ 100 ml (goed)
Verzadigde dampdruk: 590 mbar

Overige informatie

Publieke grenswaarde: 6 mg/m³ (8 uur)
MAK: 4,83 mg/m³
TLV-TWA: 4,83 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte oogirritatie

VRW → AGW: lichte irritatie van ogen en bovenste luchtwegen (tranenvloed, speekselvloed)

AGW → LBW: ernstige irritatie van ogen en bovenste luchtwegen (tranenvloed, speekselvloed), bemoeilijkte ademhaling, benauwdheid, ademnood, ataxie, verminderde coördinatie, bewustzijnsdaling

Boven LBW: coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Propyleenoxide veroorzaakt irritatie van de ogen en de bovenste luchtwegen.
- Propyleenoxide is een genotoxische alkyleerde verbinding.
- In hoge concentraties kan propyleenoxide neurotoxische effecten veroorzaken.
- Zowel de duur van de blootstelling als concentratie is van invloed op de ernst van de effecten.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn

Oogcontact: *damp*: roodheid en pijn, *bijtend.*
Vloeistof: roodheid en pijn, *bijtend*, (evt. brandwonden).

Carcinogeniteit

IARC classificatie: 2B
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken (propyleen oxide wordt door de huid opgenomen), afspoelen met water en arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen: geen.
Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 75-56-9 **Propylene oxide** **$CH_3CH(-O-)CH_2$, cyc** **UN-nr: 1280**

Basis for the Dutch Intervention Values

VRW: AEGL values adopted, 2hr value added

AGW: Different point of departure and rationale, 2hr value added

LBW: AEGL values adopted except for 10-min value, 2hr value added

Date: 28-11-2008 | AEGL document: Final, 2010

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	180	180	180	180	180	180	Slight irritation in humans
AGW	2600	1400	910	600	400	270	Irritation in workers
LBW	6100*	3200	2100	1400	930	620	Lethality animals

* value higher than 10% of LEL

Derivation of the Dutch Intervention Values

VRW: As starting point for the derivation of the VRW, four exposure levels at different time points 380 ppm (920 mg/m^3, 117 min), 525 ppm (1270 mg/m^3, 121 min), 392 ppm (950 mg/m^3, 135 min), and 460 ppm (1111 mg/m^3, 116 min)) measured in the breathing zone of workers were averaged (440 ppm or 1063 mg/m^3). The effects observed were undefined irritation and some eye irritation. A total uncertainty factor of 6 was applied. A factor 3 for intraspecies differences, because irritation is a point of contact effect and is not expected to vary greatly among individuals, and a modifying factor 2 was applied, because the defined effects are above a VRW but below the AGW endpoint. The resulting value of 73 ppm (177 mg/m^3) was set equal across time because mild irritation is not expected to vary greatly across time.

AGW: The available experimental animal data addressing AGW relevant effects are not consistent with the limited data available for workers showing that workers are capable of performing their job at concentrations of about 400 to 1500 ppm (970 to 3625 mg/m^3) for 2 to 3 hours. Although the data on workers' experience are limited they are therefore considered to be the best point of departure for derivation of AGW values. Based on the available exposure data 500 ppm (1200 mg/m^3) is chosen as point of departure by a weight of evidence approach. An interspecies factor of 1 was applied combined with a factor for intraspecies differences of 2 because the mechanism of toxicity, irritation, not expected to vary greatly among individuals and a larger factor would bring the AGW values for longer durations too close to the corresponding VRW values. Although the mechanism of action appears the be a direct irritant effect, it is not appropriate to set values equal across time, because the irritation is no longer considered mild, but is part of the continuum of respiratory tract irritation leading to death. Time scaling was performed using the equation $C^n \times t = k$, with n=1.7 (derived from a rat lethality study).

LBW: The LBW derivation is based on the lowest calculated 4-hour $BMCL_{01}$ value of 1161 ppm (2806mg/m^3) in rats. This choice is supported by dog lethality data. Not selecting the very low $BMCL_{01}$ values of mice (282 and 673 ppm, and 682 and 1627 mg/m^3, respectively) as starting point is supported by studies with monkeys, being exposed to 300 ppm for 6 hours/day, 5 d/w for 2 years or 457 ppm (1105 mg/m^3), 6hr/day, 7 d/wk for 6 months and human exposure to 1520 ppm (3673 mg/m^3) for 171 min, causing irritation, but not enough to cease working. An intraspecies factor of 3 was applied, because the mechanism of toxicity, irritation, is a point of contact effect and is not expected to vary greatly among individuals. An interspecies factor of 1 was applied, because of the supporting data in dogs and monkeys. Time scaling was performed using the equation $C^n \times t = k$, with n=1.7 (derived from a rat lethality study). The 10-min value was also derived by time scaling supported by the data on workers' exposures.

Additional toxicological information (including relevant results of a general literature search, if any)

Propylene oxide is a direct alkylating agent that has been shown to alkylate proteins and DNA. In addition, propylene oxide possesses irritant properties, such as inducing lacrimation and mucous discharge. Propylene oxide reacts at the site of entry. Possible neurotoxic effects have been observed as well in both rodents and

dogs following inhalation exposure to very high levels of propylene oxide (1500 and 2000 ppm, and 3625 and 4834 mg/m^3, respectively). The severity of the effects depends on exposure duration as well as the height of the exposure.

Propylene oxide does not have reproductive effects. Developmental toxicity was limited to decreased foetal growth and increased incidence of rib dysmorphology or a reduced number of ossified sacral-caudal vertebrae in rats.

H302: Harmful if swallowed; H312: Harmful in contact with skin; H315: Causes skin irritation; H319: Causes serious eye irritation; H332: Harmful if inhaled; H335: May cause respiratory irritation; H340: May cause genetic defects; H350: May cause cancer.

Carcinogenicity and derivation of the CRP value

IARC classification: 2B (possibly carcinogenic to humans)

Derivation of the carcinogenic risk potency (CRP): not derived

Propylene oxide is considered to be a threshold carcinogen and repeated exposure would be required to induce carcinogenesis. Therefore, it is inappropriate to conduct a carcinogenicity assessment for an acute exposure scenario. A one-time exposure event to high concentrations of propylene oxide would not be expected to result in tumour development.

Odour and derivation of the LOA value

Sweet and alcoholic odour.

OT_{50}: 1.3 ppm (3.2 mg/m^3)[AEGL (2010)]
LOA = 11.8 * OT_{50} * 1.33 = 51 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies below all the proposed intervention values (VRW, AGW, and LBW at all time points).

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **180**	*AEGL-1* 180	*ERPG-1* 120		*IDLH:* 967 mg/m^3 (10 min)
AGW level **910**	*AEGL-2* 701	*ERPG-2* 604		
LBW level **2100**	*AEGL-3* 2100	*ERPG-3* 1800		

Stofdocument deel A

CAS-nr: 141-57-1

Propyltrichloorsilaan

$C_3H_7Cl_3Si$

VN-nr: 1816

GEVI: X83

Synoniemen: (n-propyltrichloorsilaan, trichloorpropylsilaan (Engels: propyl trichlorosilane)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	4,4	4,4	4,4	4,4	4,4	4,4
Alarmeringsgrenswaarden	AGW (mg/m³)	280	130	82	51	32	32
Levensbedreigende waarden	LBW (mg/m³)	830	390	250	150	97	97

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,135 ppm; 1 ppm = 7,38 mg/m³

Explosiegrens: geen data

Boven 31°C: damp met lucht explosief

Geur: scherpe, irriterende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze, rokende vloeistof

Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,2

Molecuulmassa: 177,5 g/mol

Zuurgraad: geen data

LogKow: geen data

Wateroplosbaarheid: reactie

Verzadigde dampdruk: 38,4 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: irritatie van ogen en luchtwegen, tranenvloed, hoesten, lichte benauwdheid

AGW → LBW: ernstige irritatie van ogen en luchtwegen, pijn op de borst, benauwdheid, longontsteking, longoedeem

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Chloorsilanen reageren zeer snel met water onder vorming van chloorwaterstof (HCl). De acute toxiciteit van propyltrichloorsilaan wordt veroorzaakt door chloorwaterstof.
- Inhalatie van chloorwaterstof veroorzaakt een type I inhalatie intoxicatie.
- Chloorwaterstof veroorzaakt irritatie van de slijmvliezen van ogen en luchtwegen.
- Chloorwaterstof kan bij inhalatie longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, brandwonden

Oogcontact: bijtend, roodheid en pijn, hoornvliesbeschadiging, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: n.v.t.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen, en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**:* geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 141-57-1 **Propyl trichlorosilane** $C_3H_7Cl_3Si$ **UN-nr: 1816**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same rationale as AEGL (analogy with HCl), 2h value added

LBW: Same rationale as AEGL (analogy with HCl), 2h value added

Date: November 2015 | AEGL document: final 2012

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	4.4	4.4	4.4	4.4	4.4	4.4	Based on HCl (Threshold of irritation in humans)
AGW	280	130	82	51	32	32	Based on HCl (one-third of LBW)
LBW	830	390	250	150	97	97	Based on HCl (Threshold of lethality in animals)

Derivation of the Dutch Intervention Values

VRW: Since no appropriate data exist for propyl trichlorosilane, VRW values for hydrogen chloride will be used (on ppm-basis) to derive VRW values for propyl trichlorosilane. The use of hydrogen chloride as a surrogate for propyl trichlorosilane was deemed appropriate since it is believed that the hydrolysis product, HCl, is responsible for the adverse effects. Because three moles of hydrogen chloride are produced for every mole of propyl trichlorosilane, a molar adjustment factor of 3 was applied to the hydrogen chloride VRW values.

Derivation of VRW values for HCl

The hydrogen chloride VRW values were based on a no-adverse-effect-level of 1.8 ppm (2.73 mg/m³) in exercising asthmatics with an exposure duration of 45 min. Because the test subjects were considered a sensitive subpopulation and the endpoint was essentially a no-effect level, no uncertainty factor was applied to account for sensitive human subpopulations. The VRW values were held constant for all specified exposure periods since mild irritant effects represent threshold effects and generally do not vary over time.

AGW: Since no appropriate data exist for propyl trichlorosilane, AGW values for hydrogen chloride will be used (on ppm-basis) to derive AGW values for propyl trichlorosilane. Because three moles of hydrogen chloride are produced for every mole of propyl trichlorosilane, a molar adjustment factor of 3 was applied to the hydrogen chloride AGW values.

Derivation of AGW values for HCl

The AGW values of HCl for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data. The only study of HCl that addressed effects that meet the definition of an AGW, severe nasal lesions, was a study on hydrogen halides by Stavert et al. (1991). Nevertheless, this study was not considered a suitable basis for derivation of AGW values because 6% of the animals died after exposure to HCl at 1300 ppm (1974 mg/m³), only one concentration was tested and the number of animals tested was inconsistent.

LBW: Since no appropriate data exist for propyl trichlorosilane, LBW values for hydrogen chloride will be used (on ppm-basis) to derive LBW values for propyl trichlorosilane. Because three moles of hydrogen chloride are produced for every mole of propyl trichlorosilane, a molar adjustment factor of 3 was applied to the hydrogen chloride LBW values.

Derivation of LBW values for HCl

The LBW values were based on a lethality study in rats. The rat study included six exposure durations and various concentrations. Probit analyses using DoseResp was performed and yielded LC_{01} values for the 10 min, 30 min, 1-, 2-,4-, and 8hrs exposure durations of 3370, 1602, 1002, 627, 393 and 246 ppm (5116, 2433, 1522, 952, 596, and 373 mg/m³), respectively, which were used as point of departure for LBW derivation. The default total uncertainty factor of 10 (3x3) was considered

sufficient to account for inter- and intraspecies differences. The probit analyses yielded an n-value of 1.48, which was supported by the n-value of 1.59 calculated by Arts *et al.* (2000) from the C*t study. To maintain consistency with other hydrogen halogenides, the 8 hour value was set equal to the 4 hour value, as performed for the most potent hydrogen halogenide HF.

Additional toxicological information (including relevant results of a general literature search, if any)

No data concerning lethality or nonlethal toxicity in humans from propyl tichlorosilane were located in the available literature.

Chlorosilanes react violently with water to produce hydrogen chloride gas. Data suggest that the acute toxicity of chlorosilanes is due to the hydrogen chloride hydrolysis product; acute toxicity of the chlorosilanes is both qualitatively (based on clinical signs) and quantitatively (based on molar equivalents of hydrogen chloride) similar to that of HCl.

Although toxicity data are limited for individual chlorosilanes, well-conducted 1-hr inhalation toxicity studies in rats are available for a series of chlorosilanes. In general, LC_{50} values for monochlorosilanes were approximately twice the LC_{50} values for dichlorosilanes and three times the LC_{50} values for trichlorosilanes. Clinical signs were consistent with hydrogen chloride exposure and included lacrimation, salivation, dried material around or on the eyes and/or nose, green staining around the nose and mouth, and perineal urine staining. Labored breathing, rales, hypoactivity, closed or partially closed eyes, prostration, corneal opacity or opaqueness, and swollen and/or necrotic paws were also observed. Hemorrhage, congestion and/or consolidation of the lungs, ectasia of the lungs, gaseous distension of the gastrointestinal tract, absence of body fat, obstruction of nostrils, dried and/or firm nares, alopecia around the eyes and discoloration of hair were observed at necropsy.

No data concerning developmental/reproductive toxicity for exposure to chlorosilanes were located in the available literature.

H314: causes severe skin burns and eye damage. H302: harmful if swallowed. H331: toxic if inhaled, EUH071: corrosive to the respiratory tract.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived

No information was found regarding the carcinogenicity of chlorosilanes in humans and experimental animals.

Odour and derivation of the LOA value

Odour: chlorosilanes have a pungent, irritating odour

No LOA was derived due to lack of data

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **4.4**	*AEGL-1* 4.4	*ERPG-1* not derived		*IDLH*: not derived
AGW level **82**	*AEGL-2* 54	*ERPG-2* not derived		
LBW level **250**	*AEGL-3* 240	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 7697-37-2 **Salpeterzuur (70%)** HNO_3 **VN-nr: 2031**

GEVI: 885

Synoniemen: geen (Engels: nitric acid) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	4,2	4,2	4,2	4,2	4,2	4,2
Alarmeringsgrenswaarden	AGW (mg/m³)	150	100	80	40	20	10
Levensbedreigende waarden	LBW (mg/m³)	440	300	240	120	60	30

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,382 ppm; 1 ppm = 2,62 mg/m³

Explosiegrens: geen data

Geur: stekende geur

LOA: 11,8 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze tot lichtgele, aan vochtige lucht licht rokende oplossing

Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,06

Molecuulmassa: 63 g/mol

Zuurgraad: < 0,5 (100%)

LogKow: Geen data

Wateroplosbaarheid: volledig

Verzadigde dampdruk: 56 mbar

Overige informatie

Publieke grenswaarde: 1,3 mg/m³ (15 min)

MAK: niet afgeleid

TLV-TWA: 5,2 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen klachten

VRW → AGW: luchtweg- en oogirritatie, keelpijn en hoesten

AGW → LBW: kortademigheid, ernstige oogirritatie

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De damp van salpeterzuur kan bij inademen luchtwegirritatie en kortademigheid veroorzaken.
- Herstel kan enige weken duren en een terugval kan optreden
- Sterfte kan optreden door bronchopneumonia en/of longfibrose
- Allergische en asthmatische personen zijn extra gevoelig
- Het effect van blootstelling aan salpeterzuur damp kan versterkt worden door gelijktijdige blootstelling aan stikstofdioxide

Effecten bij blootstelling aan vloeistof

Huidcontact: *bijtend*, roodheid en pijn, ernstige brandwonden

Oogcontact: *bijtend*, roodheid en pijn, slecht zien, hoornvliesbeschadiging, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding, specifieke behandeling en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen: geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7697-37-2 **Nitric acid** **HNO_3** **UN-nr: 2031**

Basis for the Dutch Intervention Values

VRW: Same point of departure as for AEGL values but using different uncertainty factors, 2h value added

AGW: Different point of departure than AEGL, 2h value added

LBW: AEGL value adopted, 2h value added

Date: 06-10-2016 | AEGL Document, Final, 2014

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	4.2	4.2	4.2	4.2	4.2	4.2	NOAEL for pulmonary function in humans
AGW	150	100	80	40	20	10	1/3 LBW
LBW	440	300	240	120	60	30	Threshold for lethality in rats

Derivation of the Dutch Intervention Values

VRW: VRW values were derived from a study in which five healthy volunteers were exposed at rest to nitric acid fumes at 1.6 ppm (4.19 mg/m³) for 10 minutes. No changes in pulmonary function (vital capacity, respiratory resistance, and FEV_1) were observed. The concentration of 4.19 mg/m³ was the highest NOAEL available in humans. Anecdotal data in humans (e.g. self-exposure at 12 ppm for 1 hour, result a.o. in irritation of the respiratory tract, whereas in a second study even higher concentrations could be tolerated) indicate that higher concentrations are tolerable, This supports the use of an intraspecies factor of 1 instead of 3. The VRW was set equal for all time points because irritation is generally concentration-dependent but not time-dependent.

AGW: Due to lack of suitable data consistent with AGW-level effects, the LBW values were divided by 3.

LBW: The point of departure for LBW is a 1-hour LC_{01} of 919 ppm (2,408 mg/m³) as calculated by a log-probit analysis. The default total uncertainty factor of 10 (3 x 3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n * t = k$ with the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Nitric acid is a highly corrosive, strongly oxidizing acid. The course of toxicity following inhalation exposure to nitric acid is consistent among a number of available case reports. Nitric acid fumes may cause immediate irritation of the respiratory tract, pain, and dyspnoea which are followed by a period of recovery that may last several weeks. After this time, a relapse may occur with death caused by bronchopneumonia and/or pulmonary fibrosis. For exposure to nonlethal concentrations, allergic or asthmatic individuals are the most sensitive population.

Inhalation exposures to nitric acid fumes involve exposure to nitric acid as well as nitrogen oxides such as nitrogen dioxide (NO2) and nitric oxide (NO). Nitric acid and nitrogen dioxide are suspected to interact causing enhanced toxicity.

No information was found regarding the developmental or reproductive toxicity of nitric acid.

H314: Causes severe skin burns and eye damage

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

No information was found regarding the carcinogenicity

Odour and derivation of the LOA value

Odour: characteristic, stinging and choking odour

ODT: 0.75 mg/m³ [Ruth, 1986]

LOA = 11.8 * ODT * 1.33 = 11.8 mg/m³

(The concentration Level leading to distinct Odour

of nitric acid in humans or experimental animals.	Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value) The LOA lies between the VRW and the AGW .

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*				
VRW level **4.2**	*AEGL-1* 0.41	*ERPG-1* 2.6		*IDLH:* 66 mg/m³ (30 min)
AGW level **80**	*AEGL-2* 62	*ERPG-2* 26		
LBW level **240**	*AEGL-3* 240	*ERPG-3* 200		

Stofdocument deel A

CAS-nr: 107-44-8 **Sarin** **$C_4H_{10}FO_2P$** **VN-nr: geen** **GEVI: geen**

Synoniemen: Agent GB, isopropylmethylfosfonofluoridaat (Engels: Sarin) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,0068	0,0039	0,0020	0,0017	0,0012	0,00085
Alarmeringsgrenswaarden	AGW (mg/m³)	0,087	0,050	0,035	0,025	0,018	0,013
Levensbedreigende waarden	LBW (mg/m³)	0,38	0,19	0,13	0,099	0,070	0,052

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,17 ppm; 1 ppm = 5,88 mg/m³

Explosiegrens: Geen data

Geur: bijna geurloos, fruitig, kruidachtig

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: geen data

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa:	140,1 g/mol
Zuurgraad:	Geen data
LogKow:	0,15
Wateroplosbaarheid:	mengbaar
Verzadigde dampdruk:	2,8 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: oogpijn, hoofdpijn

VRW → AGW: pupilvernauwing, misselijkheid, braken

AGW → LBW: speekselvloed, tranenvloed, benauwdheid, spiertrillingen, verlammingsverschijnselen, bewustzijnsdaling

Boven LBW: convulsies, coma, verlamming, ademstilstand, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Het zenuwgas Sarin is een irreversibele cholinesterase remmer. Hierdoor wordt de afbraak van de neurotransmitter acetylcholine geremd en de zenuwimpuls bij de motorische eindplaat verstoord.
- Doelorganen zijn het centrale en perifere zenuwstelsel.
- De meeste effecten treden zeer snel op, echter neuropathologische effecten zoals verlamming kunnen vertraagd optreden en langdurig van aard zijn.

Effecten bij blootstelling aan vloeistof

Huidcontact: spiertrillingen, zweten, misselijkheid, braken, diarree, zwaktegevoel, bewustzijnsdaling, convulsies, ademstilstand.
Stof kan via de huid opgenomen worden!

Oogcontact: roodheid en (hevige) pijn, nauwe pupillen, slecht/wazig zien, tranenvloed, en verdere systemische effecten.

Carcinogeniteit

IARC classificatie: niet geclassificeerd.
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, specifieke behandeling en direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!) , specifieke behandeling en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: benodigde middelen (100% zuurstof, specifieke antidota zoals o.a. atropine) moeten met gebruiksaanwijzing beschikbaar zijn.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 107-44-8 **Sarin** **$C_4H_{10}FO_2P$** **UN-nr: none**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2hr value added.

AGW: AEGL value is adopted, 2hr value added.

LBW: AEGL value is adopted, 2hr value added.

Date: 24-09-2009 | AEGL document, final 2003

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.0068	0.0039	0.0020	0.0017	0.0012	0.00085	Miosis (pupil constriction) in animals
AGW	0.087	0.050	0.035	0.025	0.018	0.013	Miosis, nerve conduction in humans
LBW	0.38	0.19	0.13	0.099	0.070	0.052	Threshold of animal lethality

Derivation of the Dutch Intervention Values

VRW: VRW values can be derived from a data set for sarin-induced miosis in rats exposed to vapour for 10, 60, and 240 min. Supportive evidence is available from a dataset on sarin-induced miosis in marmosets exposed to vapor for 5 h, as well as historical human data. Starting points were the rat data: 0.068 mg/m^3, 10 minute exposure (for 10 and 30 minute VRW), 0.020 mg/m^3, 1 hr exposure, and 0.012 mg/m^3, 4hr exposure (for 2hr, 4hr and 8hr VRW derivation). An interspecies uncertainty factor of 1 and an intraspecies UF of 10 were used, resulting in a composite uncertainty factor of 10. To estimate the interspecies factor miosis data for a number of species were compared. It was determined that there was no significant difference between guinea pigs and marmosets at the 5% level. Independent investigators have concluded that the miotogenic response of mammalian eyes to sarin vapor exposure is quantitatively similar across species, including standard laboratory animals (rabbits and guinea pigs), nonhuman primates (marmosets), and humans. In consequence, the interspecies factor for the VRW end point of miosis in young adult female rats is set equal to 1. The intraspecies factor of 10 used in the derivation of the VRW is based on the known polymorphic variation in human cholinesterase and carboxylesterase activity that may make some individuals susceptible to the effects of cholinesterase inhibitors such as nerve agents. Time scaling was performed using $C^n * t = k$, with n = 2 based on experimental data on miosis and lethality.

AGW: A human study, where eight subjects were exposed to sarin at 0.5 mg/m^3 for 30 minutes, was used for AGW derivation. The study was performed under Helsinki accords and clinical supervision and was conducted with the cooperation of fully informed human subjects (“fit male servicemen”). The observed effects included miosis in eight of eight subjects, dyspnea and photophobia in some individuals (number not given), inhibition of red blood cell cholinesterase to approximately 60% of individual baseline at 3 h and 3 days postexposure, and small but measurable changes in single fibre electromyography (SFEMG) of the forearm (in five of eight subjects) which was still measurable between 4 and 15 months postexposure. Although the latter effect is considered a subclinical and reversible effect, it was considered the starting point for AGW derivation. SFEMG changes may be a precursor of intermediate syndrome and because of the steepness of the dose-response curve for nerve agents, the use of this end point for establishing AGW values is considered a protective approach. To accommodate known variation in human cholinesterase and carboxylesterase activity that may make some individuals susceptible to the effects of cholinesterase inhibitors and absorption such as nerve agents, an uncertainty factor of 10 was applied. Time scaling was performed using $C^n * t = k$, with n = 2 based on experimental data on miosis and lethality.

LBW: The acute lethal toxicity of sarin to male and female rats was evaluated for time periods of 10, 30, 60, 90, 240, and 360 min in a whole-body dynamic chamber. Ten males and 10 females were used for each concentration-time combination, and 50 males and 50 females were used for each time point. Sarin concentrations ranged from about 2 mg/m^3 to 54 mg/m^3. Lethality was assessed at 24 h and at 14 d postexposure. Female rats were reported to be more sensitive to sarin vapor toxicity than males over the range of exposure concentrations and durations studied. Based on a probit analysis of the data, the estimated LC_{01} values for the females are as follows: 11.5 mg/m^3 for 10 min, 5.8 mg/m^3 for 30 min, 4.0 mg/m^3 for 60 min, 2.1 mg/m^3 for 4 h (also used to derive the 2hr LBW), and 1.8 mg/m^3 for 6 h (used to derive the 8hr LBW). Data from animal and human studies indicate that an interspecies factor (rat-to-human) of approximately 3 for LBW derivation is reasonable considering the same mechanism of action, but where humans show to be more sensitive by a factor

of approximately 3. To accommodate known variation in human cholinesterase and carboxylesterase activity that may make some individuals susceptible to the effects of cholinesterase inhibitors such as nerve agents, a factor of 10 was applied for intraspecies variability (protection of susceptible populations). An experimentally derived n = 2 is used as the time scaling function in the equation $C^n \times t = k$.

Additional toxicological information (including relevant results of a general literature search, if any)

Sarin is a well known nerve agent, also known as agent GB. Nerve agents exert toxic effects on the central and peripheral nervous system indirectly through acetylcholine esterase inhibition, nerve agents may also affect nerve impulse transmission by additional mechanisms at neuromuscular junctions and at neurotransmitter receptor sites in the CNS. The first symptoms are related to the nerve conduction inhibition by the substance and consist of pupil constriction (miosis), headache, shortness of breath, tightness of the chest. A runny nose and lacrimation can also be observed. At increasing exposure levels or prolonged exposures sweating, diarrhea, bradycardia, tremors, overall weakness, paralysis, unconsciousness, convulsions, suppression of the respiration and death can occur. The dose-response relation is considered very steep and effects may occur rapidly. However, delayed neuropathological effects (such as paralysis) may occur.

No developmental or reproduction toxicity effects are described.

No harmonized H-statements or human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: almost odourless, fruity, spicy.

No LOA was derived.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **0.0020**	*AEGL-1* 0.0020	*ERPG-1* -		*IDLH:* not established.
AGW level **0.035**	*AEGL-2* 0.035	*ERPG-2* -		
LBW level **0.13**	*AEGL-3* 0.13	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 7783-79-1 **Seleenhexafluoride** F_6Se **VN-nr: 2194**

GEVI: geen

Synoniemen: seleniumhexafluoride (Engels: selenium hexafluoride) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,80	0,80	0,80	0,80	0,80	0,80
Alarmeringsgrenswaarden	AGW (mg/m³)	2,4	1,7	1,3	1,3	1,3	1,3
Levensbedreigende waarden	LBW (mg/m³)	7,3	5,1	4,0	4,0	4,0	4,0

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,125 ppm; 1 ppm = 8,03 mg/m³

Explosiegrens: kans op explosie door reactie met ammoniak; geen explosiegrenzen beschikbaar

Geur: geen data

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze gas

Brand: niet brandbaar

Relatieve dichtheid gas (lucht =1): 6,7

Molecuulmassa:	193 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Water-oplosbaarheid:	Niet (langzame hydrolyse)
Verzadigde dampdruk:	-

Overige informatie

Publieke grenswaarde: 0,2 mg/m³ (8 uur) als Se

MAK: niet afgeleid

TLV-TWA:0,4 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten te verwachten

VRW → AGW: keelpijn en hoesten, braken, duizeligheid, branderig gevoel achter het borstbeen

AGW → LBW: kortademigheid, longoedeem, moeizaam ademen, spierkrampen

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Seleenhexafluoride is sterk irriterend tot bijtend.
- Blootstelling aan seleenhexafluoride kan longoedeem, chemische pneumonitis en blijvende longschade veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Seleenhexafluoride kan leverschade veroorzaken. Dit effect kan vertraagd optreden.
- De stof heeft een steile concentratie-response curve; van 0-100% sterfte bij tweemaal hogere concentratie.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, bevriezingsletsel

Oogcontact: bijtend, roodheid en pijn, bevriezingsletsel.

Carcinogeniteit

IARC classificatie: 3

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp:

Algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Huid: kleding uittrekken (NIET lostrekken), direct spoelen met veel water (minimaal 20 min.), dan pas eventueel aan de huid vastgevroren kleding verwijderen en verder spoelen en onmiddellijk een arts raadplegen.

Specifieke behandeling en materialen*:* geen

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 7783-79-1 **Selenium hexafluoride** **F_6Se** **UN-nr: 2194**

Basis for the Dutch Intervention Values

VRW: Same PoD but different UF and no MF, no time scaling between 30 minutes and 8 hours, 2h value added

AGW: Same rationale as for AEGL (one-third of LBW), 2h value added

LBW: Same PoD, but different UF and no MF, no time scaling between 1 and 8 hours, 2 h value added.

Date: 06-10-2016 | AEGL document: Interim, 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.80	0.80	0.80	0.80	0.80	0.80	NOEL for effects on respiratory tract
AGW	2.4	1.7	1.3	1.3	1.3	1.3	One third of LBW
LBW	7.3	5.1	4.0	4.0	4.0	4.0	Highest non-lethal concentration in animals

Derivation of the Dutch Intervention Values

VRW: Only one study is available that addresses selenium hexafluoride toxicity in animal models. Groups of one rabbit, one guinea pig, 2 rats and 4 mice were exposed to 1, 5, 10, 25, 50 or 100 ppm (8.03, 40.1, 80.3, 201, 401, and 803 mg/m^3, respectively) for 4 hours. At 1 ppm (8.03 mg/m^3) no effects were observed. Animals exposed to 40.1 mg/m^3 showed severe irritation, difficulty in breathing and pulmonary oedema. The NOAEL of 8.03 mg/m^3 is used as basis for the VRW. The default uncertainty factor of 10 (3x3) was considered sufficient to account for intra- and interspecies differences.

AGW: In the absence of empirical data, the LBW values were divided by 3 to obtain AGW values for selenium hexafluoride. This approach is justified based on no effects in rabbit, guinea pig, rat, or mouse for 4-hour exposures at 1 ppm, difficulty breathing and pulmonary edema, but no mortality at 5 ppm, and 100% mortality at 10 ppm.

LBW: In the study as described under VRW all animals died at exposure concentrations of 80.3 mg/m^3 and higher. No mortality was observed at 4-hour exposures to 8.03 or 40.1 mg/m^3. In a similar group of animals exposed to 80.3 mg/m^3 for one hour, 0/1 rabbit, 1/1 guinea pig, 2/2 rats and 2/4 mice died. The observation period was 3 weeks in all exposures. The LBW is based on the 4-h highest concentration causing no mortality in the guinea pig, rabbit, rats, and mice (5 ppm, 40.1 mg/m^3) combined with the 1-hour exposure to 80.3 mg/m^3 that also caused high mortality. The observations in the latter exposure group indicated that the 1-hour LBW value should be below 8 mg/m^3 (*i.e.*, 80.3 mg/m^3 divided by a default UF of 10), with the notification that the ratio of the concentrations with 100% mortality and with 0% mortality was only 2 for the 4-hour exposure period. The default uncertainty factor of 10 (3x3) was considered sufficient to account for intra- and interspecies differences, resulting in a 4-hour LBW value of 4.0 mg/m^3. Taking into account the observations at 1 hour of exposure, the value of 4.0 mg/m^3 is flatlined from 1 to 8 hours of exposure. Time scaling to the 10- and 30-minute values was performed using $C^n \times t = k$, with the default value of n=3.

Additional toxicological information (including relevant results of a general literature search, if any)

Selenium hexafluoride is corrosive and severely irritating to skin, eyes, and causes respiratory distress and pulmonary edema; the irritation is immediate, but pulmonary edema may be delayed several hours.
No relevant information on reproductive or developmental toxicity in humans or experimental animals was available.

There are no harmonized H-sentences for human health available.

Carcinogenicity and derivation of the CRP value

IARC classification:

3 (not classifiable as to carcinogenicity to humans

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: No LOA was derived due to lack of data.

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)***				
VRW level **0.80**	*AEGL-1* 0.43	*ERPG-1* -		*IDLH:* 16 (10 min)
AGW level **1.3**	*AEGL-2* 0.70	*ERPG-2* -		
LBW level **4.0**	*AEGL-3* 2.1	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 7783-07-5 **Seleenwaterstof** **H_2Se** **VN-nr: 2202**
GEVI: 263

Synoniemen: waterstofselenide, seleniumhydride (Engels: Hydrogen selenide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	7,6	4,9	3,7	2,8	2,1	1,6
Levensbedreigende waarden	LBW (mg/m³)	23	15	11	8,4	6,4	4,8

Datum vaststelling: November 2015 Conversiefactor: 1 mg/m³ = 0,297 ppm; 1 ppm = 3,37 mg/m³

Explosiegrens: niet bekend

Geur: typerende geur (knoflookgeur)
LOA: 16 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas
Brand: brandbaar

Relatieve dichtheid: 2,8

Molecuulmassa: 81,0 g/mol
Zuurgraad: Geen data
LogKow: Geen data
Wateroplosbaarheid: 0,9 g/100 ml (slecht)
Verzadigde dampdruk: 9000 mbar

Overige informatie

Publieke grenswaarde: 0,1 mg/ m³ (8 uur, als Se)
MAK: 0,02 mg/m³
TLV-TWA: 0,168 mg/m³ (als Se)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: irritatie ogen en luchtwegen, misselijkheid, braken, duizeligheid, hoofdpijn, vermoeidheid, metaalsmaak in mond

AGW → LBW: ernstige irritatie luchtwegen, hoesten, benauwdheid, longoedeem, verminderde leverfunctie, bewustzijnsdaling

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Seleenwaterstof is irriterend voor de ogen en bovenste en onderste luchtwegen. Longoedeem kan ontstaan, waarbij de verschijnselen vertraagd kunnen optreden en versterkt kunnen worden door lichamelijke inspanning.
- Seleenwaterstof kan leverschade veroorzaken. Dit effect kan vertraagd optreden.
- Bij blootstelling aan seleenwaterstof kan verlamming van reukzenuw optreden waardoor geurwaarneming en geurwaarschuwing afwezig is.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, bevriezingsverschijnselen zoals roodheid en pijn.

Oogcontact: bijtend, bevriezing kan optreden, roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: 3
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: aan de huid vastgevroren kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en direct spoedeisende medische hulp inzetten..
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: n.v.t. (gas).

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 7783-07-5 **Hydrogen selenide** **H_2Se** **UN-nr: 2202**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: Same rationale as for AEGL (one-third of LBW), 2h value added

LBW: Same point of departure as AEGL, different uncertainty factors, 2h value added.

Date: November 2015 | Interim AEGL document 08/2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	No appropriate endpoints
AGW	7.6	4.9	3.7	2.8	2.1	1.6	One third of LBW
LBW	23	15	11	8.4	6.4	4.8	Lethality threshold in animals

Derivation of the Dutch Intervention Values

VRW: VRW values are not recommended, because no data with the appropriate endpoints were found in either the human or animal studies.

AGW: In the absence of sufficient human or animal data to derive AGW values, the LBW values divided by 3 were used. This approach is justified because lethality data indicated a steep concentration-response curve. The derived values are supported by the limited and poorly documented data in humans in which workers could tolerate 0.3 ppm (1.01 mg/m³) for several minutes, but 1.5 ppm (5.05 mg/m³) resulted in severe irritation that was intolerable.

LBW: The point of departure and the value of n was estimated by combining data from two experiments: a C × t study and a 1-h LC_{50} study. These experiments were performed at the same laboratory with the same species and strain. From the combined data, a 1-h LC_{01} of 33 ppm (111 mg/m³) and an n-value of 2.5 are estimated by combining all data (un-weighted). The combined data were analyzed in total (28 observations) and after excluding data at 1,410 mg/m³ and higher; mortality was 100% (2/2) at those concentrations, so the data provided little value to the analysis. Both analyses yielded a 120-min LC_{01} of 25 ppm (84 mg/m3), which is below the observed lethal concentration of 40 ppm (135 mg/m3). The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences.

Additional toxicological information (including relevant results of a general literature search, if any)

The mechanism of toxicity of selenium and selenium compounds is unknown and is likely dependent on the individual compound and on the dose level. From the limited data available it seems that the mechanism may concern two different pathways. Hydrogen selenide is highly irritating to the respiratory tract with effects progressing to pulmonary edema, bronchitis, and bronchial pneumonia at very high dose levels with a steep dose-response curve. This has been observed in humans. The second pathway is based on the finding that, in animals, deaths at longer durations occurred over a lower and relatively flat concentration range. These deaths were most likely secondary to liver damage; most deaths occurred more than 5 days after exposure, when liver damage was greatest. Glutathione depletion by high levels of selenium is most likely the mechanism of liver damage. In contact with mucus membranes, the compound is oxidized to elemental selenium which appears as a red precipitate. A distinct garlic odor on the breath can be detected in humans accidentally exposed to selenium (compounds). Human studies indicate that children seem to be less susceptible to selenium toxicity from high dietary intake than adults.

No relevant information on reproductive or developmental toxicity in humans or experimental animals was available.

H330: Fatal if inhaled

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to carcinogenicity to humans)

Odour and derivation of the LOA value

Odour: garlic-like odour

No carcinogenic risk potency (CRP) was derived.

No information was found on the human or animal chronic toxicity or carcinogenicity of hydrogen selenide. IARC classification refers to selenium and selenium compounds in general.

OT_{50}: 1.011 mg/m^3 [AIHA, 1989]
LOA = 11.8 * OT_{50} * 1.33 = 16 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

A distinct garlic odour of the breath has been reported for humans accidentally exposed to selenium or selenium compounds and is most likely the result of excretion of dimethyl selenide in expired air.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **NR**	*AEGL-1* NR	*ERPG-1* NR		*IDLH: 3.4 (30 min)*
AGW level **3.7**	*AEGL-2* 0.37	*ERPG-2* 0.67		
LBW level **11**	*AEGL-3* 1.1	*ERPG-3* 6.7		

Stofdocument deel A

CAS-nr: 7803-62-5 **Silaan** H_4Si **VN-nr: 2203**

GEVI: 23

Synoniemen: monosilaan, siliciumtetrahydride, siliciumwaterstof (Engels: silane) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	130	130	130	130	130	130
Alarmeringsgrenswaarden	AGW (mg/m³)	970	670	530	420	340	170
Levensbedreigende waarden	LBW (mg/m³)	1900*	1300*	1100	840	670	340

Datum vaststelling: 28-11-2008

Conversiefactor: 1 mg/m³ = 0,749 ppm; 1 ppm = 1,34 mg/m³

Explosiegrens: LEL = 1 vol% ≈ 13.000 mg/m³

* De volgende Interventiewaarden zijn gelijk aan of hoger dan 10% LEL : de LBW-waarden voor 10 min. en 30 min.

Geur: weerzinwekkende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: samengeperst gas

Brand: pyrofoor, zeer brandgevaarlijk

Relatieve dichtheid gas: 1,1

Molecuulmassa: 32,1 g/mol

Zuurgraad: geen data

LogKow: geen data

Wateroplosbaarheid: niet oplosbaar

Verzadigde dampdruk: geen data

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 6,7 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: irritatie, reversibele nierschade

AGW → LBW: irreversibele nierschade

Boven LBW: sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Silaan kan irritatie van de ogen en luchtwegen veroorzaken.
- Silaan kan nierschade veroorzaken.

Effecten bij blootstelling aan vloeistof

alleen mogelijk bij ongecontroleerd vrijkomen uit een drukhouder

Huidcontact: roodheid

Oogcontact: branderig gevoel

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: n.v.t.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust.

ogen: –

Ontsmetting vloeistof

huid: n.v.t. (gas), maar in geval van bevriezingswonden: aan de huid vastgevroren kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en arts raadplegen.

ogen: n.v.t. (gas), maar in geval van bevriezingswonden: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen. Blijven spoelen tijdens vervoer.

inslikken: n.v.t.

Specifieke behandeling en materialen*:* geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7803-62-5 **Silane** **H_4Si** **UN-nr: 2203**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same point of departure as for AEGL values but using different uncertainty factors, 2h value added and time scaling applied for 10-min value

LBW: Same point of departure as for AEGL values but using different uncertainty factors, 2h value added and time scaling applied for 10-min value

Date: 28-11-2008 | AEGL document: Interim, 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	130	130	130	130	130	130	Irritation in animals
AGW	970	670	530	420	340	170	Threshold of persistent kidney damage in animals
LBW	1900*	1300*	1100	840	670	340	Threshold of lethality in animals

* value ≥ 10% of LEL

Derivation of the Dutch Intervention Values

VRW: VRW values were derived from the 1000 ppm (1300 mg/m³) NOEL for irritation in mice. Male mice were exposed to 1000 ppm (1300 mg/m³) silane for 1, 2, 4 and 8 hours. No effects were observed on mortality, hematology, clinical chemistry or histopathology. Clinical signs in treated animals included increased washing of the face and lower abdominal area after exposure. In the repeated dose phase of the study, the only other finding was a slight increase in inflammatory/necrotic nasal cells in mice exposed to 1000 ppm (1300 mg/m³) silane 6 hours/day, 5 days/week for 4 weeks. Therefore, 1000 ppm (1300 mg/m³) will be the point of departure for the VRW values with no time-scaling. A total uncertainty factor of 10 was used, 3 for interspecies and 3 for intraspecies. Both were set at 3 because the only effect observed was mild irritation and this response is not expected to vary greatly among species or humans.

AGW: AGW values were determined using the 2500 ppm (3400 mg/m³) concentration from the 4 hour acute inhalation study in mice. This concentration caused reversible renal lesions. At 2500 ppm (3400 mg/m³), renal lesions observed two days post-exposure resolved within two weeks. At the next highest concentration, 5000 ppm (6700 mg/m³), renal lesions were noted both after the two day and two week observation period, thus making 2500 ppm (3400 mg/m³) the 4 hour NOEL for irreversible effects. Time-scaling was performed using the formula $C^n \times t = k$ using the default values of n = 1 and n=3 for extrapolating to longer and shorter exposure durations. In contrast to the AEGL-2, time-scaling was also applied to the 10 minute AGW value. A total uncertainty factor of 10 was used, 3 for interspecies because the mouse was identified as the most sensitive species tested, and 3 for intraspecies. In contrast the AEGL-2 values were derived using an intraspecies factor of 10.

LBW: LBW values were based on a 4 hour mouse inhalation study in which 5000 ppm (6700 mg/m³) induced irreversible renal lesions with no mortality. The highest level tested, 10,000 ppm (13,000 mg/m³), caused mortality in 6/8 mice. Time-scaling was performed using the formula $C^n \times t = k$ using default values of n=1 and n=3 for extrapolating to longer and shorter exposure durations. In contrast to the AEGL, time-scaling was also applied to the 10-min LBW. A total uncertainty factor of 10 was used, 3 for interspecies and 3 for intraspecies (in contrast the AEGL-3 values were derived using an intraspecies factor of 10). An LC_{50} study identified the mouse as being more sensitive than the rat. No deaths occurred and no gross lesions were observed in rats after a 4-hour exposure to 9600 ppm (12.800 mg/m³) silane. However, 4/10 mice died at the same concentration and in another 4 hour study, renal enlargement in mice exposed to 10,000 ppm (13,000 mg/m³) was observed. In contrast to the AEGL-3, time-scaling was also applied to the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)
No data concerning lethality or nonlethal toxicity in humans from exposure to silane were located in the available literature. Both human and animal data on silane toxicity are limited. Part of the difficulty in conducting studies is the highly explosive nature of silane. The highest concentration tested was 10,000 ppm (13,000 mg/m^3) due to safety concerns above this level. No data were located on developmental/reproductive toxicity of silane. No harmonized H-statements for human health.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived No data were located concerning carcinogenicity of silane in humans or experimental animals	Odour: repulsive odour No LOA was derived due to lack of reliable data

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **130**	*AEGL-1* 130	*ERPG-1* not derived		*IDLH*: not derived
AGW level **530**	*AEGL-2* 170	*ERPG-2* not derived		
LBW level **1100**	*AEGL-3* 360	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 10026-04-7 **Siliciumtetrachloride** Cl_4Si **VN-nr: 1818**

GEVI: X80

Synoniemen: chloorkiezel, chloorsilaan, tetrachloorsilaan (Engels: tetrachlorosilane) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	3,2	3,2	3,2	3,2	3,2	3,2
Alarmeringsgrenswaarden	AGW (mg/m³)	200	94	59	37	23	23
Levensbedreigende waarden	LBW (mg/m³)	600	280	180	110	69	69

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,141 ppm; 1 ppm = 7,07 mg/m³

Explosiegrens: geen data

Geur: scherpe stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze rokende vloeistof
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,3

Molecuulmassa:	169,9 g/mol
Zuurgraad:	geen data
LogKow:	geen data
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	260 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW	geen informatie
VRW → AGW:	irritatie van ogen en luchtwegen, tranenvloed, hoesten, lichte benauwdheid
AGW → LBW:	ernstige irritatie van ogen en luchtwegen, pijn op de borst, benauwdheid, longontsteking, longoedeem
Boven LBW:	ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Chloorsilanen reageren zeer snel met water onder vorming van chloorwaterstof (HCl). De acute toxiciteit van siliciumtetrachloride wordt veroorzaakt door chloorwaterstof.
- Inhalatie van chloorwaterstof veroorzaakt een type I inhalatie intoxicatie.
- Chloorwaterstof veroorzaakt irritatie van de slijmvliezen van ogen en luchtwegen.
- Chloorwaterstof kan bij inhalatie longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, brandwonden.

Oogcontact: bijtend, roodheid en pijn, hoornvliesbeschadiging, ernstige brandwonden.

Carcinogeniteit

IARC classificatie: niet geclassificeerd.
CRP: niet afgeleid.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust; in geval van rode ogen halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken (voorzichtig i.v.m mogelijk reeds beschadigde huid), minimaal 20 min. spoelen met veel water of douchen, en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen:.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 10026-04-7 **Tetrachlorosilane** **Cl_4Si** **UN-nr: 1818**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same rationale as AEGL (analogy with HCl), 2h value added

LBW: Same rationale as AEGL (analogy with HCl), 2h value added

Date: November 2015 | AEGL document: final 2012

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	3.2	3.2	3.2	3.2	3.2	3.2	Based on HCl (Threshold for irritation in humans)
AGW	200	94	59	37	23	23	Based on HCl (one-third of LBW))
LBW	600	280	180	110	69	69	Based on HCl (Calculated threshold for lethality in animals)

Derivation of the Dutch Intervention Values

VRW: Since no appropriate data exist for tetrachlorosilane, VRW values for hydrogen chloride will be used (on ppm-basis) to derive VRW values for tetrachlorosilane. The use of hydrogen chloride as a surrogate for tetrachlorosilane was deemed appropriate since it is believed that the hydrolysis product, HCl, is responsible for the adverse effects. Because a maximum of four moles of hydrogen chloride are produced for every mole of tetrachlorosilane, a molar adjustment factor of 4 was applied to the hydrogen chloride VRW values.

Derivation of VRW values for HCl

The hydrogen chloride VRW values were based on a no-adverse-effect-level of 1.8 ppm (2.73 mg/m^3) in exercising asthmatics with an exposure duration of 45 min. Because the test subjects were considered a sensitive subpopulation and the endpoint was essentially a no-effect level, no uncertainty factor was applied to account for sensitive human subpopulations. The VRW values were held constant for all specified exposure periods since mild irritant effects represent threshold effects and generally do not vary over time

AGW: Since no appropriate data exist for tetrachlorosilane, AGW values for hydrogen chloride will be used (on ppm-basis) to derive AGW values for tetrachlorosilane. Because a maximum of four moles of hydrogen chloride are produced for every mole of tetrachlorosilane, a molar adjustment factor of 4 was applied to the hydrogen chloride AGW values.

Derivation of AGW values for HCl

The AGW values of HCl for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data. The only study of HCl that addressed effects that meet the definition of an AGW, severe nasal lesions, was a study on hydrogen halides by Stavert et al. (1991). Nevertheless, this study was not considered a suitable basis for derivation of AGW values because 6% of the animals died after exposure to HCl at 1300 ppm (1974 mg/m^3), only one concentration was tested and the number of animals tested was inconsistent.

LBW: Since no appropriate data exist for tetrachlorosilane, LBW values for hydrogen chloride will be used (on ppm-basis) to derive LBW values for tetrachlorosilane. Because a maximum of four moles of hydrogen chloride are produced for every mole of tetrachlorosilane, a molar adjustment factor of 4 was applied to the hydrogen chloride LBW values.

Derivation of LBW values for HCl

The LBW values were based on a lethality study in rats. The rat study included six exposure durations and various concentrations. Probit analyses using DoseResp was performed and yielded LC_{01} values for the 10 min, 30 min, 1-, 2-,4-, and 8hrs exposure durations of 3370, 1602, 1002, 627,

393 and 246 ppm (5116, 2433, 1522, 952, 596, and 373 mg/m^3), respectively, which were used as point of departure for LBW derivation. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The probit analyses yielded an n-value of 1.48, which was supported by the n-value of 1.59 calculated by Arts *et al.* (2000) from the C*t study. To maintain consistency with other hydrogen halogenides, the 8 hour value was set equal to the 4 hour value, as performed for the most potent hydrogen halogenide HF.

Additional toxicological information (including relevant results of a general literature search, if any)

The only human exposure data located were from an accidental release of terachlorosilane at a chemical plant. Symptoms of due to exposure generally resolved within 24 hours, and included lacrimation, rhinorrhea, burning in the mouth and throat, headache, coughing, and wheezing. No tetrachlorosilane air concentrations were reported.

Chlorosilanes react violently with water to produce hydrogen chloride gas. Data suggest that the acute toxicity of chlorosilanes is due to the hydrogen chloride hydrolysis product; acute toxicity of the chlorosilanes is both qualitatively (based on clinical signs) and quantitatively (based on molar equivalents of hydrogen chloride) similar to that of HCl.

Although toxicity data are limited for individual chlorosilanes, well-conducted 1-hr inhalation toxicity studies in rats are available for a series of chlorosilanes. In general, LC_{50} values for monochlorosilanes were approximately twice the LC_{50} values for dichlorosilanes and three times the LC_{50} values for trichlorosilanes. Tetrachlorosilane had an LC_{50} value similar to the trichlorosilanes; however, there were experimental difficulties at the lowest concentration tested. Clinical signs were consistent with hydrogen chloride exposure and included lacrimation, salivation, dried material around or on the eyes and/or nose, green staining around the nose and mouth, and perineal urine staining. Labored breathing, rales, hypoactivity, closed or partially closed eyes, prostration, corneal opacity or opaqueness, and swollen and/or necrotic paws were also observed. Hemorrhage, congestion and/or consolidation of the lungs, ectasia of the lungs, gaseous distension of the gastrointestinal tract, absence of body fat, obstruction of nostrils, dried and/or firm nares, alopecia around the eyes and discoloration of hair were observed at necropsy.

No data concerning developmental/reproductive toxicity for exposure to tetrachlorosilane were located in the available literature.

H319: Causes skin irritation. H315: Causes serious eye irritation. H335: May cause respiratory irritation.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified.

No carcinogenic risk potency (CRP) was derived

No data concerning carcinogenicity for exposure to tetrachlorosilane were located in the available literature.

Odour and derivation of the LOA value

Odour: pungent odour

No LOA was derived due to lack of data.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **3.2**	*AEGL-1* 3.2	*ERPG-1* 5.3		*IDLH:* not derived
AGW level **59**	*AEGL-2* 39	*ERPG-2* 35		
LBW level **180**	*AEGL-3* 180	*ERPG-3* 260		

Stofdocument deel A

CAS-nr: 7803-52-3 **Stibine** **H_3Sb** **VN-nr: 2676**

GEVI: geen

Synoniemen: antimoonwaterstof, antimoonhydride (Engels: stibine) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	22	15	7,6	3,8	1,9	0,94
Levensbedreigende waarden	LBW (mg/m³)	140	99	50	25	12	6,2

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,193 ppm; 1 ppm = 5,19 mg/m³

Explosiegrens: geen data

Geur: typerende, vieze, walgingwekkende, zwavelwaterstof-achtige (rotte eieren) geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos onder druk tot vloeistof verdicht gas
Brand: zeer brandgevaarlijk

Relatieve dichtheid gas: 4,3

Molecuulmassa:	124,8 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	0,1 g/100 ml (slecht)
Verzadigde dampdruk:	1000 mbar

Overige informatie

Publieke grenswaarde: 0,50 mg/m³ (8 uur)
MAK: niet afgeleid
TLV-TWA: 0,52 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW**:* irritatie van ogen en luchtwegen, hoesten, keelpijn, pijnlijke ogen

AGW → LBW: irritatie van onderste luchtwegen, benauwdheid, longoedeem, verlies van gezichtsvermogen, buikpijn, misselijkheid, spierpijn, zwaktegevoel, hoofdpijn, duizeligheid, hemolyse, nierfunctiestoornissen

Boven LBW: ademnood, coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Stibine werkt bijtend op de luchtwegen en ogen
- Inademing van stibine kan longoedeem veroorzaken, waarbij de verschijnselen pas na enkele uren kunnen optreden en versterkt kunnen worden door lichamelijke inspanning
- Stibine kan hemolyse veroorzaken; hemolytische effecten kunnen progressief zijn en enkele dagen na blootstelling aanhouden.
- Secundair aan hemolyse kan nierschade en uiteindelijk nierfalen ontstaan
- **Let op:** steile concentratie-respons curve.

Effecten bij blootstelling aan vloeistof

Huidcontact: bevriezingsverschijnselen zoals roodheid, pijn, blaren.

Oogcontact: roodheid en pijn, ernstige brandwonden, verlies van gezichtsvermogen

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: n.v.t. (gas), *maar in geval van bevriezingswonden*: aan de huid vastgevroren kleding NIET lostrekken, spoelen met veel water / kleding verwijderen en onmiddellijk arts raadplegen.

ogen: n.v.t. (gas), maar *bij bevriezing:* minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas)

***Specifieke behandeling en materialen**: geen.*
Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 7803-52-3 **Stibine** **H_3Sb** **UN-nr: 2676**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL values are adopted, 2 hr values added

LBW: AEGL values are adopted, 2 hr values added

Date: 16-12-2010 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Insufficient data
AGW	22	15	7.6	3.8	1.9	0.94	No effect level for irreversible toxicity (kidney and lung) in rats and guinea pigs
LBW	140	99	50	25	12	6.2	Highest exposure with no lethality in rats and guinea pigs

Absence of a VRW value does not imply that exposure below the AGW concentration is without adverse effects.

Derivation of the Dutch Intervention Values

VRW: VRW values are not recommended because data are not available from human or animal studies consistent with VRW endpoints.

AGW: AGW values are based upon studies where 10 rats (5/sex) and 10 guinea pigs (5/sex) were exposed for 30 minutes to 29.1, 191 or 333 ppm (151, 992, or 1729 mg/m³) stibine and observed for 14 days. Exposure to 191 ppm (992 mg/m³) in both species resulted in renal tubular dilation and calcification that would result in scarring. Pulmonary inflammation was also found in one guinea pig at this exposure. Eye irritation and closure were observed in rats. All animals experienced generalized depressed activity, but none were judged to have an impaired ability to escape. Exposure at 29.1 ppm (151 mg/m³) was defined as the no effect level for irreversible renal effects.
This concentration, 29.1 ppm (151 mg/m³), was used as the point of departure for the derivation of AGW values as it was the highest exposure level without an AGW effect. A total uncertainty factor of 10 was applied to account for interspecies extrapolation and intraspecies variability. A factor of 3 was applied for interspecies variability because similar mortality rates were reported from pulmonary edema for rats (70%) and guinea pigs (70%) at 333 ppm (1729 mg/m³) and similar lesions (renal tubular dilation, pulmonary edema) were reported in both species at 191 ppm (992 mg/m³). An uncertainty factor of 3 was applied for intraspecies variability. Although the mechanism of toxicity is unknown, the point of departure is based on contact irritation in the lung, and that respiratory irritant action is not expected to vary a great deal among individuals. Time extrapolation was performed using $C^n \times t = k$, where the defaults n = 3 and n = 1 are applied for extrapolations to shorter and longer durations, respectively.

LBW: The LBW values are based on the same study as used for the derivation of the AGW values. One guinea pig exposed to 191 ppm (992 mg/m³) for 30 min died and cortical necrosis of the cerebrum was found in that animal. However, this lesion and death were not considered to be treatment-related. At 333 ppm (1729 mg/m³) 70% mortality in rats and 70% mortality in guinea pigs was observed. These deaths appeared to be caused by pulmonary edema. The highest concentration with no treatment-related mortality (191 ppm (992 mg/m³), 30-min exposure) was identified as the point of departure for the LBW derivation. The same uncertainty factors and rationale used for AGW values were applied to LBW calculations. Time extrapolation was performed using $C^n \times t = k$, where the defaults n = 3 and n = 1 are applied for extrapolations to shorter and longer durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Stibine is a respiratory irritant that induces pulmonary inflammation, edema, and congestion. Stibine is recognized as a haemolytic poison that causes the rapid breakdown of erythrocytes. The relatively brief time to death following acute exposure is consistent with death as a consequence of pulmonary edema rather than death from renal failure subsequent to haemolysis

Exposure to stibine gas could be detected by measuring the antimony concentration in the blood and urine of humans. However, there is no way to distinguish between stibine exposure and exposure to other antimony compounds. Complete elimination was reported of antimony following a weekend of no workplace stibine exposure (not detected in urine samples).

There are no studies found on potential developmental or reproductive effects of stibine in humans or experimental animals.

No harmonized H-statements for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No information concerning potential carcinogenicity was located.

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: disagreeable hydrogen sulfide-like odour

No odour threshold data were located.

No LOA was derived.

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)***

VRW level **NR**	*AEGL-1* NR	*ERPG-1* ID*		*IDLH:* 26 (30 minutes)
AGW level **7.6**	*AEGL-2* 7.8	*ERPG-2* 2.6		
LBW level **50**	*AEGL-3* 50	*ERPG-3* 7.8		

* ID = insufficient data.

Stofdocument deel A

CAS-nr: 10102-44-0 **Stikstofdioxide** **NO_2** **VN-nr: 1067**

GEVI: 265

Synoniemen*[65,66]*: dinitrotetroxide, stikstofperoxide, (di)stikstoftetroxide

Status: B-stof

(Engels: nitrogen dioxide)

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,96	0,96	0,96	0,96	0,96	0,96
Alarmeringsgrenswaarden	AGW (mg/m³)	44	30	24	19	10	4,8
Levensbedreigende waarden	LBW (mg/m³)	220	150	120	96	48	24

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,523 ppm; 1 ppm = 1,91 mg/m³

Explosiegrens: geen kwalitatieve data; kans op explosie door reactie met vele stoffen

Geur: stekende geur

LOA: 3,6 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: roodbruin onder druk tot vloeistof gedrukt gas of gele zeer vluchtige vloeistof
Brand: niet brandbaar, doch bevordert brand van andere stoffen

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,6

Molecuulmassa:	46,0 g/mol
Zuurgraad:	Geen data
LogKow:	-0.58
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	960 mbar

Overige informatie

Publieke grenswaarde: 0,4 mg/m³ (8 uur), 1 mg/m³ (15 min)
MAK: 0,95 mg/m³
TLV-TWA: 5,7 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: irritatie luchtwegen en ogen

VRW → AGW: irritatie luchtwegen en ogen, hoesten, bloeddrukdaling, hoofdpijn, misselijkheid

AGW → LBW: ernstige irritatie luchtwegen en ogen, benauwdheid, pijn op de borst, longoedeem

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Stikstofdioxide veroorzaakt irritatie van de slijmvliezen van luchtwegen en ogen.
- Inhalatie van stikstofdioxide veroorzaakt een type II inhalatoire intoxicatie waarbij de stof diep doordringt tot de lagere luchtwegen.
- Een kenmerk van een stikstofdioxide-intoxicatie na de acute fase is een schijnbaar herstel gevolgd door schade van de lagere luchtwegen
- Blootstelling aan stikstofdioxide kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: *vloeistof: bevriezingsletsel*.
Oogcontact: *damp:* roodheid en pijn, branderig gevoel, hoornvliesbeschadiging, *vloeistof: bevriezingsletsel*.

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

inademing: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, spoelen met veel water / kleding verwijderen en onmiddellijk arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas > 21°C).

Ontsmetting vloeistof n.v.t. (gas).

Specifieke behandeling en materialen*: geen*.

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

[65] Het roodbruine stikstofdioxide is onder normale omstandigheden in chemisch evenwicht met het kleurloze distikstoftetraoxide
[66] Nitreuze dampen bestaan uit een mengsel van stikstofdioxide en stikstofmonoxide.

Stofdocument deel B

CAS-nr: 10102-44-0 **Nitrogen dioxide** NO_2 **UN-nr: 1067**

Basis for the Dutch Intervention Values

VRW: AEGL values are adopted, 2 hour values added

AGW: Same point of departure, different value for n, 2 hour values added

LBW: Same point of departure, different UFs and different value for n, 2 hour values added

Date: 06-10-2016 | AEGL final 2012

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.96	0.96	0.96	0.96	0.96	0.96	Mild symptoms of discomfort in exercising asthmatics
AGW	44	30	24	19	10	4.8	Respiratory symptoms in healthy volunteers.
LBW	220	150	120	96	48	24	Marked respiratory irritation and severe lung histopathology in monkey

Derivation of the Dutch Intervention Values

VRW: The VRW values were based on human data. Exposure of asthmatics (n=13) during exercise to 0.5 ppm (0.96 mg/m³) nitrogen dioxide for 2 hour resulted in clinical signs (slight burning of eyes, slight headache, chest tightness or labored breathing) in 7/13 subjects, but no changes in pulmonary function. The 2h exposure to 0.96 mg/m³ nitrogen dioxide was used as point of departure for the VRW. Since asthmatics are potentially the most susceptible population, no uncertainty factor was applied for intraspecies differences. The concentration of 0.96 mg/m³ was adopted for all time points, because adaptation to mild sensory irritation occurs. In addition, animal responses to nitrogen dioxide have demonstrated a much greater dependence on concentration than on time; therefore, extending the 2-hour concentration to 8 hour should not exacerbate the human response.

AGW: As starting point for the derivation of the AGW, results from a human study with healthy volunteers (n=10-14/group) with 2h exposure to 0.5-30 ppm (0.96-57 mg/m³) nitrogen dioxide were used. Exposure to 57 mg/m³ for 2 h resulted in marked irritation, discomfort and respiratory effects. This exposure concentration was used as point of departure for the AGW. The effects observed are considered a threshold for AGW, because the effects noted by the subjects would not impair the ability to escape and the effects were reversible after cessation of exposure. The default intraspecies uncertainty factor of 3 was considered sufficient to account for intraspecies differences. For time-scaling $C^n \times t = k$ was used, using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively.

LBW: The LBW values were based on monkey data. Monkeys (2-6/group) were exposed to 10, 15, 35 or 50 ppm (19.1, 28.7, 66.9, 95.5 mg/m³) for 2h. Signs of marked irritation and severe lung histopathology were observed from exposure to nitrogen dioxide at 95.5 mg/m³ for 2 h. This was used as point of departure. For interspecies differences, an uncertainty factor of 1 was used. A larger interspecies uncertainty factor is not considered necessary, because the end point in the monkey study is below the definition of the LBW, and the respiratory tracts of humans and monkeys are similar. Furthermore, the mechanism of action with the target at the alveoli of nitrogen dioxide does not vary between species. The default intraspecies uncertainty factor of 3 was considered sufficient to account for intraspecies differences. However, the resulting LBWs then would conflict with human data (see AGW) and therefore, the intraspecies factor is lowered to 1. For time-scaling $C^n \times t = k$ was used, using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. The derived values are supported by human data from a welder with pulmonary edema (confirmed on x-ray), who was exposed to approximately 90 ppm (172 mg/m³) for up to 40 minutes.

Additional toxicological information (including relevant results of a general literature search, if any)

Nitrogen oxide is an irritant to the mucous membranes and may cause coughing and dyspnea during exposure. After less severe exposure, symptoms may persist for several hours before subsiding. With more severe exposure, pulmonary edema ensues with signs of chest pain, cough, dyspnea, cyanosis, and moist rales on auscultation. Death from nitrogen dioxide inhalation is caused by bronchospasm and pulmonary edema. Toxicity from acute exposure can be described in one of three categories: 1) immediate death after very heavy exposure, 2) delayed symptoms with development of edema within 48 hours, and 3) apparent recovery from immediate effects but later chronic chest disease of varying severity.

There is no human data on reproductive toxicity. Evaluation of the postnatal effects of prenatal exposure to nitrogen dioxide (6h/day during pregnancy) showed that pup viability and body weight of the 5.3 ppm (10 mg/m^3) were significantly less than the controls on day 21 of lactation. Exposure to ≥0.53 ppm (1 mg/m^3) in rats resulted in developmental delays and exposure to ≥0.053 ppm (0.1 mg/m^3) lead to disturbances in neuromotor development.

H314: Causes severe skin burns and eye damage, H330: Fatal if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: pungent, bleach odour

ODT: 0.23 mg/m^3 [Nagata, 2003; corrected value derived from 0.12 ppm]
LOA = 11.8 * ODT * 1.33 = 3.6 mg/m^3
(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/ODT) + 0.5. A correction factor of 1.33 is applied to this value)

Note, AIHA (1986) states that the reference range of odour values (0.058-0.14 ppm, i.e. 0.11 – 0.27 mg/m^3) is not acceptable.

The LOA lies below the AGW and LBW values.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **0.96**	*AEGL-1* 0.96	*ERPG-1* 1.9		*IDLH:* 38 mg/m^3 (30 minutes)
AGW level **24**	*AEGL-2* 23	*ERPG-2* 29		
LBW level **120**	*AEGL-3* 38	*ERPG-3* 57		

Stofdocument deel A

CAS-nr: 10102-43-9 **Stikstofmonoxide** **NO** **VN-nr: 1660**

GEVI: geen

Synoniemen*[67]*: stikstof (II)oxide (Engels: nitric oxide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Let op! De hieronder gepresenteerde* Interventiewaarden *zijn de waarden voor stikstofmonoxide, maar deze zijn gebaseerd op de waarden van stikstofdioxide. Stikstofmonoxide wordt in de lucht omgezet in het meer toxische stikstofdioxide. Stikstofdioxide dient gemeten te worden in het geval van een calamiteit met stikstofmonoxide. Zie voor informatie het stofdocument van stikstofdioxide.							
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,63	0,63	0,63	0,63	0,63	0,63
Alarmeringsgrenswaarden	AGW (mg/m³)	29	20	16	13	6,3	3,1
Levensbedreigende waarden	LBW (mg/m³)	143	99	79	63	31	16

Datum vaststelling: 06-10-2016

Conversiefactor stikstofmonoxide: 1 mg/m³ = 0,801 ppm; 1 ppm = 1,25 mg/m³

Conversiefactor stikstofdioxide: 1 mg/m³ = 0,523 ppm; 1 ppm = 1,91 mg/m³

Explosiegrens: geen gegevens

Geur: reukloos

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas, wordt bruin aan de lucht

Brand: niet brandbaar, maar bevordert brand van andere stoffen

Relatieve dichtheid gas (lucht =1): 1,03

Molecuulmassa:	30,0 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	0,006 g/100 ml (zeer slecht)
Verzadigde dampdruk:	-

Overige informatie

Publieke grenswaarde: 0,25 mg/m³ (8 uur)

MAK: 0,63 mg/m³

TLV-TWA: 31 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: irritatie luchtwegen en ogen

VRW → AGW: irritatie luchtwegen en ogen, hoesten, bloeddrukdaling, hoofdpijn, misselijkheid

AGW → LBW: ernstige irritatie luchtwegen en ogen, benauwdheid, pijn op de borst, longoedeem

Boven LBW: ademnood, sterfte

NB: De hierboven beschreven effecten zijn gerelateerd aan blootstelling aan stikstofdioxide. Als gevolg van directe blootstelling aan stikstofmonoxide kunnen ook cardiovasculaire effecten en methemoglobinevorming ontstaan; hiervoor zijn geen goede concentratie-effect relaties bekend.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De toxiciteit van stikstofmonoxide is primair een gevolg van door oxidatie tot stikstofdioxide en secundair door methemoglobine vorming.
- Stikstofdioxide veroorzaakt irritatie van de slijmvliezen van luchtwegen en ogen.
- Inhalatie van stikstofdioxide veroorzaakt een type II inhalatoire intoxicatie waarbij de stof diep doordringt tot de lagere luchtwegen.
- Een kenmerk van een stikstofdioxide-intoxicatie na de acute fase is een schijnbaar herstel gevolgd door schade van de lagere luchtwegen
- Blootstelling aan stikstofdioxide kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Vorming van methemoglobine (als direct effect van stikstofmonoxide) leidt tot een verminderde zuurstofafgifte naar de weefsels.

Effecten bij blootstelling aan gas

Huidcontact: bijtend, roodheid, pijn, brandwonden

Oogcontact: bijtend, roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

inademing: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Huid: verontreinigde kleding uittrekken, minimaal 20 min. Spoelen met veel water of douchen en (bij brandwonden) arts raadplegen.

Ogen: minimaal 15 min. Spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Inslikken: n.v.t. (gas).

Ontsmetting vloeistof n.v.t. (gas).

Specifieke behandeling en materialen*: geen (in het ziekenhuis kan later desgewenst het methemoglobinegehalte worden bepaald .*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

[67] Nitreuze dampen bestaan uit een mengsel van stikstofdioxide en stikstofmonoxide

Stofdocument deel B

CAS-nr : 10102-43-9 **Nitric oxide** **NO** **UN-nr: 1660**

Basis for the Dutch Intervention Values

VRW: AEGL rationale adopted, 2 hour values added

AGW: AEGL rationale adopted, 2 hour values added

LBW: AEGL rationale adopted, 2 hour values added

Date: 06-10-2016 AEGL Final 2012

Dutch Intervention Values (mg/m³)

Note that the presented Intervention Values are those of nitric oxide! The values are based on nitrogen dioxide, because nitric oxide is converted in the atmosphere to the more toxic compound nitrogen dioxide. Nitrogen dioxide levels should be monitored in case of an incident with nitric oxide.

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.63	0.63	0.63	0.63	0.63	0.63	Based on nitrogen dioxide (Mild symptoms of discomfort in asthmatics)
AGW	29	20	16	13	6.3	3.1	Based on nitrogen dioxide (Respiratory symptoms in healthy volunteers)
LBW	143	99	79	63	31	16	Based on nitrogen dioxide (Marked respiratory irritation and severe lung histopathology in monkey)

Derivation of the Dutch Intervention Values

VRW: Because conversion to nitrogen dioxide is expected to occur in the atmosphere, and because nitrogen dioxide is more toxic than nitric oxide, the VRW values for nitrogen dioxide are recommended for use with emergency planning for nitric oxide. Nitrogen dioxide is the most ubiquitous and the most toxic of the oxides of nitrogen; VRW values derived from nitrogen dioxide toxicity data are considered applicable to all oxides of nitrogen including nitric oxide. Monitoring nitrogen dioxide levels is recommended in case of an incident with nitric oxide.

Derivation of VRW values for nitrogen dioxide

The VRW values were based on human data. Exposure of asthmatics (n=13) during exercise to 0.5 ppm (0.96 mg/m^3) nitrogen dioxide for 2 hour resulted in clinical signs (slight burning of eyes, slight headache, chest tightness or labored breathing) in 7/13 subjects, but no changes in pulmonary function. The 2h exposure to 0.96 mg/m^3 nitrogen dioxide was used as point of departure for the VRW. Since asthmatics are potentially the most susceptible population, no uncertainty factor was applied for intraspecies differences. The concentration of 0.96 mg/m^3 was adopted for all time points, because adaptation to mild sensory irritation occurs. In addition, animal responses to nitrogen dioxide have demonstrated a much greater dependence on concentration than on time; therefore, extending the 2-hour concentration to 8 hour should not exacerbate the human response.
To express the VRWs in mg/m^3 nitric oxide, a molecular weight correction was applied to the nitrogen dioxide levels.

AGW: Because conversion to nitrogen dioxide is expected to occur in the atmosphere, and because nitrogen dioxide is more toxic than nitric oxide, the AGW values for nitrogen dioxide are recommended for use with emergency planning for nitric oxide. Nitrogen dioxide is the most ubiquitous and the most toxic of the oxides of nitrogen; AGW values derived from nitrogen dioxide toxicity data are considered applicable to all oxides of nitrogen including nitric oxide. Monitoring nitrogen dioxide levels is recommended in case of an incident with nitric oxide.

Derivation of AGW values for nitrogen dioxide

As starting point for the derivation of the AGW, results from a human study with healthy volunteers (n=10-14/group) with 2h exposure to 0.5-30 ppm (0.96-57 mg/m^3) nitrogen dioxide were used. Exposure to 57 mg/m^3 for 2 h resulted in marked irritation, discomfort and respiratory effects. This exposure concentration was used as point of departure for the AGW. The effects observed are considered a threshold for AGW, because the effects noted by the subjects would not impair the

ability to escape and the effects were reversible after cessation of exposure. The default intraspecies uncertainty factor of 3 was considered sufficient to account for intraspecies differences. For time-scaling $C^n \times t = k$ was used, using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively.
To express the AGWs in mg/m^3 nitric oxide, a molecular weight correction was applied to the nitrogen dioxide levels.

LBW: Because conversion to nitrogen dioxide is expected to occur in the atmosphere, and because nitrogen dioxide is more toxic than nitric oxide, the LBW values for nitrogen dioxide are recommended for use with emergency planning for nitric oxide. Nitrogen dioxide is the most ubiquitous and the most toxic of the oxides of nitrogen; LBW values derived from nitrogen dioxide toxicity data are considered applicable to all oxides of nitrogen including nitric oxide. Monitoring nitrogen dioxide levels is recommended in case of an incident with nitric oxide.

Derivation of LBW values for nitrogen dioxide
The LBW values were based on monkey data. Monkeys (2-6/group) were exposed to 10, 15, 35 or 50 ppm (19.1, 28.7, 66.9, 95.5 mg/m^3) for 2h. Signs of marked irritation and severe lung histopathology were observed from exposure to nitrogen dioxide at 95.5 mg/m^3 for 2 h. This was used as point of departure. For interspecies differences, an uncertainty factor of 1 was used. A larger interspecies uncertainty factor is not considered necessary, because the end point in the monkey study is below the definition of the LBW, and the respiratory tracts of humans and monkeys are similar. Furthermore, the mechanism of action with the target at the alveoli of nitrogen dioxide does not vary between species. The default intraspecies uncertainty factor of 3 was considered sufficient to account for intraspecies differences. However, this factor is lowered to 1, because the resulting LBWs would conflict with human data (see AGW). For time-scaling $C^n \times t = k$ was used, using default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. The derived values are supported by human data from a welder with pulmonary edema (confirmed on x-ray), resulting from exposure to approximately 90 ppm (172 mg/m^3) for up to 40 minutes. Similar results for LBW-values would be obtained using data of rats exposed to nitrogen dioxide at 72 ppm (138 mg/m^3) for 1 h (signs of severe respiratory distress and ocular irritation) and using an uncertainty factor of 3.

To express the LBWs in mg/m^3 nitric oxide, a molecular weight correction was applied to the nitrogen dioxide levels.

Additional toxicological information (including relevant results of a general literature search, if any)

The toxicity of nitric oxide is associated with methaemoglobin formation and oxidation to nitrogen dioxide.
Inhaled nitric oxide is absorbed into the bloodstream and binds to haemoglobin forming nitrosylhaemoglobin, which is rapidly oxidized to methaemoglobin The affinity of nitric oxide for haemoglobin is about 1,500 times greater than that of carbon monoxide and the binding and formation of methaemoglobin is dependent on nitric oxide concentration and time. Methaemoglobin formation results in hypoxia, which occurs due to the decreased oxygen-binding capacity of methaemoglobin, as well as the increased oxygen-binding affinity of other subunits in the same haemoglobin molecule, which prevents them from releasing oxygen at normal tissue oxygen levels.

The relative toxicities of nitric oxide and nitrogen dioxide are complex. At concentrations >833 ppm for 1 h, nitric oxide was more toxic than nitrogen dioxide; however, at lower concentrations, nitrogen dioxide was more toxic. It appears that for nitric oxide, if the concentration is not high enough to be lethal from methemoglobin formation, the animal recovers completely. On the other hand, concentrations of nitrogen dioxide that are not rapidly lethal may cause more persistent effects and in some cases cause death from pulmonary edema after a delay of several days.

No information on the reproductive and developmental toxicity of nitric oxide.

No harmonized H-sentences for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

Derivation of the carcinogenic risk potency (CRP): No CRP derived

Odour and derivation of the LOA value

Odour: odourless

No LOA derived

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*				
VRW-level **0.63**	*AEGL-1* 0.96	*ERPG-1* -		*IDLH: 125 mg/m³ (30 min)*
AGW level **16**	*AEGL-2* 23	*ERPG-2* -		
LBW level **79**	*AEGL-3* 38	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 7783-54-2 **Stikstoftrifluoride** F_3N **VN-nr: 2451**

GEVI: 25

Synoniemen: fluorstikstof, trifluoramine, trifluorammonia (Engels: nitrogen trifluoride) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	3.600	1.200	600	290	150	75
Alarmeringsgrenswaarden	AGW (mg/m³)	9.200	3.100	1.600	790	400	200
Levensbedreigende waarden	LBW (mg/m³)	15.000	5.000	2.600	1.300	650	330

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,339 ppm; 1 ppm = 2,95 mg/m³

Explosiegrens: geen data

Geur: muffe, schimmelachtige geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas
Brand: niet brandbaar, bij vele reacties kans op brand en explosie

Relatieve dichtheid gas (lucht=1): 2,4

Molecuulmassa:	71,0 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	Slecht
Verzadigde dampdruk:	Geen data

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 30 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen klachten

VRW → AGW: cyanose (blauwkleuring van de lippen, tong, huid en slijmvliezen)

AGW → LBW: klachten door zuurstoftekort in weefsels: zwakte, hoofdpijn, duizeligheid, braken, lethargie, verwardheid, benauwdheid, ernstige cyanose, versnelde ademhaling, versnelde hartslag

Boven LBW: ademnood, convulsies, coma, verlaagde hartslag, hartritmestoornissen, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Stikstoftrifluoride induceert de omzetting van hemoglobine in methemoglobine. Hemoglobinetekort kan leiden tot zuurstofgebrek in weefsels (anoxie).
- Blootstelling kan leiden tot aan anoxie gerelateerde klachten en schade aan longen en andere organen.
- De vorming van methemoglobine is reversibel, maar kan gevolgd worden door hemolytische anemie (hemoglobinetekort door afbraak van rode bloedcellen).
- De afbraak van rode bloedcellen kan mogelijk enige dagen aanhouden, waardoor effecten vertraagd op kunnen treden.
- Pasgeborenen zijn gevoeliger voor methemoglobine vorming dan volwassenen.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, branderig gevoel, blaren

Oogcontact: bijtend, slecht zien, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, specifieke behandeling en onmiddellijk arts raadplegen.

Ontsmetting vloeistof
huid: spoelen met veel water / kleding uittrekken en arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: n.v.t. (gas).

***Specifieke behandeling en materialen**: Bij vergiftiging door deze stof is specifieke eerste hulp noodzakelijk; de benodigde middelen (100% zuurstof en specifieke antidota zoals o.a. methyleenblauw) moeten met gebruiksaanwijzing ter plekke beschikbaar zijn.*

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7783-54-2 **Nitrogen trifluoride** **F_3N** **UN-nr: 2451**

Basis for the Dutch Intervention Values

VRW: AEGL values adopted, 2 h value added

AGW: AEGL values adopted, 2 h value added

LBW: AEGL values adopted, 2h value added

Date: 06-10-2016 | AEGL document, interim 2009

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	3,500	1,200	590	300	150	74	15% MetHb formation in dogs
AGW	9,200	3,100	1,600	790	400	200	Impaired ability to escape in humans
LBW	15,000	5,000	2,600	1,300	650	330	Lethality in rats

Derivation of the Dutch Intervention Values

VRW: VRW levels were based on studies in 6 dogs and 6 monkeys which were exposed to 290, 510, 1075, 2000, 3500, 7000 ppm (856, 1506, 3175, 5907, 10,337, 20,673 mg/m³) nitrogen trifluoride for 15, 30 or 60 minutes. Exposure to 2000 ppm (5907 mg/m³) for 60 minutes was used as point of departure. This exposure resulted in 15% MetHb formation in dogs and 10% in monkeys. A MetHb concentration ≤15% is without clinical signs or symptoms. Hematology changes (decreases in erythrocyte count, Hb, and hematocrit of approximately 16%), seen only in dogs, were reversible. The dog is the most sensitive species for effects on hematology parameters and compared with rodents, the dog is more hematologically similar to humans regarding hematopoiesis and blood cell kinetics. Therefore, an interspecies factor of 1 was considered sufficient. An intraspecies uncertainty factor of 10 was applied because infants, lacking the NADH cofactor for methemoglobin reductase, are especially sensitive to MetHb-forming chemicals. In addition, some humans may be anemic, have hereditary methemoglobinemia, or have defective hemoglobins, resulting in higher sensitivity to MetHb-generating chemicals. Time scaling was applied using a chemical specific n-value of 1.0 derived from a dog lethality study.

AGW: AGW levels were based on the estimated concentration of nitrogen trifluoride which induces 43% MetHb concentration. A MetHb concentration of 40-45% is predicted to induce weakness, fatigue, dizziness and lethargy in humans. These symptoms are the threshold for an impaired ability to escape and meet the definition of an AGW-level. A concentration of nitrogen trifluoride inducing 43% MetHb was estimated as the midpoint between the 15% MetHb concentration that defines the VRW levels and the 70% MetHb predicted threshold value for lethality as cited in several reviews and referenced in the key and supporting studies. The AGW values for each exposure duration were calculated as the midpoint concentration between each VRW and LBW value. Inter- and intraspecies uncertainty factors are already accounted for in derivation of the VRW and LBW values.

LBW: LBW values were based on the threshold of lethality in dogs. Death was caused by anoxia due to methemoglobin-formation. The dog was chosen because, compared to rodents, the dog is more similar to humans regarding MetHb reductase activity and hematopoiesis. The threshold for lethality at each LBW exposure duration was calculated using the probit-based, dose response program of ten Berge (2006). The threshold was set at 1%, which is similar to the benchmark dose BMC_{01}. The data indicated a time-scaling n-value of 1. LC_{01} values for 10 min, 30 min, 1 hour, 2 hour, 4 hour and 8 hour were 148,100, 50,370, 25,510, 12,920, 6,540, 3,312 mg/m³). The dog is the most sensitive species for effects on hematology parameters and compared with rodents, the dog is more hematologically similar to humans regarding hematopoiesis and blood cell kinetics. Therefore, an interspecies factor of 1 was considered sufficient. An intraspecies uncertainty factor of 10 was applied because neonates, lacking the NADH cofactor for methemoglobin reductase, are especially sensitive to MetHb-forming chemicals.

Additional toxicological information (including relevant results of a general literature search, if any)

No human clinical toxicological data are available.

The primary toxic effect of nitrogen trifluoride is methemoglobinemia as a result of the oxidation of hemoglobin to methemoglobin (MetHb). Methemoglobin is unable to carry oxygen to the tissues, resulting in tissue anoxia.

This may result in headache, dizziness, weakness and cyanosis.

Methemoglobinemia may be followed by hemolytic anemia that can cause enlargement of the spleen and pathological changes in liver and kidney. At the cessation of exposure methemoglobin reverts to hemoglobin within several hours. In contrast, hemolytic anemia may take weeks to resolve, and may even worsen for some time after cessation of exposure.

Neonates are deficient of NADH-methemoglobin reductase. NADH (the cofactor for methemoglobin reductase) lacks full activity until infants are four months of age. Neonates are therefore more sensitive to methemoglobin-generating chemicals than adults.

There was no evidence of maternal or developmental toxicity in a developmental toxicity study in which groups of 8 rats were exposed to 0, 5, 20, 50, or 100 ppm (0, 15, 60, 150, or 300 mg/m^3) nitrogen trifluoride for 6 hours/day on gestational day 6-20. There is no evidence from standard short-term test to suggest nitrogen trifluoride presents a genotoxic or mutagenic hazard.

No harmonized H-sentences for human health.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived. There is no evidence from standard short-term test to suggest nitrogen trifluoride presents a genotoxic or mutagenic hazard.	Odour: mouldy No LOA was derived due to lack of suitable data.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **590**	*AEGL-1* 590	*ERPG-1* N.A.		*IDLH:* 3000 mg/m^3 (30 minutes)
AGW level **1600**	*AEGL-2* 1600	*ERPG-2* 1200		
LBW level **2600**	*AEGL-3* 2500	*ERPG-3* 2400		

Stofdocument deel A

CAS-nr: 12504-13-1 **Strontiumfosfide** Sr_3P_2 **VN-nr: 2013**

GEVI: geen

Synoniemen: - (Engels: strontium phosphide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	81	27	14	6,8	3,4	1,7
Levensbedreigende waarden	LBW (mg/m³)	150	49	24	12	6,1	3,0

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,0740 ppm; 1 ppm = 13,519 mg/m³

Explosiegrens: geen data
Kans op explosie door vorming van fosfine met vocht uit de lucht.

Geur: geen informatie

LOA: niet afgeleid.

Fysisch-chemische eigenschappen

Uiterlijk: vaste stof
Brand: kan spontaan ontbranden door vorming van fosfine met vocht uit lucht.

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa: 325 g/mol

Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: reactie
Verzadigde dampdruk: geen data

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling
(gebaseerd op vrijkomen van fosfine)

*Onder **AGW***: irritatie aan ogen, huid, neus en luchtwegen, hoofdpijn, misselijkheid, braken, zwakte, paresthesie, duizeligheid, tremor
AGW → LBW: benauwdheid, longoedeem, bewustzijnsdaling, hartritmestoornissen, nier- en leverfunctiestoornissen
Boven LBW: convulsies, cardiovasculaire collaps, myocardinfarct, ademnood, coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De toxiciteit van strontiumfosfide wordt veroorzaakt door vorming van fosfine bij contact met vocht uit de lucht en luchtwegen.
- Fosfine verstoort door effecten op de celademhaling de zuurstofopname en energievoorziening van de cel.
- Fosfine werkt irriterend op de ogen, huid en luchtwegen.
- Hoge blootstelling kan tot longoedeem leiden. Dit kan pas na enkele uren optreden en kan worden versterkt door lichamelijke inspanning.
- Kinderen zijn mogelijk gevoeliger voor toxiciteit door fosfine.

Effecten bij blootstelling aan vloeistof

Huidcontact: geen informatie

Oogcontact: geen informatie

Carcinogeniteit

IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
ogen: spoelen met water (evt. contactlenzen verwijderen).

Ontsmetting vaste stof
huid: verontreinigde kleding uittrekken, afspoelen met water.
ogen: spoelen met water (evt. contactlenzen verwijderen).
inslikken: mond laten spoelen (uitspugen!), rust, GEEN mond-op-mondbeademing, actieve kool (carbomix) toedienen, en direct spoedeisende medische hulp inzetten..

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 12504-13-1 **Strontium phosphide** Sr_3P_2 **UN-nr: 2013**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 24-09-2009 AEGL document: Final 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended due to insufficient data
AGW	81	27	14	6.8	3.4	1.7	Irritation nasal mucosa rats (phosphine)
LBW	150	49	24	12	6.1	3.0	Lethality rats (phosphine)

Derivation of the Dutch Intervention Values

VRW: No data are available for strontium phosphide. As toxicity of strontium phosphide is due to phosphine, which is formed due to reaction of strontium phosphide with moisture, data on phosphine could be used to derive intervention values. However, no appropriate data were available for derivation of VRW values for phosphine. Therefore VRW values are not recommended. This does not imply that exposure below AGW is without adverse effects.

AGW: Since no appropriate data exist for strontium phosphide, AGW values for phosphine will be used (on ppm-basis) to derive AGW values for strontium phosphide. The use of phosphine as a surrogate for strontium phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because two moles of phosphine are produced for every mole of strontium phosphide, a molar adjustment factor of 2 was applied to the strontium phosphide AGW values.

Derivation of AGW values for phosphine

The phosphine AGW values were based on red mucoid nasal discharge in rats exposed to 10 ppm (14 mg/m³) phosphine for 6 hours, corresponding to 67.60 mg/m³ strontium phosphide. Since this endpoint is less severe than effects defined by AGW, the resulting values should be protective.
The default uncertainty factor of 3 was applied to account for interspecies variability. An uncertainty factor of 10 was applied to account for intraspecies variability since the human data suggest that children may be more sensitive than adults when exposed to presumably similar phosphine concentrations. For example, in two reports, exposed children died, but exposed adults survived. Time scaling was performed using the equation $C^n \times t = k$, and an n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine).

LBW: Since no appropriate data exist for strontium phosphide, LBW values for phosphine will be used (on ppm-basis) to derive LBW values for strontium phosphide. The use of phosphine as a surrogate for strontium phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because two moles of phosphine are produced for every mole of strontium phosphide, a molar adjustment factor of 2 was applied to the strontium phosphide LBW values.

Derivation of LBW values for phosphine

The highest concentration yielding no deaths in rats (18 ppm = 25 mg/m³) for 6 hours was used as point of departure for the calculation of the LBW values, corresponding to 121.7 mg/m³ strontium phosphide. The default uncertainty factor of 3 for interspecies and an intraspecies factor of 10 were applied for reasons provided above. Time scaling was performed using the equation $C^n \times t = k$ and a chemical specific n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine). These values are considered protective since workers were repeatedly exposed for “brief” periods of time to phosphine concentrations up to 35 ppm (49 mg/m³) with no life-threatening effects and workers exposed to >50 ppm (>70 mg/m³) for 2-5 minutes experienced only odour.

Additional toxicological information (including relevant results of a general literature search, if any)

When strontium phosphide reacts with moisture, phosphine gas will be formed. Phosphine is considered to induce acute toxic effects following oral and inhalation exposure. Children are thought to be more vulnerable to phosphine exposure. Common clinical signs after exposure to phosphine are headache, vomiting, coughing, shortness of breath, paresthesia, weakness, tremors and jaundice. Pulmonary congestion, pleural effusion, and congestive heart failure may be observed upon post-mortem examination.

In vitro, phosphine reacts with cytochrome c and cytochrome c oxidase, thereby inhibiting mitochondrial oxygen uptake. In vitro studies have also shown that phosphine can react with the heme moiety of hemoglobin in the presence of oxygen. Cell death and loss of cell membrane integrity accounted for the increased liver enzymes, bronchiolytic effects, cloudy swelling of renal tubular epithelia, and hemorrhagic myocardial lesions.

No reproductive or developmental data were found.

No harmonised H-statements for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not evaluated.

No carcinogenic risk potency (CRP) was derived.

No data concerning carcinogenicity of strontium phosphide are available.

Fumigation workers exposed long-term to phosphine have a higher incidence of both stable and less stable chromosomal aberrations. Molecular analysis of these lesions suggests that the breakpoints are near proto-oncogenes involved in non-Hodgkin's lymphoma, possibly contributing to the increased incidence of lymphomas in pesticide workers.

Odour and derivation of the LOA value

Odour: no information.

Pure phosphine is odourless at concentrations up to 200 ppm. Technical-grade phosphine has a garlic-like odour (may be due to impurities).

For phosphine, no LOA was derived due to lack of reliable data. Ruth (1986) reported an odour range of 0.028-3.6 mg/m^3 for phosphine.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **NR**	*AEGL-1* NR	*ERPG-1* not derived		*IDLH:* not derived
AGW level **14**	*AEGL-2* 13	*ERPG-2* not derived		
LBW level **24**	*AEGL-3* 24	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 100-42-5 **Styreen** $H_2C=C(C_6H_5)H$ **VN-nr: 2055**
GEVI: 39

Synoniemen: ethenylbenzeen, fenyletheen, vinylbenzeen (Engels: styrene) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	87	87	87	87	87	87
Alarmeringsgrenswaarden	AGW (mg/m³)	990	680	540	540	540	540
Levensbedreigende waarden	LBW (mg/m³)	21000**	8300*	4700*	2600	1500	1500

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,231 ppm; 1 ppm = 4,33 mg/m³

Explosiegrens: LEL = 0,8 vol% ≈ 35.000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

** berekende interventiewaarde hoger dan 50% LEL

Geur: doordringende, iets zoetige geur

LOA: 2,4 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot lichtgele vloeistof
Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,02

Molecuulmassa: 104,2 g/mol
Zuurgraad: geen data
LogKow: 3,2
Wateroplosbaarheid: 0,03 g/100 ml (niet)
Verzadigde dampdruk: 7 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: 86 mg/m³
TLV-TWA: 87 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: mogelijk lichte irritatie

VRW → AGW: irritatie van ogen, huid, neus en luchtwegen, keelpijn, hoofdpijn, vermoeidheid

AGW → LBW: duizeligheid, misselijkheid, braken, tranenvloed, bewustzijnsdaling, verminderde coördinatie

Boven LBW: coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Styreen werkt irriterend op de ogen, huid en luchtwegen.
- Styreen kan depressie van het centrale zenuwstelsel veroorzaken, met mogelijk coma en sterfte tot gevolg.
- Bij fysieke inspanning en bij mensen die eerder zijn blootgesteld aan styreen is verhoogde gevoeligheid voor de effecten van styreen mogelijk.

Effecten bij blootstelling aan vloeistof

Huidcontact: prikkeling, roodheid en pijn
Stof kan door de huid worden opgenomen.
Oogcontact: prikkeling, roodheid en pijn, tranenvloed

Carcinogeniteit

IARC classificatie: 2B
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*
Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 100-42-5 **Styrene** **$H_2C=C(C_6H_5)H$** **UN-nr: 2055**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 16-12-2010 | AEGL document: Interim 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	87	87	87	87	87	87	Threshold of irritation and CNS effects in humans
AGW	990	680	540	540	540	540	CNS effects in humans
LBW	21000**	8300*	4700*	2600	1500	1500	$BMDL_{05}$ for lethality in animals

* value higher than 10% of LEL, ** value higher than 50% of LEL

Derivation of the Dutch Intervention Values

VRW: In an evaluation of reactions related to chemosensory irritation of styrene in humans, the ratings for irritation at 20 ppm (87 mg/m³) indicated only marginal effects in this respect. No increase in irritation or headaches compared to control was noted at 20 ppm (87 mg/m³) in a further study. At 50 ppm (220 mg/m³), a marginal increase in subjective symptoms ratings for eye and nose irritation, headache, and fatigue was described in one, but not in a second study. At 100 ppm (430 mg/m³), signs of irritation and of mild subjective CNS effects were reported in some studies, but no such effects were seen in others. Complaints of eye and nose irritation were more frequent at about 200 ppm and the severity increased with a further increase in concentration. Therefore, 20 ppm (87 mg/m³) was selected as point of departure to derive VRW. Because this concentration represents a NOAEL for local as well as CNS effects and in other studies effects at 50 and 100 ppm (220 and 430 mg/m³) were only weak or absent, an intraspecies factor of 1 is applied. The value of 20 ppm (87 mg/m³) was used for all timepoints since slight irritation and subjective discomfort that were reported at higher concentrations did not increase within several hours of exposure.

AGW: The AGW is based on the CNS effects observed in 9 healthy male volunteers following exposed for 1h, 2h or 7h (with a 30 min break) to 51.4, 99.4, 116.7, 216.1, 376 ppm (223, 431, 506, 937, 1630 mg/m³) for time periods of 1 hour, 7 hours, 2 hours, 1 hour and 1 hour respectively. Exposure to 376 ppm (1630 mg/m³) for one hour resulted in: nausea in one subject; feeling of being inebriated in two subjects, and unability to normally perform tests of coordination and manual dexterity in three of five subjects. The effects described address a level of CNS depression that seems still below a level for an impairment of the ability to escape and therefore a concentration of 376 ppm (1600 mg/m³) is considered a NOAEL for CNS effects. This concentration is close to the range where irritation in humans becomes intolerable: Exposed subjects reported immediate lacrimation at 300-400 ppm (1300-1700 mg/m³) and described the irritation above 500 or 600 ppm (2200 or 2600 mg/m³) as very strong or even intolerable. An intraspecies uncertainty factor of 3 was considered adequate to protect sensitive subgroups including groups exposed to styrene during longer periods of light exercise. The value was scaled to shorter periods of time using the equation $C^n \times t = k$, using n=3. Toxicokinetic studies with humans exposed to styrene concentrations at 70-200 ppm (300-870 mg/m³) show that most of the increase of the styrene concentration in blood is seen during the first 30 minutes of exposure and that there is no or very little increase at 1 – 3 hours at these concentrations. Therefore, for longer exposure times no additional extrapolation is necessary and the 1h AGW value is applied to longer periods of time.

LBW: The LBW is based on lethality observed in rats (10/sex/group; 20/sex/group at highest conc) exposed for 4 hours to 2983, 3766, 4814, 5911, 6621, 7218, 8407 ppm (12930, 16323, 20865, 25620, 28698, 31285, 36439 mg/m³). A $BMDL_{05}$ for female rats of 3409 ppm (rounded to 3400 ppm; 15,000 mg/m³) was calculated, which was used as a point of departure to derive LBW values. An interspecies factor of 3 and an intraspecies factor also of 3 were used. The interspecies uncertainty factor of 3 is based on limited data indicating no gross differences in the concentration of styrene in blood between rats and humans. An intraspecies uncertainty factor of 3 was applied to account for sensitive individuals since the threshold for CNS impairment is not expected to vary much among individuals. Time scaling was performed using the relationship $C^n \times t = k$ and a value of n = 1.2, which was derived from extrapolation of the LC_{50} in rats for 4-

and 6 hours. The 8-hour AGW was assigned the same value as the 4-hour AGW, as toxicokinetic data indicate that there is, at the most, little increase of the internal dose after 4 hours of exposure; moreover, lower values which would be derived by default calculations are not supported by toxicological data for humans. In contrast to the 10 minute AEGL-3 value, that was set equal to the 30 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Individuals with a high level of physical activity during exposure may be considered more susceptible than individuals at rest because the concentration of styrene in blood is strongly affected by physical activity.

Individual cases of respiratory or skin sensitization to styrene have been described. Taking into account the wide use of styrene both in industry and in consumer products, sensitization seems to be a rare event. However, sensitized individuals may not be able to tolerate styrene concentrations that are without effect in non-sensitized individuals and may not be protected by the intervention values developed for styrene.

Styrene is irritating to eyes and the respiratory tract. In a number of controlled studies with human volunteers, irritation and effects on the CNS were investigated.

In rats, exposure to high concentrations of styrene leads to progressive CNS depression with narcosis and, finally, death. Pulmonary lesions were also described in these studies but only at concentrations leading to severe or lethal CNS effects.

No data are available indicating potential reproductive or developmental toxicity of styrene in humans after inhalation exposure.

H315: Causes skin irritation; H319: Causes serious eye irritation; H332: Harmful if inhaled; H316d: Suspected of damaging the unborned child; H372: Causing damage to hearing organs through prolonged or repeated exposure.

Carcinogenicity and derivation of the CRP value

IARC classification: 2B (possibly carcinogenic to humans)

No carcinogenic risk potency (CRP) was derived.

With respect to carcinogenicity, IARC concluded that the increased risks for cancers of the lymphatic and hematopoetic system are small, statistically unstable and often based on subgroup analyses. The findings are not very robust and that it cannot be ruled out that the observations are the results of chance, bias or confounding. The balance of epidemiologic studies does not suggest a causal association between styrene and any human cancer, because of the limited power of these studies. However the inconclusive results do not rule out the possibility that the observed increase of lung tumors in mice are of relevance to humans.

Odour and derivation of the LOA value

Odour: pungent, slightly sweetish odour.

OT_{50}: 0.15 mg/m^3 [AEGL]

LOA = 11.8 * OT_{50} * 1.33 = 2.4 mg/m^3

(The concentration Level leading to distinct Odour Awareness (l=3) is calculated using the formula: l = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is far below the VRW values.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **87**	*AEGL-1* 87	*ERPG-1* 220		*IDLH:* 3000 (30 minutes)
AGW level **540**	*AEGL-2* 560	*ERPG-2* 1100		
LBW level **4700**	*AEGL-3* 4800	*ERPG-3* 4300		

Stofdocument deel A

CAS-nr: 7791-25-5 **Sulfurylchloride** SO_2Cl_2 **VN-nr: 1834**

GEVI: X668

Synoniemen: - (Engels: sulfuryl chloride) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	38	26	21	17	13	6,6
Levensbedreigende waarden	LBW (mg/m³)	114	79	63	50	39	20

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,178 ppm; 1 ppm = 5,62 mg/m³

Explosiegrens: geen data

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot gele vloeistof
Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,5

Molecuulmassa: 135 g/mol
Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: reactie
Verzadigde dampdruk: 133 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: irritatie van slijmvliezen van ogen, neus en keel, tranenvloed, keelpijn, lichte benauwdheid, hoesten

AGW → LBW: ernstige irritatie van ogen, neus en keel, benauwdheid, longoedeem, pijn op de borst, bloed ophoesten

Boven LBW: ademnood, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Sulfurylchloride kan irritatie en schade aan de ogen en luchtwegen veroorzaken.
- De corrosieve effecten en schade aan weefsels wordt waarschijnlijk veroorzaakt door de afbraakproducten zwavelzuur en zoutzuur, die worden gevormd bij contact met water.
- Sulfurylchloride kan een type I inhalatoire intoxicatie veroorzaken. Hierbij kan longoedeem ontstaan welke pas na enkele uren kan optreden en versterkt kan worden door lichamelijke inspanning. Bij afwezigheid van lokale irritatie, is geen longoedeem te verwachten.

Effecten bij blootstelling aan vloeistof

Huidcontact: *bijtend*, roodheid, pijn, (chemische) brandwonden

Oogcontact: *bijtend*, roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en zo nodig arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 7791-25-5 **Sulfuryl chloride** **SO_2Cl_2** **UN-nr: 1834**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 16-12-2010 AEGL document: Final, 2011

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	38	26	21	17	13	6.6	One third of LBW values
LBW	114	79	63	50	39	20	$BCML_{05}$ for lethality in rats

Derivation of the Dutch Intervention Values

VRW: No exposure-response data are available to differentiate VRW type effects from those that may progress to more serious effects. The lowest concentrations tested in available animal studies were associated with evidence of respiratory tract damage. The continuum of toxic responses is likely a function of the corrosive action of the sulfuryl chloride degradation products, hydrochloric and sulfuric acid. The sulfuryl chloride concentrations at which the corrosive activity of these products becomes more than minor irritation is unclear. Therefore, VRW values are not recommended.

AGW: The reviewed toxicity studies were conducted primarily to assess lethality. Because lethality threshold estimates tended to be less than non lethal experimental exposures and because of the apparent steep exposure-response curve for sulfuryl chloride, AGW values were estimated by a three-fold reduction of the LBW values.

LBW: A 4-hour $BMCL_{05}$ of 70.1 ppm (390 mg/m³) calculated from a study in rats was used as the point-of-departure for deriving LBW values. An interspecies uncertainty factor of 3 was used because the effects of sulfuryl chloride consist of contact tissue damage of degradation products (sulfuric acid and hydrochloric acid), and not from metabolites. An intraspecies uncertainty factor of 3 was used to account for individual variability in direct contact toxic response to corrosive agents. Temporal scaling for LBW values was performed $C^n \times t = k$ equation using default values for n, i.e. n=1 and n=3 for extrapolation to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-3 value that was set equal to the 30 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

There are no human exposure data regarding inhalation of sulfuryl chloride.

Toxicity data for sulfuryl chloride are limited to lethality studies in rats. Because sulfuryl chloride decomposes to hydrochloric acid, and sulfuric acid upon contact with water, it may be assumed that much of its toxicity is attributable to corrosive activity of these products on contacted tissues (e.g., respiratory tract). Exposure of test animals to nonlethal concentrations of sulfuryl chloride was associated with signs of ocular and respiratory irritation, body weight loss, and respiratory tract damage.

No information was available regarding the developmental/reproductive toxicity of sulfuryl chloride.

H314: Causes severe skin burns and eye damage; H335: May cause respiratory irritation.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Results of genotoxicity assays of sulfuryl chloride are equivocal and no carcinogenicity bioassays have been conducted.

Odour and derivation of the LOA value

Odour: pungent odour

No LOA was derived due to lack of data.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* 1.7		*IDLH:* not derived
AGW level **21**	*AEGL-2* 20	*ERPG-2* 17		
LBW level **63**	*AEGL-3* 61	*ERPG-3* 84		

Stofdocument deel A

CAS-nr: 2699-79-8 **Sulfurylfluoride** SO_2F_2 **VN-nr: 2191**

GEVI: 26

Synoniemen: PT8, sulfuryldifluoride (Engels: sulfuryl fluoride) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	160	110	91	72	57	29
Levensbedreigende waarden	LBW (mg/m³)	490	340	270	220	170	86

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,235 ppm; 1 ppm =4,24 mg/m³

Explosiegrens: geen data

Geur: geurloos

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas

Brand: niet brandbaar

Relatieve dichtheid gas (lucht=1): 3,5

Molecuulmassa	102,1 g/mol
Zuurgraad:	Geen data
LogKow:	0,1
Wateroplosbaarheid:	1,7 g/100 ml (matig)
Verzadigde dampdruk:	16.000 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 21 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: Irritatie van slijmvliezen van ogen neus en keel, bewustzijnsdaling, slaperigheid

AGW → LBW: Ernstige irritatie van ogen, neus en keel, misselijkheid, buikpijn, braken, bewustzijnsdaling, gevoelloosheid extremiteiten, tremoren, benauwdheid

Boven LBW: Longoedeem, cyanose, convulsies, ademstilstand, hartstilstand, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Sulfurylfluoride is irriterend voor de huid, ogen en luchtwegen.
- De stof kan inwerken op het centrale zenuwstelsel met als gevolg bewustzijnsdaling, convulsies en sterfte.
- De stof veroorzaakt laesies in de luchtwegen, nieren en lever.
- De uitwerking kan vertraagd intreden.
- De toxiciteit van fluoride wordt veroorzaakt door remming van enkele enzymsystemen, hypocalciëmie, cardiovasculaire insufficiëntie en een direct toxische werking op spier- en zenuwweefsel.

Effecten bij blootstelling aan vloeistof

Huidcontact: bevriezingsletsel.

Oogcontact: roodheid, bevriezingsletsel.

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas:

Algemeen: frisse lucht, rust, GEEN mond-op-mondbeademing, halfzittende houding en onmiddellijk spoedeisende hulp inzetten

Huid (bij bevriezing): minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.

Ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), bij bevriezingsletsel naar oogarts brengen, blijven spoelen tijdens vervoer.

Specifieke behandeling en materialen:

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 2699-79-6 **Sulfuryl fluoride** SO_2F_2 **UN-nr: 2191**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: Same rationale as for AEGL (one-third of LBW), time scaling applied to 10 min value, 2h value added

LBW: AEGL value adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 06-10-2016 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended (insufficient data)
AGW	160	110	91	72	57	29	One third of LBW
LBW	490	340	270	220	170	86	Highest concentration causing no mortality in mice

Derivation of the Dutch Intervention Values

VRW: The available human and animal data indicate that there is very little margin between exposures having no effects and lethal exposures, therefore VRW values were not derived.

AGW: In the absence of empirical data and the presence of a steep concentration response relationship, the AGW values were derived by dividing the LBW values by 3. In 4-hr acute studies with the most sensitive species tested (mouse), no signs of toxicity were found at 404 or 596 ppm (1720 or 2530 mg/m³), but mortality occurred at 603 ppm (2560 mg/m³) (100%) and 692 ppm (2940 mg/m³) (90%), respectively, in two different strains of mouse. Rats exposed for 4 hours to 790 ppm (3360 mg/m³) had cyanosis, and 10% of the male rats and 100% of the female rats died at the next highest concentration of 1000 ppm (4250 mg/m³).

LBW: For deriving LBW values, exposure response data for mice exposed to sulfuryl fluoride for 4 hr at concentrations of 404, 603, and 1003 ppm (1720, 2530 and 4260 mg/m³) were used. The 603 (2560 mg/m³) and 1003 ppm (4260 mg/m³) exposures resulted in 100% mortality in mice within 5 days following exposure. The highest concentration at which no mortality occurred (404 ppm, 1720 mg/m³) was used for LBW derivation. The default uncertainty factor of 10 (3x3) was considered sufficient to account for intra- and interspecies differences. Time scaling was performed using the equation $C^n \times t = k$, with the default values of n=1 and n=3 for extrapolation to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-3 value that was set equal to the 30 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Sulfuryl fluoride is a severe irritant of skin, eyes and respiratory tract, and a central nervous system depressant. The toxicity of sulfuryl fluoride is probably due to the fluoride ion that binds to calcium and magnesium leading to the formation of an insoluble salt. If calcium is bound, it cannot longer fulfil its role in physiological processes. Increased fluoride can disrupt the Krebs cycle and can result in ventricular fibrillations and cardiovascular collapse from extracellular release of potassium.

The few available animal studies on reproduction and developmental toxicity showed no indications for reproductive toxicity of sulfuryl fluoride.

H331: Toxic if inhaled; H373: May cause damage to organs through prolonged repeated exposure.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

There are no indications for carcinogenicity or genotoxicity in humans.

Odour and derivation of the LOA value

Odor: odorless

No LOA was derived.

Other standards and guidelines (1h values in mg/m³, unless otherwise indicated)

VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH:* 850 (30 min)
AGW level **91**	*AEGL-2* 89	*ERPG-2* -		
LBW level **270**	*AEGL-3* 270	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 56-23-5 **Tetrachloorkoolstof** CCl_4 **VN-nr: 1846** **GEVI: 60**

Synoniemen: koolstoftetrachloride, tetrachloormethaan, tetra (Engels: Carbon tetrachloride) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	580	370	280	210	160	120
Levensbedreigende waarden	LBW (mg/m³)	5.900	3.800	2.900	2.200	1.600	1.200

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,156 ppm; 1 ppm = 6,40 mg/m³

Explosiegrens: geen data

Geur: zoete, stekende, etherachtige, niet onaangename geur

LOA: 460 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,5

Molecuulmassa:	153,8 g/mol
Zuurgraad:	Geen data
LogKow:	2,6 (berekend)
Wateroplosbaarheid:	0,1 g/100 ml (slecht)
Verzadigde dampdruk:	120 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: 3,2 mg/m³ (30min)

TLV-TWA: 32 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW: oogirritatie, hoofdpijn, misselijkheid en braken

AGW → LBW: agitatie, verwardheid, duizeligheid bewustzijnsdaling, verstoorde lever- en nierfunctie

Boven LBW: ernstige lever- en nierschade met convulsies, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De primaire doelorganen van tetrachloorkoolstof zijn de lever, nieren en het CZS.
- De hepatotoxiciteit is het gevolg van reactieve metabolieten, die worden gevormd door het (door ethanol induceerbare) CYP2E1 enzym.
- Effecten op de lever en nieren kunnen vertraagd optreden.
- Gevoelige groepen zijn alcoholisten en mensen die eerst zijn blootgesteld aan ethanol, alifatische alcoholen en ketonen. Deze stoffen versterken de levereffecten en waarschijnlijk niereffecten van tetrachloorkoolstof.
- Ook pulmonaire, cardiovasculaire en hematologische effecten zijn beschreven.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, droge huid.

Oogcontact: roodheid, pijn.

Carcinogeniteit

IARC classificatie: 2B

CRP (1 hr): 3.723 mg/m³

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust en arts raadplegen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken en minimaal 20 min. spoelen met veel water of douchen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 56-23-5 **Carbon tetrachloride** CCl_4 **UN-nr: 1846**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with the AEGL

AGW: Same point of departure as for AEGL, but using different uncertainty factor, 2 h value added,

LBW: Different point of departure, using the same uncertainty factor, 2 hr added.

Date: November 2015 | AEGL document: Final 2014

Proposal for the Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Inadequate data
AGW	580	370	280	210	160	120	Threshold for CNS effects (Davis, 1934)
LBW	5,900	3,800	2,900	2,200	1,600	1,200	Threshold for lethality (LC_{01}) in rats (Adams, 1952)

Derivation of the Dutch Intervention Values

VRW: A study in which four human volunteers were exposed to 76 ppm for 4 hours under controlled conditions was considered for derivation of the VRW. These human volunteers were already exposed 24 hours earlier to the same concentration for 2.5 hours. No symptoms or signs of toxicity were reported in any of the tested subjects. This study was however not used for derivation of the VRW, because the values that produced no effect were also the no-effect level for the CNS effects, which is an AGW level effect. Therefore, derivation of the VRW values is not recommended.

AGW: The AGW values are based on the highest no-effect level for CNS effects in a human exposure study. As point of departure the no-effect level of 76 ppm (486 mg/m³) in humans exposed to carbon tetrachloride for 4 hours was used. An uncertainty factor of 3 was applied to account for interindividual variation. Time scaling was performed using the equation C^n x t = k, where n=2.5, based on lethality data in the rat (see LBW).
This approach deviates from the AEGL-2 derivation, where an uncertainty factor of 10 was applied.

LBW: The point of departure for the LWB values was based on the results of one rat lethality study, in which animals were exposed to 19,000, 12,000, 7,300, 4,600, 3,600 and 3,000 ppm (120,000, 77,000, 47,000, 29,000, 23,000 and 19,000 mg/m³, respectively) for various durations. This study from Adams et al (1952) was used, because multiple time and concentration points were used and because the resulting LC_{01} calculated in Doseresp yielded the most conservative LBW values.

PBPK modeling shows that the amount of toxic metabolites produced in humans would be approximately half the amount in rodents. Therefore the toxicokinetic component of the interspecies uncertainty factor is considered to be 0.5. The toxicodynamic component of the interspecies uncertainty factor is considered to be 3. The total interspecies uncertainty factor of 1.5 (0.5 x 3 = 1.5) is therefore applied. An intraspecies uncertainty factor of 10 was used to account for variation between individuals based on known variability in the metabolism of carbon tetrachloride. Therefore the total uncertainty factor is 15. The n-value used in the equation C^n x t = k was determined to be 2.5, using the same data set.
This approach deviates from the AEGL-3 derivation, where the LC_{01} was calculated based on pooled data of two rat lethality studies.

Additional toxicological information (including relevant results of a general literature search, if any)

Case reports of human fatalities resulting from acute exposure to carbon tetrachloride are available that provide a clinical picture of dizziness, nausea, abdominal pain and oliguria/anuria with death being attributed to renal failure and hepatotoxicity. The liver, kidneys and central nervous system appear to be the primary targets for carbon tetrachloride toxicity. Most research has been focused on hepatotoxicity of carbon tetrachloride. The narcotic properties are well documented, but the precise mechanism of action is unclear. Also pulmonary, cardiovascular en hematological responses have been documented. Humans primarily exposed to ethanol, aliphatic alcohols and ketons are at risk for a potentiated carbon tetrachloride

hepatotoxicity.

The metabolism of carbon tetrachloride is mediated by ethanol-inducible CYP2E1 and the resulting reactive metabolites appear to be critical for toxicological effects of carbon tetrachloride. Biotransformation of carbon tetrachloride results in the formation of radicals that can bind to macromolecules including proteins and lipids and resulting in tissue damage.

Carbon tetrachloride is not teratogenic or toxic for reproduction. Embryotoxic and foetotoxic effects were only observed at levels that also induced maternal toxicity.

H331: Toxic if inhaled; H311: Toxic in contact with skin; H301: Toxic if swallowed; H351: Suspected of causing cancer; H372: Causes damage to organs through prolonged or repeated exposure

Carcinogenicity and derivation of the CRP value

IARC classification: 2B (possibly carcinogenic to humans)

Derivation of the carcinogenic risk potency (CRP):

10^{-4} risk level after inhalation: 17 x 10^{-3} mg/m^3 [EPA]

CRP = (10^{-4} risk level * average life span in hours)/DRCF

= (17 x 10^{-3} * 613,200) /2.8 = 3,723 mg/m^3

In the Netherlands carbon tetrachloride is not classified as a genotoxic carcinogen. The risk level above is based on route-to-route exposure from oral exposure data. Epidemiologic data do not demonstrate carcinogenicity in workers occupationally exposed to carbon tetrachloride.

Odour and derivation of the LOA value

Odour: sweet, pungent, ether like, not unpleasant odour

OT_{50}: 29.44 mg/m^3 [Nagata, 2003]

LOA = 11.8 * OT_{50} * 1.33 = 460 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies below the 10 min VRW and below AGW and LBW values for all time points.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **NR**	*AEGL-1* NR	*ERPG-1* 130		*IDLH:* 1,280 (30 minutes)
AGW level **280**	*AEGL-2* 82	*ERPG-2* 640		
LBW level **2,900**	*AEGL-3* 2,100	*ERPG-3* 4,800		

Stofdocument deel A

CAS-nr: 116-14-3 **Tetrafluorethyleen** $CF_2=CF_2$ **VN-nr: 1081**

GEVI: 239

Synoniemen: perfluorethyleen, TFE, FC-1114 (Engels: tetrafluoroethylene) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	4.100	2.900	2.300	1.800	1.400	940
Levensbedreigende waarden	LBW (mg/m³)	25.000	17.000	14.000	11.000	8.700	4.300

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,240 ppm; 1 ppm = 4,16 mg/m³

Explosiegrens: LEL= 10 vol% ≈ 416.000 mg/m³

Geur: reukloos

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos onder druk tot vloeistof verdicht gas

Brand: zeer brandgevaarlijk

Relatieve dichtheid gas (lucht = 1): 3,5

Molecuulmassa:	100 g/mol
Zuurgraad:	geen data
LogKow:	1,2
Wateroplosbaarheid:	0,01 g/100 ml (zeer slecht)
Verzadigde dampdruk:	30.000 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA (8 uur): 8,3 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen

VRW → AGW: lichte irritatie van de ogen en luchtwegen, versnelde ademhaling, hoofdpijn

AGW → LBW:, coordinatiestoornissen, spierzwakte

Boven LBW: ademnood, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof kan inwerken op de nieren, met als gevolg nierbeschadiging.

Effecten bij blootstelling aan vloeistof

Huidcontact: bevriezingsverschijnselen

Oogcontact: bevriezingsverschijnselen

Carcinogeniteit

IARC classificatie: 2A

CRP: 412 mg/m³

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust en arts raadplegen..

ogen: *uit*spoelen met water (evt. contactlenzen verwijderen).

Ontsmetting vloeistof (= bevriezingsletsel)

huid: kleding uittrekken (NIET lostrekken), direct spoelen met veel water (minimaal 20 min.), dan pas eventueel aan de huid vastgeplakte kleding verwijderen en verder spoelen en arts raadplegen

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Specifieke behandeling en materialen*: N.B.: adembescherming hulpverleners (inhalatoir carcinogeen).*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 116-14-3 **Tetrafluoroethylene** **$CF_2=CF_2$** **UN-nr: 1081**

Basis for the Dutch Intervention Values

VRW: Not recommended, in contrast to AEGL

AGW: Same point of departure as for AEGL values but using different uncertainty factors, 2h value added, time scaling applied to 10 min value

LBW: Same point of departure as for AEGL values but using different uncertainty factors, 2h value added, time scaling applied to 10 min value

Date: 06-10-2016	AEGL document: Final, 2015

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	4,100	2,900	2,300	1,800	1,400	940	Threshold for irreversible renal lesions (necrosis) in rats
LBW	25,000	17,000	14,000	11,000	8,700	4,300	$BMCL_{05}$ level for lethality in hamsters

Derivation of the Dutch Intervention Values

VRW: VRW values are not recommended, because there are no exposure-response data in humans or animals consistent with VRW-level effects. The lack of VRW-values does not necessarily mean that exposure below AGW-levels is without any effects.

AGW: Several studies showed effects that are considered to be AGW-level effects. A study in rats showed no statistical significant increase in urinary glucose concentrations and enzyme activity levels in rats when exposed to 3,000 ppm (12,480 mg/m³) for 6 hours. Necrosis was observed at the next exposure level. The exposure to 12480 mg/m³ for 6 hours was therefore considered to be the threshold for irreversible renal lesions and was used as the point of departure for derivation of the AGW values. This is supported by data of repeated exposure studies that result in reversible renal effects. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n \times t = k$, with the default values of n=1 and n=3 when extrapolating to longer and shorter exposure durations, respectively. In contrast to the 10-minute AEGL-2 value, time scaling was also applied for the 10-minute AGW value.

LBW: For derivation of the LBW values a benchmark concentration approach was applied to the data from a 4-hour study of tetrafluoroethylene in hamsters. The 4-h $BMCL_{05}$ concentration of 20,822 ppm (86,620 mg/m³) was used as the point of departure. The $BMCL_{05}$ concentration is also supported by the highest 4-h non-lethal concentration (20,700 ppm, corresponding to 83,200 mg/m³) that was found in a study in rats. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n \times t = k$, with the default values of n=1 and n=3 when extrapolating to longer and shorter exposure durations, respectively. In contrast to the 10-minute AEGL-3 value, time scaling was also applied for the 10-minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Renal toxicity from tetrafluoroethylene results from a reactive metabolite formed after a series of metabolic steps in the kidney; there is a correlation between the covalent binding of the reactive thiol of the cysteine conjugate with renal proteins and nephrotoxicity. In animal models the toxicity of tetrafluoroethylene is characterized by proximal tubular necrosis and is observed clinically as an increase in urinary glucose and protein, cellular enzyme activity and blood urea nitrogen. The mitochondrion might be the target of the reactive metabolite. At high concentrations, death from tetrafluoroethylene may be due to pulmonary congestion.

The mechanism of action that leads to renal tumor formation may be attributed to renal tubular damage via the processing of the glutathione conjugate. Cell necrosis followed by chronic regeneration of the epithelium in the kidney (increased cell proliferation) results in greater opportunity for error in DNA synthesis and mutation.

No information on developmental or reproductive effects of tetrafluoroethylene was found.

No harmonized H-sentences for human health.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: 2A (probably carcinogenic to humans) Derivation of the carcinogenic risk potency (CRP): 10^{-4} risk level after inhalation: 1.88 x 10^{-3} mg/m^3 [NRC, 2001] CRP = (10^{-4} risk level * average life span in hours)/DRCF = (1.88 x 10^{-3} * 613,200) /2.8 = 412 mg/m^3	Odour: odourless gas No LOA was derived (due to lack of data).

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **NR**	*AEGL-1* 92	*ERPG-1* 830		*IDLH: not established*
AGW level **2,300**	*AEGL-2* 230	*ERPG-2* 4,200		
LBW level **14,000**	*AEGL-3* 1,500	*ERPG-3* 42,000		

Stofdocument deel A

CAS-nr: 109-99-9 **Tetrahydrofuraan** **$(CH_2)_4O$, cyclisch** **VN-nr: 2056** **GEVI: 33**

Synoniemen: butyleenoxide, diethyleenoxide, 1,4-epoxybutaan (Engels: tetrahydrofuran) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	1500	660	400	250	150	91
Alarmeringsgrenswaarden	AGW (mg/m³)	4800*	2200	1300	820	500	310
Levensbedreigende waarden	LBW (mg/m³)	17.000*	7900*	4800*	3000	1800	1100

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,333 ppm; 1 ppm = 3,00 mg/m³

Explosiegrens: LEL = 1,5 vol% ≈ 45.000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

Geur: ether-achtig

LOA: 1460 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,3

Molecuulmassa: 72,1 g/mol

Zuurgraad: geen data

LogKow: 0,5

Wateroplosbaarheid: volledig

Verzadigde dampdruk: 193 mbar

Overige informatie

Publieke grenswaarde: 300 mg/m³ (8 uur)

MAK: 150 mg/m³

TLV-TWA: 600 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: irritatie van ogen en bovenste luchtwegen, keelpijn, hoesten

AGW → LBW: ernstige irritatie van ogen en luchtwegen, benauwdheid, misselijkheid, hoofdpijn, duizeligheid, bewustzijnsdaling, lethargie

Boven LBW: ademnood, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Tetrahydrofuraan is irriterend voor de ogen en luchtwegen.
- De stof heeft een depressieve werking op het centrale zenuwstelsel.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn

Stof kan door de huid opgenomen worden

Oogcontact: roodheid en pijn

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust en arts raadplegen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken en minimaal 20 min. spoelen met veel water of douchen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 109-99-9 **Tetrahydrofuran** **$(CH_2)_4O$, cyclisch** **UN-nr: 2056**

Basis for the Dutch Intervention Values

VRW: Based on toxicological information in ERPG document

AGW: Based on toxicological information in ERPG document

LBW: Based on toxicological information in ERPG document

Date: 16-12-2010 | ERPG document: post-balloted draft, 2005

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	1500	660	400	250	150	91	No effects in human volunteers
AGW	4800*	2200	1300	820	500	310	Threshold for CNS depression in animals
LBW	17,000*	7900*	4800*	3000	1800	1100	Estimated threshold for lethality in animals

* value higher than 10% of LEL

Derivation of the Dutch Intervention Values

VRW: Since human data are available these were used for the derivation of VRW values. As point of departure for the derivation of VRW values 4 hour exposure to 150 ppm (450 mg/m³) was chosen. This was considered a no effect level for the irritating and narcotic effects of tetrahydrofuran. Several human kinetic studies were performed with tetrahydrofuran using, respectively, a 6 minute exposure to 100 or 400 ppm (300 or 1200 mg/m³) a 20 minute exposure to 100 ppm (300 mg/m³), a 4 hour exposure to 150 ppm (450 mg/m³) and 2 times 3 hours exposure to 200 ppm (600 mg/m³). In none of these studies any adverse effects of exposure were reported. It is noted that the purpose of these studies was to study the kinetics rather than the toxicity of tetrahydrofuran in humans. An intraspecies factor of 3 was applied to account for sensitive individuals. Time-scaling was performed using the equation $C^n \times t = k$, using the chemical specific value for n of 1.4, as calculated from rat lethality data.

The choice of the point of departure was supported by observations in experimental animals. In rabbits exposed for 4 hours to 250 ppm (750 mg/m³) a reversible decline in tracheal ciliary activity was observed. In rats exposure to 100 or 200 ppm (300 or 600 mg/m³) for 3 hours did not result in significant effects except slight local irritation such as redness of the nose and eyelids.

AGW: As point of departure for the derivation of AGW values exposure to 2500 ppm (7500 mg/m³) for 6 hours was chosen. At this exposure concentration and duration mild sedative effects were noted in rats (12/24 rats showed a decreased alerting response, 0/12 male rats and 2/12 female rats showed lethargy). At the next highest concentration of 5000 ppm (15,000 mg/m³) 12/24 rats showed a decreased alerting response and 12/24 had no observable alerting response. In this group 12/12 male rats and 11/12 female rats exhibited lethargy. After exposure to 500 ppm (1500 mg/m³) for 6 hours no adverse effects were observed. Because the point of departure concerns a LOAEL for central nervous system depression, a modifying factor of 2 was applied. An inter- and intraspecies factor of 3 each were applied to account for differences between species and individuals. Time-scaling was performed using the equation $C^n \times t = k$, using the chemical specific value for n of 1.4, as calculated from rat lethality data.
The choice of the point of departure was supported by several other observations in experimental animals. In a study in rats sleeping was observed after 6 hours exposure to concentrations of 4900 ppm (14.700 mg/m³) or higher. In another report it is indicated that blood concentrations 60 mg/dl tetrahydrofuran cause weak central nervous system depression in experimental animals whereas concentrations below 50 mg/dl had no effect. In rats, mice, rabbits, and cats exposure for 6 hours to 1000 and 2000 ppm (3000 and 6000 mg/m³) tetrahydrofuran resulted in blood levels of 2-17 mg/dl and 26-84 mg/dl, respectively. Inhalation of 1000 ppm (3000 mg/m³) tetrahydrofuran for 6 hours/day 5 days/week for one year did not cause any symptoms in rats, cats, or rabbits. Daily inhalation of 3000 ppm (9000 mg/m³) for 8 hours did not cause any signs of poisoning in rats. Finally, a study in rabbits, cats, guinea pigs and rats showed irritation of the mucous membranes and slight anesthetic effects after 3 and 8 hours exposure to 3400 ppm (10.200 mg/m³) [ERPG document, and references

therein].
Data on developmental toxicity in rats and mice were not used for derivation of AGW. In rats exposed for 6 hours/day on day 6-15 of gestation to tetrahydrofuran, the mean number of implantations per dam and the incidence of malformed fetuses were not exposure related. At the highest concentrations tested (4940 ppm (14815 mg/m^3) and 4934 ppm (14797 mg/m^3)) the fetal variations of reduced weight and less ossified sternae were significantly different from controls. However, these data were considered as non-relevant for deriving the AGW.

LBW: As point of departure the 4 hour LC_{50} for rats of 18,000 ppm (54,000 mg/m^3) was chosen. This value was divided by 3 to derive an estimated threshold for lethality. Inter- and intraspecies factor of 3 each were applied to account for differences between species and individuals. Time-scaling was performed using the equation $C^n \times t = k$, using the chemical specific value for n of 1.4, as calculated from rat lethality data.

Although no information was available on the LC_{50} value that was used for the derivation of the LBW values, the choice of the point of departure was supported by several other reports, though the contained information was equally limited. Two other 4-hour LC_{50} of 21,357 and 22,374 ppm (64,051 and 67,102 mg/m^3), a 3-hour LC_{50} of 21,000 ppm (63,000 mg/m^3), and two 1-hour LC_{50} values of 61,020 and 82,377 ppm (183,004 and 247,055 mg/m^3) were reported for rats. Reported 8 hour LC_{50} values for dogs, cats and rats were respectively 25,000 ppm, 16,000 ppm and 18,000 ppm (75,000- 48,000- and 54,000 mg/m^3). No mortality was observed in rats exposed for 3 hours to 5000 ppm (15,000 mg/m^3). A study in mice and rats showed lethality after 2 hour exposure to measured tetrahydrofuran levels of 6100 ppm (18,300 mg/m^3) and higher. The highest concentration that did not result in lethality was 8140 ppm (24,400 mg/m^3) for rats and 4070 ppm (12,200 mg/m^3) for mice. The use of the latter value as point of departure for LBW derivation would result in the most conservative LBW values (7200, 3300, 2000, 1200, 740, and 450 mg/m^3 for 10 minutes, 30 minutes, 1 hour, 2 hour, 4 hour and 8 hour exposure respectively, when using the same uncertainty factors). However, these values are inconsistent with the observation that there were no effects in human volunteers after exposure for 2 times 3 hours to 200 ppm (600 mg/m^3) tetrahydrofuran [ERPG document, and references therein].

Additional toxicological information (including relevant results of a general literature search, if any)

Tetrahydrofuran is irritating to the eyes and respiratory tract. The compound has CNS depressant activity.

Tetrahydrofuran poisonings after occupational exposure were reported in two plumbers. Both men were repairing plastic pipes in confined spaces with glue containing tetrahydrofuran; they used no protective measures. Both men had signs of irritation of mucous membranes, mild CNS effects, and cytolitic hepatitis. Complaints included nausea, headache, blurred vision, dizziness, chest pain, cough, dyspnoea and epigastric pain. The clinical course was suggestive of an occupational toxic hepatitis [Garnier *et al*., 1989].

No information on reproduction/developmental toxicity of tetrahydrofuran in humans was located. In inhalation developmental toxicity studies in rats and mice developmental toxicity was observed at concentrations that induced maternal toxicity (1800 ppm (5400 mg/m^3) and higher) [ERPG document].

H319: Causes serious eye irritation; H335: May cause respiratory irritation; H351: suspected of causing cancer

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

No data concerning carcinogenicity of tetrahydrofuran in humans was found. There is some evidence of carcinogenicity of tetrahydrofuran in experimental animals:

Chronic inhalation (6 hr/day, 5 days/week, 105 weeks) to 0-1800 ppm (0- 5400 mg/m^3) of tetrahydrofuran resulted in an increased incidence of renal tubule adenoma or carcinoma (combined) in male rats. However, this may have been due to alpha2microglobulin accumulation, a mode of action not relevant to humans. In female mice exposed to 1800 ppm (5400 mg/m^3), the incidence of hepatocellular neoplasms was increased.

Odour and derivation of the LOA value

Odour: ether-like

OT_{50}: 93 mg/m^3 [ERPG document, AIHA]
LOA = 11.8 * OT_{50} * 1.33 = 1460 mg/m^3

(The concentration Level leading to distinct Odour Awareness (l=3) is calculated using the formula: $l = 2.33 * \log (C/OT_{50}) + 0.5$. A correction factor of 1.33 is applied to this value)

The LOA is higher than the VRW values, the 1-8-hour AGW values and the 8-hour LBW value.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*				
VRW level **400**	*AEGL-1* not derived	*ERPG-1* 300		*IDLH:* 6000 mg/m^3 (30 minutes)
AGW level **1300**	*AEGL-2* not derived	*ERPG-2* 1500		
LBW level **4800**	*AEGL-3* not derived	*ERPG-3* 15,000		

Stofdocument deel A

CAS-nr: 509-14-8 **Tetranitromethaan** $C(NO_2)_4$ **VN-nr: 1510**

GEVI: 559

Synoniemen: TNM (Engels: tetranitromethane) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	7,8	5,4	4,3	3,4	2,7	1,4
Levensbedreigende waarden	LBW (mg/m³)	26	18	14	11	9,0	4,5

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,123 ppm; 1 ppm = 8,15 mg/m³

Explosiegrens: geen data

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot lichtgele vloeistof

Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,06

Molecuulmassa: 196,0 g/mol
Zuurgraad: geen data
LogKow: - 0,8
Wateroplosbaarheid: niet
Verzadigde dampdruk: 11,2 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
TLV-TWA: 0,041 mg/m³
MAK: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: irritatie aan ogen en luchtwegen, keelpijn, hoesten, lichte benauwdheid

AGW → LBW: ernstige irritatie aan ogen en luchtwegen, benauwdheid, longoedeem, hoofdpijn, speekselvloed, misselijkheid, verlies gezichtsvermogen, blauwe lippen en nagels en/of huid (nabij LBW)

Boven LBW: ademnood, bloed ophoesten, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Tetranitromethaan werkt zeer irriterend op de luchtwegen en de ogen.
- Toxiciteit treedt met name op in de longen, waar de stof longoedeem en bloedingen kan veroorzaken, met mogelijk sterfte tot gevolg. De verschijnselen van longoedeem kunnen pas na enkele uren optreden en versterkt worden door lichamelijke inspanning.
- Tetranitromethaan kan lichte methemoglobinemie veroorzaken bij zeer hoge concentraties (nabij LBW).

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn, branderig gevoel, blaren, brandwonden.

Oogcontact: bijtend, tranenvloed, slecht zien

Carcinogeniteit

IARC classificatie: 2B

CRP: 56 mg/m³

Beknopte medische informatie

***Ontsmetting* damp**

algemeen: frisse lucht, rust, halfzittende houding, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, spoelen met veel water / kleding uittrekken en direct spoedeisende medische hulp inzetten. [68]

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), actieve kool (carbomix) toedienen, GEEN braken opwekken specifieke behandeling en direct spoedeisende medische hulp inzetten..

***Specifieke behandeling en materialen**: 100% zuurstof en specifieke antidota zoals o.a. methyleen- of toluïdineblauw*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

[68] Door schokken, stoten of verhitten kan de stof een explosie geven. Het is een sterk oxidatiemiddel, waardoor brandgevaar bestaat. Daarom bij huidblootstelling altijd eerst spoelen met (veel) water.

Stofdocument deel B

CAS-nr: 509-14-8 **Tetranitromethane** **$C(NO_2)_4$** **UN-nr: 1510**

Basis for the Dutch Intervention Values

VRW: Not recommended due to insufficient data, in accordance with AEGL

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 16-12-2010 AEGL document: Final, 2005

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Insufficient data
AGW	7.8	5.4	4.3	3.4	2.7	1.4	Mild reversible lung irritation in animals
LBW	26	18	14	11	9.0	4.5	$BMDL_{05}$ for lethality in animals

Derivation of the Dutch Intervention Values

VRW: VRW values were not derived due to insufficient data. No studies were located with endpoints clearly within the scope of VRW.

AGW: AGW values were based on a 4-hour rat LC_{50} study, in which 10 ppm (82 mg/m³) was the NOEL for lethality from extreme lung irritation and was the lowest concentration tested. Because 10 ppm is a lethality NOEL in this study and is near the point of departure for LBW, a modifying factor of 3 was applied to 10 ppm obtain a concentration (3.3 ppm; 27 mg/m³) that would cause only mild reversible lung irritation. A total uncertainty factor of 10 was used: 3 for interspecies extrapolation because the key study tested the most sensitive species, and 3 to account for sensitive humans because mild lung irritation from a gas with a steep dose response is not likely to vary greatly among humans. Scaling across time was performed using $C^n \times t = k$, with default values of n=1 and n=3 for extrapolating to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-2 value that was set equal to the 30 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: LBW values were derived from above mentioned 4-hour rat LC_{50} study, from which a lethality $BMDL_{05}$ of 11 ppm (87 mg/m³) was calculated. The $BMDL_{05}$ of 11 ppm is consistent with the empirical lethality NOEL of 10 ppm (82 mg/m³) found in the key study and in a repeated exposure study with rats and mice. A total uncertainty factor of 10 was applied: 3 for interspecies extrapolation (key study tested the most sensitive species), and 3 for human variability (NOEL for lethality from extreme lung irritation from a gas with a steep dose response is not likely to vary greatly among humans). Scaling across time was performed using $C^n \times t = k$, with default values of n=1 and n=3 for extrapolating to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-3 value that was set equal to the 30 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

No quantitative human tetranitromethane inhalation exposure studies were located. No studies were located identifying populations more susceptible to tetranitromethane toxicity.

Tetranitromethane is a severe respiratory and eye irritant in humans and animals, although its precise mechanism of toxicity is unknown. In two well-conducted rat and mouse studies. Tetranitromethane toxicity occurred predominantly in the respiratory tract, where it caused pulmonary edema, hemorrhage, and death at sufficiently high concentrations.

No human developmental or reproductive studies were located with tetranitromethane exposure by any route.

No harmonized H-statements for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: 2B (possibly carcinogenic to humans)

Odour and derivation of the LOA value

Odour: no data

Derivation of the carcinogenic risk potency (CRP): 10^{-4} risk level after inhalation: 2.55 x 10^{-4} mg/m^3 [AEGL] CRP = (10^{-4} risk level * average life span in hours)/DRCF = (2.55 x 10^{-4} * 613,200) /2.8 = 56 mg/m^3 The ability of tetranitromethaan to induce neoplasms in animals was demonstrated in a study in which lifetime exposure of mice to 0.5 or 2 ppm (4 or 16 mg/m^3) and rats to 2 or 5 ppm (16 or 41 mg/m^3) clearly increased the incidence of lung tumors in both species. No human carcinogenicity data were located.	No LOA was derived.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* not derived		*IDLH:* 33 (30 minutes)
AGW level **4.3**	*AEGL-2* 4.3	*ERPG-2* not derived		
LBW level **14**	*AEGL-3* 14	*ERPG-3* not derived		

Stofdocument deel A

CAS-nr: 7719-09-7 **Thionylchloride** **Cl_2-O-S** **VN-nr: 1836**

GEVI: X88

Synoniemen: zwaveloxychloride (Engels: thionyl chloride) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	3,7	3,7	3,7	3,7	3,7	3,7
Alarmeringsgrenswaarden	AGW (mg/m³)	64	44	35	18	8,8	4,4
Levensbedreigende waarden	LBW (mg/m³)	370	250	200	100	50	25

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,202 ppm; 1 ppm = 4,95 mg/m³

Explosiegrens:
kans op explosie door reactie met water

Geur: scherpe, verstikkende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot lichtgele of rode rokende vloeistof
Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,4

Molecuulmassa:	119,0 g/mol
Zuurgraad:	geen data
LogKow:	geen data
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	129 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-ceiling: 4,95 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: *geen effecten*

VRW → AGW: keelpijn, hoesten, irritatie van de ogen, huid en luchtwegen.

AGW → LBW: kortademigheid, ademnood, longoedeem

Boven LBW: sterfte door ademstilstand

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt zeer irriterend tot bijtend op de ogen, de huid en de luchtwegen.
- Blootstelling aan thionylchloride kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Thionylchloride reageert met water tot SO_2 en HCl.
- Zwaveldioxide veroorzaakt longfunctie-veranderingen als gevolg van reflectoire bronchoconstrictie.
- De effecten kunnen sterker zijn bij astmatici (vergelijkbaar met SO_2).

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, brandwonden

Oogcontact: bijtend, roodheid en pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en bij brandwonden arts raadplegen.

ogen: zie hierboven.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7719-09-7 **Thionyl chloride** **Cl_2-O-S** **UN-nr: 1836**

Basis for the Dutch Intervention Values

VRW: Based on AEGL-1 for SO_2

AGW: AEGL value adopted, different UF, 2h value added

LBW: Same PoD, different UF, 2h value added

Date: 06-10-2016 | AEGL Document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	3.7	3.7	3.7	3.7	3.7	3.7	VRW values for SO_2 (LOAEL for bronchoconstriction in exercising asthmatics)
AGW	64	44	35	18	8.8	4.4	LOAEL for dyspnea in rats thionylchloride)
LBW	370	250	200	100	50	25	Threshold for lethality in rats thionylchloride

Derivation of the Dutch Intervention Values

VRW: VRW values for thionyl chloride could not be derived based on substance specific data, due to a lack of relevant human and animal data consistent with VRW effects. However, it was reported that at an ambient humidity of around 50% almost complete hydrolysis of thionyl chloride to a mixture of sulfur dioxide and hydrogen chloride occurs (1 mol thionyl chloride results in 1 mol SO_2 and 2 mol HCl). Comparison of the toxicity profiles of thionyl chloride, HCl and SO_2 shows that on ppm basis HCl is of less importance than SO_2. Therefore, the VRW values (on ppm basis) for SO_2 were taken. The VRW values for sulfur dioxide are based on a LOAEL for bronchoconstriction in exercising asthmatics of 0.75 ppm, equal to 2.0 mg/m³ SO_2 and corresponding with 3.7 mg/m³ thionyl chloride. No uncertainty factors were applied because the point of departure is a study in humans, using a sensitive population (exercising asthmatics). No time scaling was applied, because the data show the magnitude of bronchoconstriction appears to decrease with extended exposure.

AGW: In a study in rats, 5 animals/sex/concentration, dyspnea was observed after exposure to 71 ppm (351 mg/m³) and 407 ppm (2,015 mg/m³) thionyl chloride for one hour. The other concentration levels were 769 ppm (3,807 mg/m³), 2,121 ppm (10,499 mg/m³) and 3,441 ppm (17,033 mg/m³). In a second study in rats (6 animals/sex/concentration), lung discoloration occurred after an exposure to 196 ppm (970 mg/m³) and 371 ppm (1,836 mg/m³) thionyl chloride for one hour. The other concentration levels were 593 ppm (2,935 mg/m³), 954 ppm (4,722 mg/m³) and 1241 ppm (6,143 mg/m³). The value of 71 ppm (351 mg/m³) was used as point of departure for derivation of the AGW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using $C^n \times t = k$, with the default values of n=1 and n=3 when extrapolating to longer and shorter exposure durations, respectively.

LBW: In a study in rats, 5 animals/sex/concentration, dyspnea was observed after exposure to 71 ppm (351 mg/m³) and 407 ppm (2,015 mg/m³) thionyl chloride for one hour. The other concentration levels were 769 ppm (3,807 mg/m³), 2,121 ppm (10,499 mg/m³) and 3,441 ppm (17,033 mg/m³). In a second study in rats (6 animals/sex/concentration), lung discoloration occurred after an exposure to 196 ppm (970 mg/m³) and 371 ppm (1,836 mg/m³) for one hour. The other concentration levels were 593 ppm (2,935 mg/m³), 954 ppm (4,722 mg/m³) and 1241 ppm (6,143 mg/m³). The data sets from two studies in rats were used for derivation of the LBW values. In the first study the animals only displayed moderate dyspnea and reddened and swollen noses at 407 ppm (2,015 mg/m³). No mortality occurred at 769 ppm, but wheezing and necrotic changes was observed and at 2121 ppm (10.499 mg/m³) 80% lethality occurred. In the second study no mortality was observed in the 371 ppm (1,836 mg/m³) exposure group. Lethality was observed at 593 ppm (2935 mg/m3) and higher. A benchmark dose concentration was calculated from the combined data. The resulting model, however, did not fit the model sufficiently. The calculated benchmark dose concentration for either study was not used to derive LBW values because of the high variability between the two. In the absence of knowledge of which value is “more accurate”, 407 ppm (2,015 mg/m³) for one hour was chosen as the point of departure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences.

Time scaling was performed using $C^n \times t = k$, with the default values of n=1 and n=3 when extrapolating to longer and shorter exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Thionyl chloride ($SOCl_2$) is rapidly hydrolyzed. Moist air reacts with thionyl chloride and forms sulfur dioxide and hydrogen chloride. The sulfur dioxide acts on the respiratory system by injuring cells lining the airway passages. Sulfur dioxide is a water-soluble irritant, which causes upper-airway irritation and may induce increased airway resistance via reflex bronchoconstriction. The exact mechanism for this bronchoconstriction is unknown. Asthma and physical exercise increase the bronchoconstrictive effect. With regard to respiratory tract, the effects occur rapid (within several minutes). The influence of exposure duration diminishes over time, showing even a decrease in effect level after several hours. The hydrogen chloride dissolves in the nasal passages and is not metabolized. Inhaled hydrogen chloride irritates the respiratory tract. The epithelial barrier in the alveolar zone breaks down and begins to leak, causing pulmonary edema.

No information on developmental or reproductive effects of thionyl chloride was found.

H332: Harmful if inhaled; H314: Causes severe skin burns and eye damage; H302: Harmful if swallowed

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: pungent, suffocating odour.

No LOA was derived (due to lack of data).

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **3.7**	*AEGL-1* NR	*ERPG-1* 0.99		*IDLH: -*
AGW level **12**	*AEGL-2* 12	*ERPG-2* 9.9		
LBW level **200**	*AEGL-3* 69	*ERPG-3* 50		

Stofdocument deel A

CAS-nr: 7550-45-0 **Titaantetrachloride** $TiCl_4$ **VN-nr: 1838**

GEVI: X80

Synoniemen: Titaan(IV)chloride, titaniumtetrachloride (Engels: Titanium tetrachloride) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	100	34	15	13	5,2	2,4
Levensbedreigende waarden	LBW (mg/m³)	300	100	45	38	16	7,1

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,127 ppm; 1 ppm = 7,89 mg/m³

Explosiegrens: geen gegevens

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze hygroscopische vloeistof

Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,07

Molecuulmassa:	189,7 g/mol
Zuurgraad:	geen data
LogKow:	geen data
Wateroplosbaarheid:	Reactie, hydroliseert
Verzadigde dampdruk:	12,7 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: geen informatie, mogelijk irritatie

AGW → LBW: irritatie luchtwegen, benauwdheid, longoedeem

Boven LBW: sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Titaniumtetrachloride is zeer corrosief (bijtend)
- Titaniumtetrachloride hydroliseert in contact met water tot HCl, titaanoxychloride ($TiOCl_2$) en gehydrateerd titaandioxide $Ti(OH)_4$ in de lucht en luchtwegen.
- De toxiciteit wordt met name veroorzaakt door de vorming van HCl.
- HCl kan type I inhalatoire intoxicatie veroorzaken waarbij longoedeem kan ontstaan. De verschijnselen van longoedeem kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Personen met verminderde longfunctie kunnen gevoeliger zijn voor blootstelling aan titaniumtetrachloride.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid, pijn, brandwonden

Oogcontact: bijtend, roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd.

CRP: n.v.t.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 7550-45-0 **Titanium tetrachloride** **$TiCl_4$** **UN-nr: 1838**

Basis for the Dutch Intervention Values

VRW: Not recommended in accordance with the AEGL

AGW: Different point of departure

LBW: AEGL value is adopted, 2hr value added

Date: 24-09-2009 | AEGL document; Interim 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	100	34	15	13	5.2	2.4	One third of LBW value
LBW	300	100	45	38	16	7.1	Threshold for animal mortality, one-third of rat LC_{50}

Derivation of the Dutch Intervention Values

VRW: Not recommended due to insufficient data on VRW type of effects.

AGW: The AGW value is derived by taking one-third of the LBW value.
The rationale for this approach is based on that HCl is mainly responsible for the toxic effects of titaniumtetrachloride. Furthermore, the experimental data from animal studies were not appropriate for deriving AGW values. Although an exposure of rats to 1.3 ppm (10.3 mg/m³) titanium tetrachloride for 6 hours/day, 5 days/week for 4 weeks could be used as threshold for AGW-effects, this would result in too low AGW levels.

LBW: Empirical rat LC_{50} values for the 30 min (390 ppm; 3,077 mg/m³), 60 min (171 ppm; 1,349 mg/m³), 120 min (143 ppm; 1,128 mg/m³) and 240 min (59 ppm; 466 mg/m³) exposure durations were used to derive the point of departure for the respective LBW time points by taking one-third of the LC_{50} values. An interspecies uncertainty factor of 3 was applied to the values because titanium tetrachloride is an irritant and the mechanism of action is therefore not expected to vary greatly among species. An intraspecies uncertainty factor of 3 was chosen because the mechanism of irritation is also not expected to vary greatly among subpopulations. Therefore, a total uncertainty factor of 10 was applied. Using n = 0.88 in the equation $C^n * t = k$, based on experimental lethality data, the 15-minute LC_{50} (713 ppm; 5,626 mg/m³) value was used to extrapolate to 10 minutes, while the 240 minute LC_{50} value (59 ppm; 466 mg/m³) was used to extrapolate to 480 minutes.

Additional toxicological information (including relevant results of a general literature search, if any)

Titanium tetrachloride is highly corrosive, hydrolyzing upon contact with moisture releasing heat, hydrochloric acid, and orthotitanic acids, thereby causing direct tissue damage in the lung. Data indicate that the fine particulate oxychloride intermediates generated from titanium tetrachloride hydrolysis are able to penetrate deep into the lung where hydrolysis is completed, resulting in direct contact irritation and producing bronchitis or pneumonia. Symptoms that may occur are coughing, chest tightness, eye and respiratory irritation.

No data are available on the reprotoxic or developmental toxic properties of titanium tetrachloride.

H314: causes severe skin burns and eye damage.

Carcinogenicity and derivation of the CRP value

IARC classification: Not classified

No carcinogenic risk potency (CRP) was derived.

A two-year rat study revealed squamous cell carcinomas in the area of the alveoli in few (5/143) of the high-concentration exposed rats (1.3 ppm; 10.3 mg/m³). The relevance of these findings to humans is uncertain. Furthermore, it is unknown whether a single acute exposure could result in this type of tumor.

Odour and derivation of the LOA value

Odour: pungent odor

No LOA was derived due to lack of reliable data.

Other standards and guidelines (1h values in mg/m³, unless otherwise indicated)

VRW level **NR**	*AEGL-1* NR	*ERPG-1* 5		*IDLH:* not established
AGW level **15**	*AEGL-2* 7.8	*ERPG-2* 20		
LBW level **45**	*AEGL-3* 44	*ERPG-3* 100		

Stofdocument deel A

CAS-nr: 108-88-3 **Tolueen** C_6H_5-CH_3 **VN-nr: 1294**

GEVI: 33

Synoniemen: methylbenzeen, toluol, fenylmethaan (Engels: toluene) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	260	260	260	260	260	260
Alarmeringsgrenswaarden	AGW (mg/m³)	5.400*	2.900	2.100	1.700	1.200	960
Levensbedreigende waarden	LBW (mg/m³)	38.000**	20.000*	14.000*	10.000*	6.900*	5.400*

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,261 ppm; 1 ppm = 3,83 mg/m³

Explosiegrens: LEL = 1,2 vol% ≈ 46.000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

** berekende interventiewaarde hoger dan 50% LEL

Geur: zoete, stekende, benzeenachtige geur

LOA: 9,6 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,06

Molecuulmassa:	92,1 g/mol
Zuurgraad:	geen data
LogKow:	2,7
Wateroplosbaarheid:	0,05 g/100 ml (zeer slecht)
Verzadigde dampdruk:	29 mbar

Overige informatie

Publieke grenswaarde: 150 mg/m³ (8 uur)

MAK: 190 mg/m³ H

TLV-TWA: 192 mg/m³ H

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	Prikkeling en lichte irritatie van ogen en luchtwegen, hoesten
VRW → AGW:	verminderde reactiesnelheid, opwinding, onrust, irritatie van ogen en luchtwegen, keelpijn, lichte hoofdpijn, vermoeidheid, verwardheid
AGW → LBW:	Duizeligheid, verwarring, slaperigheid, misselijkheid, zwakte gevoel, coördinatiestoornissen
Boven LBW:	Bewusteloosheid, ademhalingsdepressie, coma en sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof kan inwerken op het centrale zenuwstelsel. In eerste instantie kan excitatie optreden, doorgaans snel gevolgd door depressie, met als gevolg bewustzijnsverlaging tot bewusteloosheid.
- De stof werkt irriterend op de ogen, de huid en de luchtwegen.
- Beschadiging van de lever en nieren kan optreden.
- De stof kan reprotoxische (fertiliteit en spontane abortussen) en ontwikkelingseffecten veroorzaken na inhalatie van hoge concentraties. De concentraties waarbij deze effecten optreden kunnen niet worden gekwantificeerd, maar het kan niet uitgesloten worden dat deze effecten optreden rondom de AGW waarden.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, droge huid, hoofdpijn en sufheid. De stof wordt door de huid opgenomen!

Oogcontact: roodheid en pijn.

Carcinogeniteit

IARC classificatie: 3

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 108-88-3 **Toluene** **C_6H_5-CH_3** **UN-nr: 1294**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 06-10-2016 | AEGL document: Final, 2014

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	260	260	260	260	260	260	Threshold for discomfort (irritation, neurotoxicity) in humans
AGW	5,400*	2,900	2,100	1,700	1,200	960	NOAEL for doubling reaction time in rats
LBW	38,000**	20,000*	14,000*	10,000*	6,900*	5,400*	Threshold for lethality in rats

* value higher than 10% of LEL; ** value higher than 50% of LEL

Derivation of the Dutch Intervention Values

VRW: Effects (including irritation and neurobehavioural effects) found in multiple clinical, occupational-monitoring and metabolism studies were below the definition of the VRW level effects. Based on a weight of evidence of all the human data an 8 hour exposure to 200 ppm (766 mg/m3) is considered a NOAEL for discomfort in humans and is used as a point of departure for derivation of the VRW values. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. This results in a derived VRW value of 255 mg/m^3. The concentration was considered appropriate for all durations, because at 255 mg/m^3 a steady-state is expected to be reached fairly rapidly. At concentrations of 80-200 ppm (306-766 mg/m^3) toluene approaches a steady-state in the blood within 15-30 minutes. For this reason and because the POD is also threshold for irritation, flatlining was also applied to the 10 min timepoint.

AGW: In a study in rats groups of four adult rats were exposed to 1,200 ppm (4,596 mg/m^3), 1,600 ppm (6,128 mg/m^3), 2,000 ppm (7,660 mg/m^3) or 2,400 ppm (9,192 mg/m^3) for up to 70 minutes. Their reaction time to a signal detection task was measured. A NOAEL for doubling of the reaction time was determined resulting in an exposure of 1,600 ppm (6,128 mg/m^3) for 34 minutes. This was used as point of departure for derivation of the AGW values. PBPK modelling based on the data in rats and humans was used to derive the AGW values. The toluene concentration in rat brain at the point of departure was calculated, divided by the uncertainty factor and the corresponding AGW values for the respective exposure durations were calculated using the PBPK-model. Considering that PBPK modeling eliminates the toxicokinetic component of the uncertainty factor and the fact that the CNS effects are similar in humans and animals an interspecies uncertainty factor of 1 was considered to be sufficient. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. The total uncertainty factor is 3. The PBPK model resulted in the AGW values of 1,400 ppm (5,362 mg/m^3), 760 ppm (2,911 mg/m^3), 560 ppm (2,145 mg/m^3), 310 ppm (1,187 mg/m^3) and 250 ppm (958 mg/m^3) for respectively the 10-min, 30-min, 1-h, 4-h and 8-h exposure durations.

LBW: Groups of male rats were exposed to concentrations of toluene at 810 ppm (3,102 mg/m^3), 1,660 ppm (6,358 mg/m^3) and 3,100 ppm (11,873 mg/m^3) for 4 hours and at 6,250 ppm (23,938 mg/m^3) for 2 hours. No deaths occurred following the exposures to toluene. The exposure to 6,250 ppm (23,938 mg/m^3) for 2 hours was considered to be the NOAEL for lethality and was used as point of departure for derivation of the LBW values. PBPK modelling based on the data in rats and humans was used to derive the LBW values. The LBW values were calculated using the PBPK-model to estimate the toluene concentration in brain at the LBW point of departure as dose metric and derive the respective values in a similar way as for the AGW. Considering that PBPK modeling eliminates the toxicokinetic component of the uncertainty factor an interspecies uncertainty factor of 1 was considered to be sufficient. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Using the total uncertainty factor of 3, the PBPK model resulted in the LBW values of 10,000 ppm (38,300 mg/m^3), 5,200 ppm (19,916 mg/m^3), 3,700 ppm (14,171 mg/m^3),

2,670 ppm (10,227 mg/m^3), 1,800 ppm (6,894 mg/m^3) and 1,400 ppm (5,362 mg/m^3) for respectively the 10-min, 30-min, 1-h, 2-h, 4-h and 8-h exposure durations.

Additional toxicological information (including relevant results of a general literature search, if any)

The mechanism of toxicity for CNS effects is described as the interaction of toluene with proteins in the membrane. Furthermore, it is suggested that toluene might change the binding of neurotransmitters to membranes receptors. High concentrations of toluene could result in renal toxicity with metabolic acidosis. The metabolites of toluene are benzoic acid and hippuric acid.

In the EU RAR it was concluded that toluene causes developmental toxicity in rats in the absence of maternal toxicity. The available human data on developmental and reproductive toxicity only included continuous occupational exposure and abuse situations. They do indicate an increased risk for late spontaneous abortions. Furthermore, data in humans, rats and limited data in mice provide similar developmental effects (lower birth weight, delayed postnatal development and developmental neurotoxicity). Only very high levels were tested in humans.

H304: May be fatal if swallowed and enters airways; H361d: Suspected of damaging the unborn child; H336: May cause drowsiness or dizziness; H373: May cause damage to the central nervous system through prolonged exposure; H315: Causes skin irritation.

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to carcinogenicity to humans)

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: sweet, pungent, benzene-like odour

Odour threshold: 0.61 mg/m^3 [AIHA, 1989]
LOA = 11.8 * ODT * 1.33 = 9.6 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/ODT) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies below all intervention values.

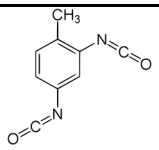
***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **260**	*AEGL-1* 250	*ERPG-1* 190		*IDLH: 1,900 mg/m^3 (30 minutes)*
AGW level **2,100**	*AEGL-2* 2,100	*ERPG-2* 1,200		
LBW level **14,000**	*AEGL-3* 14,000	*ERPG-3* 3,800		

Stofdocument deel A

CAS-nr: 584-84-9 **Tolueen-2,4-diisocyanaat**

$C_9H_6N_2O_4$



VN-nr: 2078
GEVI: 60

Synoniemen: 2,4-TDI, 2,4-tolueendiisocyanaat, 4-methyleen-m-fenyleendiisocyanaat (Engels:Toluene 2,4-Diisocyanate)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,15	0,15	0,15	0,073	0,073	0,073
Alarmeringsgrenswaarden	AGW (mg/m³)	1,7	1,2	0,60	0,30	0,15	0,15
Levensbedreigende waarden	LBW (mg/m³)	6,8	4,7	3,7	3,0	2,3	1,2

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,138 ppm; 1 ppm = 7,25 mg/m³

Explosiegrens: LEL = 0,9 vol% ≈ 65 000 mg/m³

Geur: zoete, fruitige, scherpe geur
LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: heldere, lichtgele vloeistof of kristallen

Brand: brandbaar, bij vele reacties kans op brand en explosie

Relatieve dichtheid van verzadigd damp-luchtmengsel: 1,0

Molecuulmassa:	174,2 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	Reactie
Verzadigde dampdruk:	0,04 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 0,007 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	mogelijk lichte irritatie
VRW → AGW:	irritatie aan ogen, neus en luchtwegen, keelpijn, hoesten, rhinitis, tranenvloed, hoofdpijn
AGW → LBW:	ernstige luchtwegirritatie, onregelmatige ademhaling, benauwdheid, longoedeem, bloed ophoesten
Boven LBW:	ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Tolueen-2-4-diisocyanaat is sterk irriterend voor de ogen en luchtwegen. Bij hoge concentraties werkt tolueen-2,4- diisocyanaat bijtend.
- Bij hoge concentraties kan tolueen-2,4-diisocyanaat longontsteking (chemische pneumonitis) en longoedeem veroorzaken, waarbij de verschijnselen pas na enkele uren kunnen optreden en worden versterkt door lichamelijk inspanning.
- Blootstelling kan een astmatische reactie veroorzaken.
- De stof is sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact.
  Kruisgevoeligheid met andere diisocyanaten is mogelijk.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren

Oogcontact: bijtend, roodheid, pijn

Carcinogeniteit

IARC classificatie tolueen diisocyanaten: 2B
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en onmiddellijk arts raadplegen.
ogen: desgewenst uitspoelen met water (evt. contactlenzen verwijderen).

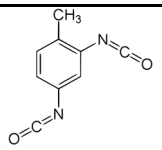
Ontsmetting vloeistof
huid: overmaat stof opdeppen, verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en arts raadplegen.

Specifieke behandeling en materialen: geen.
Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 584-84-9
$C_9H_6N_2O_4$

Toluene 2,4-diisocyanate



UN-nr: 2078

***B*asis for the Dutch Intervention Values**	
VRW:	AEGL values are adopted, 2 h value added
AGW:	AEGL values are adopted (except 10 min value for which time scaling was applied), 2 h value added
LBW:	AEGL values are adopted, (except 10 min value for which time scaling was applied), 2 h value added
Date: 24-09-2009	AEGL document: Final, 2004

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.15	0.15	0.15	0.073	0.073	0.073	Light irritation (nose and throat), chest tightness in exposed humans
AGW	1.7	1.2	0.60	0.30	0.15	0.15	Irritation eyes and respiratory tract (humans)
LBW	6.8	4.7	3.7	3.0	2.3	1.2	Lethality animals

Derivation of the Dutch Intervention Values

VRW: A human volunteer study with healthy and asthmatic individuals was used as starting point for the derivation of the VRW values. Volunteers were exposed to a mixture of 2,4-TDI and 2,6-TDI in a ratio of 80:20, respectively. Asthmatic individuals tolerated exposures of 0.01 ppm (0.073 mg/m³) for one hour followed by a rest period of 45 minutes and a second exposure to 0.02 ppm (0.15 mg/m³) for another hour. Healthy adults (control group) were exposed for 2 hours at 0.02 ppm (0.15 mg/m³). Both groups reported eye and throat irritation, cough, chest tightness, rhinitis, dyspnea and/or headache. There was no indication whether the effects were worse in asthmatics at the 0.01 ppm or 0.02 ppm (0.073 and 0.15 mg/m³, respectively) level. Therefore, the 0.02 ppm (0.15 mg/m³) was identified as the basis of for the 10-, 30-min and 1-hour time points and the 0.01 ppm (0.073 mg/m³) concentration was identified as basis for the 2-, 4- and 8-hour time points. Because asthmatic subjects tolerated 0.02 ppm (0.15 mg/m³) for 1 hour after pre-exposure at 0.01 ppm (0.073 mg/m³), it is assumed that the asthmatic population could tolerate the lower concentration for a longer duration. No additional uncertainty factors were applied, because a human study was used as starting point and because asthmatic persons are considered a sensitive population. However, it is recognized that individuals with pre-existing allergic sensitization to this substance might not be protected at those concentrations and might experience airway reactivity with symptoms characteristic of an asthmatic attack, such as coughing, wheezing, chest tightness, and difficulty in breathing. The 0.01 ppm (0.073 mg/m³) exposure concentration for the longer time periods is reasonable because data suggest that the adverse health effects of inhaled 2,4-TDI are concentration dependent rather than concentration × time dependent. The proposed values are supported by the fact that in an additional study healthy subjects tolerated approximately 0.01 ppm (0.073 mg/m³) for 4 hours with no adverse effects while a slightly higher concentration of 0.03 ppm (0.22 mg/m³) resulted in symptoms similar to the point of departure study in 100% of workers at a manufacturing plant.

AGW: Humans exposure to 0.5 ppm (3.63 mg/m³) 2,4-TDI for 30 minutes resulted in eye and throat irritation and lacrimation. The next higher concentration of 1.3 ppm (9.4 mg/m³) was intolerable after 10 minutes. A 30 minute exposure to 3.63 mg/m³ was used as point of departure for deriving AGW values. Although ocular and respiratory tract irritation associated with 2,4-TDI exposure appears to be more concentration dependent than duration dependent, longer exposure periods can result in excessive fluid accumulation in the respiratory tract, which could lead to more severe consequences than defined under AGW. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was done using the equation $C^n \times t = k$, with the default values of n=1 and n=3 for extrapolation to longer and shorter durations, respectively. The 4-hr value was used for the 8-hour time point, because extrapolation to 8-hr resulted in a concentration similar to one that caused only mild effects in workers exposed for more than 7 hours and on 8-hour work

shifts.

LBW: Several lethality studies in different species are available. A 4-hour lethality study in mice appeared to provide the lowest LC_{50} value, viz. 9.7 ppm (70 mg/m^3). The specific TDI isomers studied were not identified. This value was taken as point of departure and was divided by 3 to estimate a threshold of lethality of 3.2 ppm (23 mg/m^3). Extrapolation of the probit regression line, obtained from a graph in the selected study, shows that a concentration of approximately 4 ppm would result in 1% lethality. Therefore, one-third of the LC_{50} is considered to be a reasonable estimate of the threshold for lethality. A total uncertainty factor of 10 was applied, including 3 to account for sensitive individuals and 3 for interspecies extrapolation. Use of greater factors would result in values similar to concentrations that would produce only mild irritation in human inhalation studies. Time scaling was performed using the equation $C^n \times t = k$, with the default values of n=1 and n=3 for extrapolation to longer and shorter durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Toluene 2,4-diisocyanate is a corrosive substance, acting immediately at the point of contact. The degree of irritation seems to depend more on the exposure concentration, than the exposure-duration. Immediately after exposure, a decrease in respiratory rate can be detected in animals as well as humans. This rate becomes more graded after the initial exposure. Repeated exposure can induce asthmatic reactions in sensitized persons.

Sensitization with the risk to develop subsequent allergic reactions can occur from repeated exposure over a long period of time to relatively low concentrations or from at least one exposure at a high concentration. Therefore the sensitisation endpoint cannot be used for the derivation of intervention values. Substance is not reproductive toxic.

H315: Causes skin irritation; H317: May cause an allergic skin reaction; H319: Causes serious eye irritation; H330: Fatal if inhaled; H334: May cause allergy or asthma symptoms or beathing difficulties if inhaled; H335: May cause respiratory irritation; H351: Suspected of causing cancer.

Carcinogenicity and derivation of the CRP value

IARC classification toluene diisocyanates: 2B (possibly carcinogenic to humans).

No carcinogenic risk potency (CRP) was derived.

Although carcinogenicity data for TDI are conflicting, it can be concluded that carcinogenicity is route-specific. The oral carcinogenicity may be due to the formation of toluene diamide (TDA) that is not formed after inhalation exposure. Based on the similar behaviour of TDA and 2,4-TDI, IARC has classified TDI in accordance with TDA. USEPA has not classified 2,4-TDI. For this inhalation scenario, CRP calculation is not applicable.

Odour and derivation of the LOA value

Odour: Pungent odour (sweet and fruity)

No LOA was derived due to lack of reliable data.

Direct odour recognition has been reported at 0.05 ppm (0.36 mg/m^3) and above.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)[69]

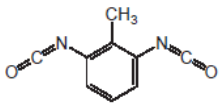
VRW level 0.15	*AEGL-1 0.14*	*ERPG-1 0.07*		*IDLH:* 18 (30 min)
AGW level 0.60	*AEGL-2 0.59*	*ERPG-2 1.09*		
LBW level 3.7	*AEGL-3 3.63*	*ERPG-3 4.35*		

[69] Note that the AEGL and ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL and ERPG, respectively.

Stofdocument deel A

CAS-nr: 91-08-7
$C_9H_6N_2O_2$

Toluеen-2,6-diisocyanaat



VN-nr: 2078
GEVI: 60

Synoniemen: 2,6-TDI, 2,6-Tolueendiisocyanaat, 2-methyl-m-fenyleendiisocyanaat (Engels: 2,6-Toluene Diisocyanate)

Status: geen

Interventiewaarden		10	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m³)**	0,15	0,15	0,15	0,073	0,073	0,073
Alarmeringsgrenswaarden	**AGW (mg/m³)**	1,7	1,2	0,60	0,30	0,15	0,15
Levensbedreigende waarden	**LBW (mg/m³)**	6,8	4,7	3,7	3,0	2,3	1,2

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,138 ppm; 1 ppm = 7,25 mg/m³

Explosiegrens: 0,9 vol% ≈ 65 000 mg/m³

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot lichtgele vloeistof
Brand: moeilijk brandbaar, bij vele reacties kans op brand en explosie

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,00

Molecuulmassa: 174,2 g/mol

Zuurgraad: Geen data

LogKow: 3,7

Wateroplosbaarheid: Reactie

Verzadigde dampdruk: 0,02 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid.

MAK: niet afgeleid

TLV-TWA: 0,007 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: prikkeling van neus en ogen

VRW → AGW: irritatie aan ogen, neus en luchtwegen, keelpijn, hoesten, rhinitis, tranenvloed, hoofdpijn

AGW → LBW: ernstige luchtwegirritatie, onregelmatige ademhaling, benauwdheid, longoedeem, bloed ophoesten

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Tolueen-2-6-diisocyanaat is sterk irriterend voor de ogen en luchtwegen. Bij hoge concentraties werkt de stof bijtend.
- Bij hoge concentraties kan tolueen-2,6-diisocyanaat longontsteking (chemische pneumonitis) en longoedeem veroorzaken, waarbij de verschijnselen pas na enkele uren kunnen optreden en worden versterkt door lichamelijk inspanning.
- Blootstelling kan een astmatische reactie veroorzaken.
- De stof is sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact.
- Kruisgevoeligheid met andere diisocyanaten is mogelijk.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn, blaren.

Oogcontact: roodheid en pijn

Carcinogeniteit

IARC classificatie: 2B

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp, *algemeen:* frisse lucht, rust, halfzittende houding en onmiddellijk arts raadplegen.

Ontsmetting vloeistof

huid: overmaat stof opdeppen, verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), (oog)arts raadplegen, blijven spoelen of druppelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en arts raadplegen.

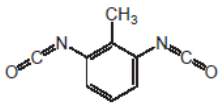
Specifieke behandeling en materialen*: geen.*

Neem contact op met het NVIC (Tel: 030 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 91-08-7
$C_9H_6N_2O_2$

2,6-Toluene Diisocyanate



UN-nr: 2078

Basis for the Dutch Intervention Values

VRW: AEGL values are adopted, 2 h value added

AGW: AEGL values are adopted (except 10 min value for which time scaling was applied), 2 h value added

LBW: AEGL values are adopted (except 10 min value for which time scaling was applied), 2 h value added

Date: 16-10-2018 | AEGL document: Final, 2004

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.15	0.15	0.15	0.073	0.073	0.073	Light irritation (nose and throat), chest tightness in exposed humans
AGW	1.7	1.2	0.60	0.30	0.15	0.15	Irritation eyes and respiratory tract (humans)
LBW	6.8	4.7	3.7	3.0	2.3	1.2	Lethality in mice

Derivation of the Dutch Intervention Values

VRW: A human volunteer study with healthy and asthmatic individuals was used as starting point for the derivation of the VRW values. Volunteers were exposed to a mixture of 2,4-TDI and 2,6-TDI in a ratio of 80:20, respectively. Asthmatic individuals tolerated exposures of 0.01 ppm (0.073 mg/m³) for one hour followed by a rest period of 45 minutes and a second exposure to 0.02 ppm (0.15 mg/m³) for another hour. Healthy adults (control group) were exposed for 2 hours at 0.02 ppm (0.15 mg/m³). Both groups reported eye and throat irritation, cough, chest tightness, rhinitis, dyspnea and/or headache. There was no indication whether the effects were worse in asthmatics at the 0.01 ppm or 0.02 ppm (0.073 and 0.15 mg/m³, respectively) level. Therefore, the 0.02 ppm (0.15 mg/m³) was identified as the basis of for the 10-, 30-min and 1-hour time points and the 0.01 ppm (0.073 mg/m³) concentration was identified as basis for the 2-, 4- and 8-hour time points. Because asthmatic subjects tolerated 0.02 ppm (0.15 mg/m³) for 1 hour after pre-exposure at 0.01 ppm (0.073 mg/m³), it is assumed that the asthmatic population could tolerate the lower concentration for a longer duration. No additional uncertainty factors were applied, because a human study was used as starting point and because asthmatic persons are considered a sensitive population. However, it is recognized that individuals with pre-existing allergic sensitization to this substance might not be protected at those concentrations and might experience airway reactivity with symptoms characteristic of an asthmatic attack, such as coughing, wheezing, chest tightness, and difficulty in breathing. The 0.01 ppm (0.073 mg/m³) exposure concentration for the longer time periods is considered reasonable because data suggest that the adverse health effects of inhaled 2,6-TDI are concentration dependent rather than concentration × time dependent. The proposed values are supported by the fact that in an additional study healthy subjects tolerated approximately 0.01 ppm (0.073 mg/m³) for 4 hours with no adverse effects while a slightly higher concentration of 0.03 ppm (0.22 mg/m³) resulted in symptoms similar to the point of departure study in 100% of workers at a manufacturing plant.

AGW: Human exposure to 0.5 ppm (3.63 mg/m³) 2,6-TDI for 30 minutes resulted in eye and throat irritation and lacrimation. The next higher concentration of 1.3 ppm (9.4 mg/m³) was intolerable after 10 minutes. A 30 minute exposure to 3.63 mg/m³ was used as point of departure for deriving AGW values. Although ocular and respiratory tract irritation associated with 2,6-TDI exposure appears to be more concentration dependent than duration dependent, longer exposure periods can result in excessive fluid accumulation in the respiratory tract, which could lead to more severe consequences than defined under AGW. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$, with the default values of n=1 and n=3 for extrapolation to longer and shorter durations, respectively. The 4-hr value was also used for the 8-hour time point, because extrapolation to 8-hr resulted in a concentration similar to one that caused only mild effects in workers exposed for more than 7 hours and on 8-hour work shifts.

LBW: Several lethality studies in different species are available. A 4-hour lethality study in mice appeared to

provide the lowest LC_{50} value, viz. 9.7 ppm (70 mg/m^3). The specific TDI isomers studied were not identified. This value was taken as point of departure and was divided by 3 to estimate a threshold of lethality of 3.2 ppm (23 mg/m^3). Extrapolation of the probit regression line, obtained from a graph in the selected study, shows that a concentration of approximately 4 ppm would result in 1% lethality. Therefore, one-third of the LC_{50} is considered to be a reasonable estimate of the threshold for lethality. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$, with the default values of n=1 and n=3 for extrapolation to longer and shorter durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Toluene 2,6-diisocyanate is a corrosive substance, acting immediately at the point of contact. The degree of irritation seems to depend more on the exposure concentration, than the exposure-duration. Immediately after exposure, a decrease in respiratory rate can be detected in animals as well as humans. This rate becomes more graded after the initial exposure. Repeated exposure can induce asthmatic reactions in sensitized persons.

Sensitization with the risk to develop subsequent allergic reactions can occur from repeated exposure over a long period of time to relatively low concentrations or from at least one exposure at a high concentration. Therefore the sensitisation endpoint cannot be used for the derivation of intervention values.

Substance is not reproductive toxic.

H315: Causes skin irritation; H317: May cause an allergic skin reaction; H319: Causes serious eye irritation; H330: Fatal if inhaled; H334: May cause allergy or asthma symptoms or beathing difficulties if inhaled; H335: May cause respiratory irritation; H351: Suspected of causing cancer.

Carcinogenicity and derivation of the CRP value

IARC classification:

Toluene diisocyanates as a group are classified by IARC as category 2B (possibly carcinogenic to humans).

No carcinogenic risk potency (CRP) was derived.

Although carcinogenicity data for TDI are conflicting, it can be concluded that carcinogenicity is route-specific. The oral carcinogenicity may be due to the formation of toluene diamide (TDA) that is not formed after inhalation exposure. Based on the similar behaviour of TDA and 2,6-TDI, IARC has classified TDI in accordance with TDA. USEPA has not classified 2,6-TDI. For this inhalation scenario, CRP calculation is not applicable.

Odour and derivation of the LOA value

Odour: Pungent odour (sweet and fruity)

No LOA was derived due to lack of reliable data.

Direct odour recognition has been reported at 0.05 ppm (0.36 mg/m^3) and above.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [70]

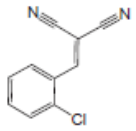
VRW level 0.15	*AEGL-1 0.14*	*ERPG-1 0.07*		*IDLH: -*
AGW level 0.60	*AEGL-2 0.59*	*ERPG-2 1.09*		
LBW level 3.7	*AEGL-3 3.63*	*ERPG-3 4.35*		

[70] Note that the AEGL and ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL and ERPG, respectively.

Stofdocument deel A

CAS-nr: 2698-41-1
$C_{10}H_5ClN_2$

Traangas (CS)



VN-nr: 3276
GEVI: 60

Synoniemen: *o*-chloorbenzylideenmalonitril, CS(-gas), OCBM, β,β-dicyano-o-chloorstyreen (Engels: tear gas (CS), o-chlorobenzylidenemalononitrile)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,0040	0,0040	0,0040	0,0040	0,0040	0,0040
Alarmeringsgrenswaarden	AGW (mg/m³)	0,25	0,25	0,25	0,25	0,25	0,25
Levensbedreigende waarden	LBW (mg/m³)	110	37	19	9,3	4,6	2,3

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,127 ppm; 1 ppm = 7,845 mg/m³

Explosiegrens: LEL = 25% ≈ 1.900.000 mg/m³

Geur: typerende (peperachtige) geur (bij hogere concentraties stekend)

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: witte kristallen of lichtgeel poeder
Brand: brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,00

Molecuulmassa:	188,6 g/mol
Zuurgraad:	Geen informatie
LogKow:	1,8
Wateroplosbaarheid:	0,0052 g/100 ml (zeer matig)
Verzadigde dampdruk:	$4{,}5\times10^{-5}$ mbar

Overige informatie

Publieke grenswaarde: niet vastgesteld

MAK: niet afgeleid

TLV-Ceiling: 0,39 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: prikkelende ogen, tranenvloed, roodheid

AGW → LBW: branderig/stekende pijn in de ogen, ooglidsamentrekking, duizeligheid, misselijkheid, braken, hoofdpijn, keelpijn en hoesten, pijn op de borst, moeizaam ademen

Boven LBW: sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- CS veroorzaakt primair lokale effecten; systemische effecten zijn echter mogelijk bij hoge concentraties.
- Bij inhalatie van zeer hoge concentraties zullen de sterke irriterende effecten op de bovenste luchtwegen de ademhaling bemoeilijken o.a. door constrictie en oedeemvorming.

Effecten bij blootstelling aan vaste stof

Huidcontact: roodheid en pijn, blaren.

Oogcontact: *bijtend*, roodheid en pijn, tranenvloed, slecht zien, mogelijke hoornvliesschade.

Carcinogeniteit

IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, en arts raadplegen.

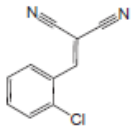
Ontsmetting vloeistof
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar (oog)arts brengen.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: 4% natriumwaterstofcarbonaatoplossing voor oogspoeling.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 2698-41-1
$C_{10}H_5ClN_2$

Tear gas CS



UN-nr: 3276

Basis for the Dutch Intervention Values

VRW: Different rationale than for AEGL, different values are derived, 2h value added

AGW: AEGL value adopted, 2h value added

LBW: Different point of departure than AEGL, 2h value added

Date: 16-10-2018 | AEGL final 2014

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.0040	0.0040	0.0040	0.0040	0.0040	0.0040	Eye irritation in humans
AGW	0.25	0.25	0.25	0.25	0.25	0.25	Ocular, nasal, mouth and throat irritation in humans
LBW	110	37	19	9.3	4.6	2.3	Acute lethality in rats

Derivation of the Dutch Intervention Values

VRW: VRW values are based on human exposure to CS. A TC_{50} (the concentration required to obtain no more than a perceptible effect on 50% of the population exposed to gas for 1 minute) of 0.004 mg/m³ for eye irritation and 0.023 mg/m³ for airway irritation was reported. An exposure to 0.004 mg/m³ was selected as point of departure for the VRW. An intraspecies uncertainty factor was not applied as the effect ('perceptible') was below the definition of the VRW. Time scaling was not applied as eye irritation is considered to be concentration-dependent rather than concentration × time-dependent.

AGW: AGW values are based on human exposure to CS at 0.75 mg/m³ for 60 min. All five subjects tolerated the exposure, but experienced ocular irritation, increased salivation, and coughing; some subjects also reported nasal, mouth, and throat irritation, nausea, and headache. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was not applied as eye irritation is considered to be concentration-dependent rather than concentration × time-dependent.

LBW: LBW values are based on an acute lethality study in rats that was considered to provide the most robust data set. Rats (10/group) were exposed to an average CS concentration of 507 mg/m³ (range 454-560 mg/m³) for 25-90 minutes. Based on these data, an LT_{50} of 66 minutes for an exposure concentration of 507 mg/m³ could be derived. The concentration of 507 mg/m³ can be considered an LC_{50} for an exposure duration of 66 minutes and was taken as point of departure for the LBW. First, a factor of 3 was applied to extrapolate to a threshold for lethality. The default uncertainty factor of 10 (3×3) was considered sufficient to account for inter- and intraspecies differences. For extrapolation to longer exposure durations, the default value of n=1 was applied. Application of a value of n=1 also for extrapolation to shorter exposure durations was supported by two rat datasets with multiple, though limited, concentration-time combinations for short exposure durations.

Additional toxicological information (including relevant results of a general literature search, if any)

CS is an SN_2 alkylating agent and, therefore, reacts directly with nucleophilic compounds. Consequently, sulfhydryl-containing enzymes and other biologic compounds are prime targets. Most notably, CS reacts rapidly with the disulfhydryl form of lipoic acid, a coenzyme in the pyruvate decarboxylase pathway.

Information on reproduction toxicity is not available for CS.

No harmonized H-sentences for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not evaluated

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: pepper-like

No LOA was derived.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)* [71]				
VRW level **0.0040**	*AEGL-1* NR	*ERPG-1* 0.005		*IDLH:* 2 mg/m³ (30 minutes)
AGW level **0.25**	*AEGL-2* 0.083	*ERPG-2* 0.1		
LBW level **19**	*AEGL-3* 11	*ERPG-3* 25		

[71] Note that the AEGL and ERPG values as presented here (in mg/m³) are derived using the conversion factors of the AEGL and ERPG, respectively.

Stofdocument deel A

CAS-nr: 71-55-6 **1,1,1-Trichloorethaan** **CH_3CCl_3** **VN-nr: 2831**

GEVI: 60

Synoniemen: methylchloroform, methyltrichloormethaan (Engels: 1,1,1-Trichloroethane) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	830	830	830	830	830	830
Alarmeringsgrenswaarden	AGW (mg/m³)	4.600	3.700	3.300	2.400	2.100	1.700
Levensbedreigende waarden	LBW (mg/m³)	24.000	24.000	24.000	19.000	15.000	12.000

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,180 ppm; 1 ppm = 5,55 mg/m³

Explosiegrens: LEL = 7,5 vol% ≈ 420.000 mg/m³

Geur: zoete, stekende geur

LOA: 34.000 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: moeilijk brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,5

Molecuulmassa:	133,4 g/mol
Zuurgraad:	geen data
LogKow:	2,5
Wateroplosbaarheid:	0,05 g/100 ml (niet)
Verzadigde dampdruk:	133 mbar

Overige informatie

Publieke grenswaarde: 555 mg/m³ (8 uur)

MAK: 1100 mg/m³

TLV-TWA: 1900 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte oogirritatie

VRW → AGW: tranenvloed, duizeligheid

AGW → LBW: verminderde reflexen, ataxie, bewustzijnsdaling, vertraagde ademhaling, hartritmestoornissen

Boven LBW: coma, ademstilstand, hartstilstand, sterfte

- Toxiciteit bij eenmalige, inhalatoire blootstelling1,1,1-Trichloorethaan werkt irriterend op de ogen
- 1,1,1,-Trichloorethaan heeft een depressieve werking op het CZS en de ademhaling.
- Een hoge concentratie kan de gevoeligheid van het hart voor adrenaline verhogen.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, droge huid.

Oogcontact: tranenvloed, roodheid en pijn.

Carcinogeniteit

IARC classificatie: 3

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust en arts raadplegen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep..

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, arts raadplegen en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen*.

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 71-55-6 **1,1,1-Trichloroethane** **CH_3CCl_3** **UN-nr: 2831**

Basis for the Dutch Intervention Values

VRW: Same point of departure as for AEGL value but using different uncertainty factors, 2h value added

AGW: 30-minute – 8-hour AEGL values are adopted; 10 minute AGW based on different point of departure; 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 16-12-2010 | AEGL document: Interim, 2000

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	830	830	830	830	830	830	Slight eye irritation and dizziness in humans
AGW	4,600	3,700	3,300	2,400	2,100	1,700	Ataxia in animals (30 min - 8h) Threshold for cardiac sensitization in animals (10 min)
LBW	24,000	24,000	24,000	19,000	15,000	12,000	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: The VRW values are developed based upon results from a controlled experiment with 6 healthy male human volunteers exposed by inhalation to 450 ppm (2500 mg/m³) 1,1,1-trichloroethane for 2 time periods of 4 hours separated by a 1.5-hour interval. Eye irritation and slight dizziness were reported by some subjects. This exposure was used as point of departure for the VRW levels. The eye irritation and slight dizziness produced by 1,1,1-trichloroethane did not increase in severity or frequency during the second 4-hour exposure period and the complaints were sporadic. Therefore, the VRW value was held constant across time. An uncertainty factor of 3 was applied to account for intraspecies differences. The AEGL-1 values were derived using an intraspecies uncertainty factor of 2 instead of 3. Among humans the Maximum Alveolar Concentration for volatile anesthetics typically varies by about 2-3 fold. Mild CNS effects like slight dizziness would be expected to occur within a similar range of variation. The VRW values are considered conservative and should be protective of the toxic effects of 1,1,1-trichloroethane. The eye irritation experienced by humans is usually characterized as “slight” even at much higher exposure concentrations as the proposed VRW values. Several chamber exposure studies using similar exposure concentrations showed similar outcomes among human subjects. Because only mild untoward effects were observed at concentrations that were 2 times the proposed value and the severity did not increase with time, this VRW value is considered appropriate.

AGW: The AGW values are based on results from an animal study in which groups of 6 rats were exposed to 0, 1500, 3000, 6000 and 12000 ppm (0, 8300, 17000, 33000 and 67000 mg/m³) 1,1,1-trichloroethane for 4 hours. The rat EC_{50} values for ataxia were used as point of departure for deriving the AGW values. This study establishes the loss of equilibrium with the observation of EC_{50} values for ataxia in rats at 30 minutes, 1, 2, and 4 hours from the start of exposure at 6740, 6000, 4240, and 3780 ppm (37000, 33000, 24000 and 21000 mg/m³). These values were used for the 30 minute, 1, 2, and 4 hour AGW values with an uncertainty factor of 10 applied, 3 each for intra- and inter-species variability for a total of 10. Extrapolation was made to the 8-hour time point using the equation $C^n \times t = k$ where n = 3.3, based on least squares fit of this data. The intra-species uncertainty factor of 3 is based on the previously described argument that the Maximum Alveolar Concentration for volatile anesthetics should not vary by more than a factor of 2-3 fold. The interspecies uncertainty factor of 3 is supported by the similarity of effects manifested in rodents compared to humans produced by agents that are CNS depressants. Human exposures to concentrations of up to 955 ppm (5300 mg/m³) for 1.3 hours are well tolerated with minimal CNS effects, which support the AGW values.

The 10 minute AGW value was based on the NOAEL for cardiac sensitization of 2500 ppm (14000 mg/m³) in dogs exposed for 10 minutes to 1,1,1-trichloroethane. Because the dog appears to be a good model for the human heart, an interspecies uncertainty factor of 1 was applied. Because this is

a conservative test, an intraspecies uncertainty factor of 3 was applied to protect sensitive individuals. The resulting 10 minute AGW value of 4700 mg/m^3 is slightly lower than the value that would have resulted from time scaling from the 30 minute AGW value (5200 mg/m^3).

LBW: The LBW values were based upon results of an animal study in which groups of 12 rats were exposed for 6 hour to 1,1,1-trichloroethane. The concentration causing no deaths in rats after 6 hour exposure, which was estimated from an exposure-concentration graph, was used to derive the LBW. The concentration-response curve crosses the X-axis between 7000 and 8000 ppm (39000 and 44000 mg/m^3). Therefore, as a conservative estimate, a value of 7000 ppm (39.000 mg/m^3) for a duration of 6 hours was used as point of departure for the derivation of LBW values. An intraspecies uncertainty factor of 3 and an interspecies uncertainty factor of 1 were applied for a total uncertainty factor of 3. The intraspecies uncertainty factor of 3 is based on the previously described argument that the Maximum Alveolar Concentration for volatile anesthetics should not vary by more than a factor of 2-3 fold. The interspecies uncertainty factor of 1 is supported by the similarity of effects manifested in rodents compared to humans produced by agents that are CNS depressants and by the observed 2 to 5-fold greater blood:air partition coefficient for 1,1,1-trichloroethane in rodents compared to humans. This principle determines the relative blood concentration for a vapor and because it is higher for rats, a higher blood concentration is achieved at lower exposure concentrations among rodents compared to humans. Time-scaling was performed using the equation $C^n \times t = k$ where n = 3, based on the rat lethality data. The 1-hour value was also used for the 10- and 30-minute values so as not to exceed the threshold for cardiac sensitization observed in a study with dogs (LOAEL: 10 minute exposure to 5000 ppm; 28000 mg/m^3).

Additional toxicological information (including relevant results of a general literature search, if any)

Studies indicate that children and particularly infants are more resistant than adults to the effects of various volatile anesthetics. The susceptibility of individuals of different ages has been extensively studied in the anesthesia literature. Minimal Alveolar Concentrations (MAC) producing lack of movement in 50% of persons exposed to that concentration show a pattern with maximal sensitivity (lowest MAC values) in newborns, pregnant women, and the elderly. The least sensitive (highest MAC values) occur in older infants, toddlers and children as compared to normal adults. The total range is 2-3 fold.

Human deaths have been reported following exposure to high concentrations of 1,1,1-trichloroethane in occupational as well as abuse situations. These deaths typically result from respiratory failure due to CNS depression or from cardiac arrhythmias following sensitization of the heart to epinephrine. Human response to 1,1,1-trichloroethane is typically characterized by eye irritation and subtle CNS effects which become measurable at levels above 450 ppm (2500 mg/m^3) at exposure durations of about 4 hours. Observable effects range from slight behavioral changes (accompanied by eye irritation in humans) at 500 ppm (2800 mg/m^3) to unconsciousness and respiratory arrest at higher concentrations (10,000-30,000 ppm, 55,000-170,000 mg/m^3). Based on the available data, a NOAEL for the threshold of subtle CNS effects is 350 ppm (900 mg/m^3) for durations up to 8 hours, the established ACGIH-TLV. Concentrations above 900 ppm (5000 mg/m^3) for periods of 70-75 minutes appear to be the threshold for loss of equilibrium concomitant with feelings of light-headedness and eye irritation. Disturbances in equilibrium occurred at 1740 ppm (9700 mg/m^3) after 5 minutes of exposure, and at levels above 2650 ppm (15,000 mg/m^3), a definite loss of equilibrium is evident after only a few minutes exposure.

Developmental toxicity, but not teratogenicity, in the form of developmental delays has been identified in rats and rabbits at concentrations that produced maternal toxicity. No developmental effects have been identified in humans. Limited epidemiological evidence on possible reproductive effects is inconclusive.

H332: Harmful if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to carcinogenicity to humans).

No carcinogenic risk potency (CRP) was derived.

No adequate epidemiological data on the carcinogenic potential of this compound in humans exists. However, a chronic inhalation study in rats and mice exposed to 1500

Odour and derivation of the LOA value

Odour: sweet, pungent odour.

Odour threshold: 2160 mg/m^3 [AIHA cited in AEGL TSD]

LOA = 11.8 * 2160 * 1.33 = 34,000 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 *

ppm (8000 mg/m^3) revealed no evidence of any carcinogenic effect.	log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value) The LOA is higher than the intervention values.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*				
VRW level **830**	*AEGL-1* 1,300	*ERPG-1* 1,900		*IDLH:* 3900 (30 minutes)
AGW level **3,300**	*AEGL-2* 3,300	*ERPG-2* 3,900		
LBW level **24,000**	*AEGL-3* 23,000	*ERPG-3* 19,000		

Stofdocument deel A

CAS-nr: 79-01-6 **Trichloorethyleen** $ClCH=CCl_2$ **VN-nr: 1710**

GEVI: 60

Synoniemen: trichlooretheen, tri, ethyleentrichloride (Engels: trichloroethylene) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	1.400	960	710	550	460	420
Alarmeringsgrenswaarde	AGW (mg/m³)	5.300	3.400	2.500	1.800	1.500	1.300
Levensbedreigende	LBW (mg/m³)	33.000	33.000	21.000	13.000	8.400	5.300

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,183 ppm; 1 ppm = 5,47 mg/m³

Explosiegrens: LEL = 7,9 vol% ≈ 430.000 mg/m³

Geur: oplosmiddelachtig, etherisch, zoet

LOA: 2400 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,3

Molecuulmassa:	131,4 g/mol
Zuurgraad:	geen data
LogKow:	Ca. 2,3
Wateroplosbaarheid:	Slecht
Verzadigde dampdruk:	77 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 273 mg/m³

Zeer vluchtig

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: irritatie ogen en luchtwegen, hoesten

AGW → LBW: benauwdheid, hoofdpijn, duizeligheid, misselijkheid, braken, bewustzijnsdaling, lethargie

Boven LBW: coma, ademnood, hartritmestoornissen, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Trichloorethyleen werkt irriterend op de ogen, huid en luchtwegen.
- Trichloorethyleen heeft een depressieve werking op het CZS.
- Het ontstaan van lever- en nierschade na blootstelling aan trichloorethyleen is beschreven.
- Bij blootstelling aan hoge concentraties kunnen mogelijk hartritmestoornissen ontstaan.

Effecten bij blootstelling aan vloeistof

Huidcontact: irritatie, roodheid, droge huid

Oogcontact: irritatie, roodheid, pijn

Carcinogeniteit

IARC classificatie: 1

CRP: 50.808 mg/m³

Beknopte medische informatie

***Ontsmetting* damp**

algemeen: frisse lucht, rust, en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken en minimaal 20 min. spoelen met veel water of douchen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 79-01-6 **Trichloroethylene** **ClCH=CCl$_2$** **UN-nr: 1710**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 24-09-2009 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	1400	960	710	550	460	420	Marginal CNS-effects in humans
AGW	5,300	3,400	2,500	1,800	1,500	1,300	CNS effects in humans
LBW	33,000	33,000	21,000	13,000	8,400	5,300	NOEL for mortality in mice

Derivation of the Dutch Intervention Values

VRW: The VRW derivation is based on the NOAEL of 300 ppm (1,600 mg/m^3) from a human volunteer study. Eight subjects exposed to 300 ppm for 2 hours showed no significant impairment of neurobehavioral function, with marginal CNS-depression present in only 1 out of 8 volunteers. For extrapolation across durations, a human PBPK model of Boyes et al. (2002) was used. The human model applied was derived from a model for rats. The peak concentration of trichloroethylene in blood after 2 hours of exposure to 300 ppm (1,600 mg/m^3) was first calculated and subsequently the external concentrations that would produce the same blood concentration for the other exposure durations were determined. The dose metric in this calculation is the peak of unchanged trichloroethylene in blood. Blood levels of trichloroethylene were found to correlate well with neurotoxic effects in rats after acute exposure and accordingly the latter are an acceptable dose metric. Following exposure to an external concentration of 300 ppm (1,600 mg/m^3) for 2 hours (the NOAEL), the model predicted a trichloroethylene concentration in blood of 4.78 mg/l. This value compares reasonably well to the peak blood concentrations of trichloroethylene as seen in various volunteer studies exposed to similar concentrations. Using the 4.78 mg/l target value external concentrations were calculated for the standard intervention value durations. For interindividual variation among humans an intraspecies factor of 3 is used. A higher factor is not necessary because the mechanism of action (general CNS depression) does not vary more than a factor of 2-3 within the human population.

AGW: Human data relevant for AGW endpoints are scant. The effects seen at 1,000 ppm (5,500 mg/m^3) are relatively mild effects for an AGW level. However, because of the lack of another reliable human NOAEL, the value of 1,000 ppm (5,500 mg/m^3) for 2 hours is considered the highest level without an AGW effect. At this concentration there was self-reported light-headedness, dizziness and lethargy and also a reduced performance in neurobehavioral tests (primarily the pegboard test). Following exposure to an external concentration of 1,000 ppm (5,500 mg/m^3) for 2 hours, the human PBPK model of Boyes et al. (2002) predicted a trichloroethylene concentration in blood of 18.3 mg/l. Although no human metabolism studies are available with appropriate exposure levels to support this calculated blood level, it should be noted that the level of 18.3 mg/l is a factor 5 lower than the blood level needed for anaesthesia (100 mg/l). Using 18.3 mg/l as the target value, the external concentrations were calculated for the standard intervention value durations. For interindividual variation among humans an intraspecies factor of 3 is used. A higher factor is not necessary because the mechanism of action (general CNS depression) does not vary more than a factor of 2-3 within the human population. In addition the severity of the effects is considered to be less than needed for AGW.

LBW: The lower 95% confidence levels of the LC_{05}-values (the Benchmark Concentration for the 5% response) derived from a rat study may be considered the most appropriate basis for deriving the LBW. The calculations with the above mentioned PBPK-model (according to the above mentioned procedure) generated values that are considered to be too low compared to the available human evidence. Therefore, an alternative approach was developed. This starts with the NOAEL for mortality observed in mice: 4,600 ppm (25,000 mg/m^3) for 4 hours. Although this concentration is probably nominal, it has been shown in many studies that actual concentrations are close to nominal levels. Therefore, the level of 4600 ppm (25000 mg/m^3) can be used. For interindividual variation among humans an intraspecies factor of 3 is used. A value of n= 1.511 is derived from the above mentioned rat study by probit analysis. Compared to rats, humans need much higher external concentrations for reaching a certain concentration in blood. Therefore, an interspecies extrapolation factor is not considered necessary.

Finally, in LBW derivation it is also taken into account that cardiac arrhythmias may occur in humans at levels of 10,000 ppm (55,000 mg/m^3) and higher and that 10,000 ppm (55,000 mg/m^3) will quickly result in complete narcosis. Therefore, this level should not be exceeded. In addition, general anaesthesia may be associated with vomiting,

which is another risk factor, especially in the absence of medical assistance. Therefore, the 10 min LBW is set equal to the 30 minute value.

Additional toxicological information (including relevant results of a general literature search, if any)

The effects on the CNS are similar to those of other solvents. This is possibly a pure physical interaction of these solvents with the membranes of the cells in the CNS. In humans it is reasonably expected that pulmonary uptake of trichloroethylene following inhalation is rapid. Based on the effects of various volatile anaesthetics maximal sensitivity is expected in newborns (particularly prematures), pregnant women, and the elderly. The least sensitive are older infants, toddlers and children compared to normal adults. The total variation, however, is not more than 2-3 fold.

No human reproductive studies are available. Developmental toxicity was examined in several epidemiological studies (chronic exposure) in which the association between both paternal and maternal exposure to trichloroethylene and spontaneous abortions was studied. Paternal exposure to trichloroethylene was not found to be a risk factor for spontaneous abortions. The number of cases were too small to allow an analysis for the association of maternal exposure to trichloroethylene and abortions.

Trichloroethylene was formerly used on a limited scale as a medical anaesthetic and analgesic. 5,000-15,000 ppm (27,000 – 82,000 mg/m^3) for producing light anaesthesia and 3,500-5,000 ppm (19,000 – 27,000 mg/m^3) for analgesia. Simultaneous exposure to alcohol and trichloroethylene gave significant effects on performance in behavioural tests, compared to those observed with after exposure to one of these substances alone (possibly due to inhibition of metabolism of tetrachloroethylene.

H315: Causes skin irritation; H319: Causes serious eye irritation; H336: May cause drowsiness or dizziness; H341: Suspected of causing genetic effects; H350: May cause cancer.

Carcinogenicity and derivation of the CRP value

IARC classification: 1 (Carcinogenic to humans)

Derivation of the carcinogenic risk potency (CRP):
10^{-4} risk level after inhalation: 0.232 mg/m^3 [AEGL]
CRP = (10^{-4} risk level * average life span in hours)/DRCF = (0.232 * 613,200) /2.8 = 50,808 mg/m^3

IARC concluded that there is sufficient evidence in humans for the carcinogenicity of trichloroethylene. Trichloroethylene causes cancer of the kidney. A positive association has been observed between exposure to trichloroethylene and non-Hodgkin lymphoma and liver cancer.
IARC reviewed a large number of occupational epidemiology studies. Two conducted meta-analyses based on a largely similar set of case–control and cohort studies of cancer of the kidney reported statistically significant meta-relative risks (meta-RR) for cancer of the kidney and exposure to trichloroethylene of 1.3 and 1.4. One meta-analysis reported a higher meta-RR of 1.6 (95% CI, 1.3–2.0) for groups with a higher exposure. A meta-analysis of cohort and case–control studies of non-hodgkin lymphoma reported statistically significant meta-RRs of 1.2 (95% CI,1.1–1.4) for non-Hodgkin lymphoma and any exposure to trichloroethylene and 1.4 (95% CI, 1.1–1.8) for higher exposure.

Odour and derivation of the LOA value

Odour: solvent like, ether-like, sweet

OT_{50}: 28 ppm (153 mg/m^3) [EPA]
LOA = 11.8 * OT_{50} * 1.33 = 2401 mg/m^3 (439 ppm)

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies above the VRW and AGW, but is lower than the LBW levels at the time points 10, 30 and 60 minutes.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **710**	*AEGL-1* 710	*ERPG-1* 550		IDLH: 5,500 (10 minutes)
AGW level **2,500**	*AEGL-2* 2,500	*ERPG-2* 2,700		
LBW level **21,000**	*AEGL-3* 21,000	*ERPG-3* 27,300		

Stofdocument deel A

CAS-nr: 10025-78-2 **Trichloorsilaan** **Cl_3HSi** **VN-nr: 1295**
GEVI: X338

Synoniemen: silicochloroform (Engels: trichlorosilane) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	3,4	3,4	3,4	3,4	3,4	3,4
Alarmeringsgrenswaarden	AGW (mg/m³)	210	100	63	39	25	25
Levensbedreigende waarden	LBW (mg/m³)	630	300	190	120	74	74

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,177 ppm; 1 ppm = 5,64 mg/m³

Explosiegrens: LEL = 1,2 vol% ≈ 68.000 mg/m³

Geur: scherpe stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze rokende vloeistof
Brand: zeer brandgevaarlijk, bij vele reacties kans op brand en explosie

Relatieve dichtheid van verzadigd damp-lucht mengsel: 3,4

Molecuulmassa:	135,5 g/mol
Zuurgraad:	geen data
LogKow:	geen data
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	667 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW	geen informatie
VRW → AGW:	irritatie van ogen en luchtwegen, tranenvloed, hoesten, lichte benauwdheid
AGW → LBW:	ernstige irritatie van ogen en luchtwegen, pijn op de borst, benauwdheid, longontsteking, longoedeem
Boven LBW:	ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Chloorsilanen reageren zeer snel met water onder vorming van chloorwaterstof (HCl). De acute toxiciteit van trichloorsilaan wordt veroorzaakt door chloorwaterstof.
- Inhalatie van chloorwaterstof veroorzaakt een type I inhalatie intoxicatie.
- Chloorwaterstof veroorzaakt irritatie van de slijmvliezen van ogen en luchtwegen.
- Chloorwaterstof kan bij inhalatie longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, brandwonden.

Oogcontact: bijtend, roodheid en pijn, hoornvliesbeschadiging, ernstige brandwonden.

Carcinogeniteit

IARC classificatie: niet geclassificeerd.
CRP: niet afgeleid.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust; in geval van rode ogen halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken (voorzichtig i.v.m mogelijk reeds beschadigde huid), minimaal 20 min. spoelen met veel water of douchen, en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen:.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 10025-78-2 **Trichlorosilane** **Cl_3HSi** **UN-nr: 1295**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same rationale as AEGL (analogy with HCl), 2h value added

LBW: Same rationale as AEGL (analogy with HCl), 2h value added

Date: November 2015 | AEGL document: Final, 2012

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	3.4	3.4	3.4	3.4	3.4	3.4	Based on HCl (Threshold for irritation in humans)
AGW	210	100	63	39	25	25	Based on HCl (one-third of LBW))
LBW	630	300	190	120	74	74	Based on HCl (Calculated threshold for lethality in animals)

Derivation of the Dutch Intervention Values

VRW: Since no appropriate data exist for trichlorosilane, VRW values for hydrogen chloride will be used (on ppm-basis) to derive VRW values for trichlorosilane. The use of hydrogen chloride as a surrogate for trichlorosilane was deemed appropriate since it is believed that the hydrolysis product, HCl, is responsible for the adverse effects. Because three moles of hydrogen chloride are produced for every mole of trichlorosilane, a molar adjustment factor of 3 was applied to the hydrogen chloride VRW values.

Derivation of VRW values for HCl

The hydrogen chloride VRW values were based on a no-adverse-effect-level of 1.8 ppm (2.73 mg/m^3) in exercising asthmatics with an exposure duration of 45 min. Because the test subjects were considered a sensitive subpopulation and the endpoint was essentially a no-effect level, no uncertainty factor was applied to account for sensitive human subpopulations. The VRW values were held constant for all specified exposure periods since mild irritant effects represent threshold effects and generally do not vary over time.

AGW: Since no appropriate data exist for trichlorosilane, AGW values for hydrogen chloride will be used (on ppm-basis) to derive AGW values for trichlorosilane. Because three moles of hydrogen chloride are produced for every mole of trichlorosilane, a molar adjustment factor of 3 was applied to the hydrogen chloride AGW values.

Derivation of AGW values for HCl

The AGW values of HCl for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data. The only study of HCl that addressed effects that meet the definition of an AGW, severe nasal lesions, was a study on hydrogen halides by Stavert et al. (1991). Nevertheless, this study was not considered a suitable basis for derivation of AGW values because 6% of the animals died after exposure to HCl at 1300 ppm (1974 mg/m^3), only one concentration was tested and the number of animals tested was inconsistent.

LBW: Since no appropriate data exist for trichlorosilane, LBW values for hydrogen chloride will be used (on ppm-basis) to derive LBW values for trichlorosilane. Because three moles of hydrogen chloride are produced for every mole of trichlorosilane, a molar adjustment factor of 3 was applied to the hydrogen chloride LBW values.

Derivation of LBW values for HCl

The LBW values were based on a lethality study in rats. The rat study included six exposure durations and various concentrations. Probit analyses using DoseResp was performed and yielded LC_{01} values for the 10 min, 30 min, 1-, 2-,4-, and 8hrs exposure durations of 3370, 1602, 1002, 627, 393 and 246 ppm (5116, 2433, 1522, 952, 596, and 373 mg/m^3), respectively, which were used as point of departure for LBW derivation. The default total uncertainty factor of 10 (3x3) was considered

sufficient to account for inter- and intraspecies differences. The probit analyses yielded an n-value of 1.48, which was supported by the n-value of 1.59 calculated by Arts *et al.* (2000) from the C*t study. To maintain consistency with other hydrogen halogenides, the 8 hour value was set equal to the 4 hour value, as performed for the most potent hydrogen halogenide HF.

Additional toxicological information (including relevant results of a general literature search, if any)

No data concerning lethality or nonlethal toxicity in humans from trichlorosilane were located in the available literature.

Chlorosilanes react violently with water to produce hydrogen chloride gas. Data suggest that the acute toxicity of chlorosilanes is due to the hydrogen chloride hydrolysis product; acute toxicity of the chlorosilanes is both qualitatively (based on clinical signs) and quantitatively (based on molar equivalents of hydrogen chloride) similar to that of HCl.

Although toxicity data are limited for individual chlorosilanes, well-conducted 1-hr inhalation toxicity studies in rats are available for a series of chlorosilanes. In general, LC_{50} values for monochlorosilanes were approximately twice the LC_{50} values for dichlorosilanes and three times the LC_{50} values for trichlorosilanes. Clinical signs were consistent with hydrogen chloride exposure and included lacrimation, salivation, dried material around or on the eyes and/or nose, green staining around the nose and mouth, and perineal urine staining. Labored breathing, rales, hypoactivity, closed or partially closed eyes, prostration, corneal opacity or opaqueness, and swollen and/or necrotic paws were also observed. Hemorrhage, congestion and/or consolidation of the lungs, ectasia of the lungs, gaseous distension of the gastrointestinal tract, absence of body fat, obstruction of nostrils, dried and/or firm nares, alopecia around the eyes and discoloration of hair were observed at necropsy.

No data concerning developmental/reproductive toxicity for exposure to trichlorosilane were located in the available literature.

H302: Harmful if swallowed; H314: Causes severe skin burns and eye damage; H332: Harmful if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified.

No carcinogenic risk potency (CRP) was derived

No data concerning carcinogenicity for exposure to trichlorosilane were located in the available literature.

Odour and derivation of the LOA value

Odour: pungent odour

No LOA was derived due to lack of data.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

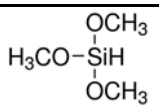
VRW level **3.4**	*AEGL-1* 3.4	*ERPG-1* 5.6		*IDLH:* not derived
AGW level **63**	*AEGL-2* 41	*ERPG-2* 17		
LBW level **190**	*AEGL-3* 190	*ERPG-3* 140		

Stofdocument deel A

CAS-nr: 2487-90-3

$C_3H_{10}O_3Si$

Trimethoxysilaan



VN-nr: 9269

GEVI: geen

Synoniemen: TMS (Engels: trimethoxysilane), Dynasylan

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	23	16	13	6,3	5,0	2,5
Levensbedreigende waarden	LBW (mg/m³)	70	49	39	19	15	7,5

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,197 ppm; 1 ppm = 5,084 mg/m³

Explosiegrens: LEL = 4,3 vol% ≈ 219.000 mg/m³

Geur: esterachtige geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 4.2

Molecuulmassa: 122,22 g/mol

Zuurgraad: Geen data

LogKow: 0,18 (QSAR)

Wateroplosbaarheid: reactie

Verzadigde dampdruk: 76 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW: keelpijn en hoesten

AGW → LBW: irritatie van ogen, huid en luchtwegen, branderig gevoel achter het borstbeen, moeizaam ademen, kortademigheid, ademnood

Boven LBW: sterfte

LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof werkt irriterend op de ogen en de luchtwegen
- Blootstelling kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Mogelijk zijn mensen met een verminderde longfunctie gevoeliger voor effecten van de stof
- Trimethoxysilaan is in het bijzonder schadelijk voor de ogen. Blootstelling aan de dampen of aerosol van de stof kan initieel zonder merkbare irritatie aan de ogen verlopen, maar na een latentietijd van 10-12 uur kan heftige (oog)pijn, roodheid en tranenvloed ontstaan, wat zich verder kan ontwikkelen tot troebeling en laesies van de cornea. In ernstige gevallen kan zelfs blindheid ontstaan.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn

Oogcontact: roodheid, pijn, slecht zien, ernstige brandwonden, mogelijk permanent verlies van gezichtsvermogen

Carcinogeniteit

IARC classificatie: niet geëvalueerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof

huid: spoelen met veel water / kleding verwijderen en onmiddellijk arts raadplegen.

ogen: zie hierboven.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*

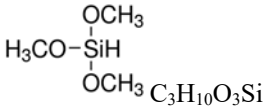
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 2487-90-3

$C_3H_{10}O_3Si$

Trimethoxysilane



$C_3H_{10}O_3Si$

UN-nr: 9269

Basis for the Dutch Intervention Values

VRW: Not recommended (in accordance with AEGL)

AGW: Same rationale as AEGL values (1/3 LBW)

LBW: Same point of departure as for AEGL values but using different uncertainty factors, different n and time scaling applied to the 10 minute value, 2h value added

Date: 16-10-2018 | AEGL document: Final, 2013

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Inadequate data
AGW	23	16	13	6.3	5.0	2.5	One-third of LBW
LBW	70	49	39	19	15	7.5	Estimated LC_{01} in rats

Derivation of the Dutch Intervention Values

VRW: The VRW values are not derived. Available human and animal data were insufficient and therefore VRW values were not recommended. The lack of VRW-values does not necessarily mean that exposure below AGW-levels is without any effects.

AGW: The AGW for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data.

LBW: The LBW values were determined by using mortality data with rats after 1h and 4h exposure. Sprague-Dawley rats (n=5/sex/concentration) were exposed to trimethoxysilane at concentrations of 19, 39, 71, or 166 ppm (97, 198, 361 or 844 mg/m³) for 4 h or 68, 155, 342, or 643 ppm (346, 788, 1739, 3269 mg/m³) for 1 h. Points of departure were the calculated LC_{01} values (lethal concentration, 1% lethality) of 76.3 ppm (388 mg/m³) for 1 h and 29.3 ppm (149 mg/m³) for 4 h. The 1 hour LC_{01} was used as PoD for the 10, 30 min and 1 hour LBW and the 4 hour LC_{01} was used for the 2 hour and 8 hour LBW values. Using the 1 hour LC_{01} as PoD for the 2 hour LBW would lead to a similar value.
Time-scaling was performed using the equation $C^n \times t = k$, using the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively. The default total uncertainty factor of 10 (3×3) was considered sufficient to account for inter- and intraspecies differences.

Additional toxicological information (including relevant results of a general literature search, if any)

The exact mechanism of toxicity of trimethoxysilane is not known. The substance is a strong ocular irritant. Epithelial tissue seems to be the target tissue for the substance, especially in the eye and respiratory tract. Animal studies show that the substance can cause lung damage, therefore subjects with a compromised lung function would be considered to be more at risk from exposure to the substance.

Data on developmental and reproductive toxicity in humans and in animals are not located.

No harmonized hazard sentences.

Carcinogenicity and derivation of the CRP value

IARC classification: not evaluated

No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value

Odour: Ester-like

No LOA was derived (due to inadequate data)

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)* [72]				
VRW level **NR**	*AEGL-1* NR	*ERPG-1* 2.5		*IDLH: not derived*
AGW level **13**	*AEGL-2* 4.2	*ERPG-2* 10		
LBW level **39**	*AEGL-3* 13	*ERPG-3* 25		

[72] Note that the AEGL and ERPG values as presented here (in mg/m³) are derived using the conversion factors of the AEGL and ERPG, respectively.

Stofdocument deel A

CAS-nr: 75-50-3 **Trimethylamine** **$(CH_3)_3$-N** **VN-nr: 1083**

GEVI: 23

Synoniemen: N,N-dimethylmethaanamine, TMA, N,N-dimethylmethylamine (Engels: Trimethylamine) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	20	20	20	20	20	20
Alarmeringsgrenswaarden	AGW (mg/m³)	590	380	290	220	160	120
Levensbedreigende waarden	LBW (mg/m³)	1900	1200	940	720	540	410

Datum vaststelling: 16-12-2010

Conversiefactor: 1 mg/m³ = 0,406 ppm; 1 ppm = 2,46 mg/m³

Explosiegrens: LEL = 2,0 vol% ≈ 49.000 mg/m³

Geur: scherp, vis- of ammoniak-achtig

LOA: 0,00124 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos onder druk tot vloeistof verdicht gas

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,0

Molecuulmassa:	59,1 g/mol
Zuurgraad:	pK_a 9,80
LogKow:	0,2
Wateroplosbaarheid:	volledig
Verzadigde dampdruk:	2200 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: 4,9 mg/m³

TLV-TWA: 12 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	geen klachten
VRW → AGW:	irritatie ogen, huid en bovenste luchtwegen, hoesten, niezen, tranenvloed
AGW → LBW:	irritatie van onderste luchtwegen, benauwdheid, longoedeem, verlies van gezichtsvermogen, coördinatieproblemen, lethargie
Boven LBW:	convulsies, ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Trimethylamine werkt irriterend tot bijtend op de ogen, de huid en de luchtwegen, waarschijnlijk door het sterk alkalische karakter van de stof.
- Depressie van het centraal zenuwstelsel kan ontstaan.
- Inademing kan, uitsluitend na verschijnselen van bijtende effecten op de slijmvliezen van de ogen en/of hogere luchtwegen, longontsteking en/of longoedeem veroorzaken. Dit kan pas na enkele uren optreden en wordt versterkt door lichamelijke inspanning.
- Expositie van de ogen aan het gas kan verlies van cornea-epitheel veroorzaken.
- In ernstige gevallen bestaat kans op verstikking door zwellingen in de keel.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, branderig gevoel, ernstige brandwonden, mogelijk ernstige bevriezings-verschijnselen zoals pijn, blaren, wonden.

Oogcontact: bijtend, tranenvloed, slecht zien, ernstige brandwonden, permanent verlies van gezichtsvermogen

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: aan de huid vastgevroren kleding NIET lostrekken, spoelen met veel water / kleding uittrekken, daarna weer spoelen en onmiddellijk arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas).

Specifieke behandeling en materialen:

Neem contact op met het NVIC (Tel: +31 (0)30 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 75-50-3 **Trimethylamine** **$(CH_3)_3$-N** **UN-nr: 1083**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 16-12-2010 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	20	20	20	20	20	20	No-effect level for nasal lesions in rats
AGW	590	380	290	220	160	120	Estimated threshold for lung lesions and neurotoxicity in rats
LBW	1900	1200	940	720	540	410	Calculated lethality threshold in rats

Derivation of the Dutch Intervention Values

VRW: The VRW was based on data from an animal study. Rats were exposed to 74-760 ppm (181.9-1868 mg/m³) trimethylamine for 6 h/day, 5 days/week for 2 weeks. The rats were sacrificed immediately or after a 14-day recovery period. All trimethylamine-treated rats had histopathological alterations in the nose, and the 760 ppm (1868 mg/m³) trimethylamine group had also lesions in the trachea and lungs. The lesion severity was dose-related being minimal at 74 ppm (181.9 mg/m³) and moderate or severe at 760 ppm (1868 mg/m³). Point of departure was 74 ppm (181.9 mg/m³). Because a no effect level for nasal lesions was not established, and the lesions were still present after the recovery period, a modifying factor of 3 was applied to this point of departure resulting in 61 mg/m³. An interspecies uncertainty factor of 3 was applied. VRW values were set equal for all exposure durations from 10 minutes to 8 hours.

These VRW values were supported by data from human occupational exposure. No toxic effects were found in workers exposed to 0.1-8 ppm (0.2-20 mg/m³) trimethylamine for 8 hours, whereas ≥20 ppm (49 mg/m³) produced moderate upper respiratory irritation (undefined exposure period).

AGW: AGW values were derived from an acute inhalation study in which 0/6 male rats died after a 4-hour exposure to 2000 ppm (4900 mg/m³), whereas 3/6 died at 3500 ppm (8600 mg/m³). During exposure, rats at both concentrations had difficulty breathing, showed nasal and oral discharge, were immobile, and did not react to sound. Because the severity of these effects exceeds the scope of AGW, the non-lethal concentration of 2000 ppm (4900 mg/m³) was divided by 3 to obtain 670 ppm (1650 mg/m³) as an estimate of the threshold for lung lesions and neurotoxicity. The 4-hour 670 ppm (1650 mg/m³) concentration was used as the point of departure for the AGW. Similar toxicity (nature and severity) was seen in rats and mice in a number of studies. An interspecies uncertainty factor of 3 was applied because animal lethality data showed little interspecies differences, and the irritating effect from a direct-acting alkaline chemical is not expected to vary greatly between species. An intraspecies uncertainty factor of 3 was applied because the effect of a direct-acting irritant is unlikely to vary greatly among humans. Time-concentration scaling was performed using $C^n \times t = k$, where n = 2.5 (calculated from rat lethality data).

LBW: LBW values were derived from a study in which rats were exposed to 18,600 ppm (45,700 mg/m³) for 6 minutes, 18,100 ppm (44,500 mg/m³) for 10 minutes, 11,200-18,200 ppm (27,500-44,800 mg/m³) for 20 minutes or 6150-8170 ppm (15,100-20,100 mg/m³) trimethylamine for 60 minutes (5 rats/sex/dose). The rats exhibited gasping, labored breathing, salivation, corneal opacity, congested or reddened lungs, and mortality. Similar effects were seen in rat and mouse acute lethality studies. The data allowed calculation of LC_{50}, $BMCL_{05}$ and BMC_{01} values for both time points. The 20- and 60-minute $BMCL_{05}$ values of 5719 ppm (14,083 mg/m³) and 3841 ppm (9,485 mg/m³), respectively were used as points of departure for deriving LBW values. Interspecies and intraspecies uncertainty factors of 3 each for a total of 10 were applied because lethality data from mice and rats suggested little interspecies variability, and the effects of an alkaline, direct-acting irritant are unlikely to vary greatly between species or among humans. Time-concentration scaling was performed using the relationship $C^n \times t = k$, where n = 2.5 (calculated from rat lethality data). The 20-minute $BMCL_{05}$ was timescaled to the 10- and 30-minute AEGL-3 exposure durations, and the 60-minute $BMCL_{05}$ was time-scaled to the 2-, 4- and 8-hour exposure durations.

Additional toxicological information (including relevant results of a general literature search, if any)

Trimethylamine is used as a warning agent for natural gas. Trimethylamine vapor has caused respiratory and eye irritation leading to respiratory tract and corneal lesions, as well as neurotoxic effects, and in some cases pathological changes in the liver, spleen, and kidneys.

No studies were located that specifically addressed the mechanism of trimethylamine toxicity. Its irritant properties are likely due to its alkalinity (pKa of 9.80 at 25°C) and corrosiveness to exposed tissues such as eyes and the respiratory mucosa. Respiratory irritation, manifest as breathing difficulties and microscopic lesions of the nose, trachea, and lungs were seen in all trimethylamine toxicity animal studies. The lesions were the most severe in the upper respiratory tract, consistent with the trimethylamine high water-solubility.

There were limited animal data on species variability, which involved only rats and mice. These data indicated that there was little variability in trimethylamine acute toxicity between rats and mice.

It is known that some people have a decreased capacity to metabolize pungent trimethylamine to the non-odourous and less toxic trimethylamine oxide. This hereditary autosomal recessive metabolic disorder is known as trimethylaminuria ("fish malodour syndrome"). This condition occurs much more frequently in women than men, and results in high concentrations of trimethylamine in the plasma, urine, sweat, and breath.

No human data were located on potential reproductive or developmental trimethylamine toxicity.

H315: Causes skin irritation; H318: May cause serious eye damage; H332: Harmful if inhaled; H335: May cause respiratory irritation

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

No studies were found that examined the carcinogenic potential of trimethylamine in humans or animals. Because mechanisms have been proposed by which the known carcinogen N-nitrosidimethylamine can be formed from trimethylamine and trimethylamine oxide in the presence of nitrosating agents, there is some concern about the neoplastic potential of trimethylamine. However, a 2-year mouse and rat inhalation study with the related dimethylamine, which can also potentially form N-nitrosidimethylamine, showed no tumor formation despite severe chronic nasal lesions.

Odour and derivation of the LOA value

Odour: pungent, fishy odour, that becomes similar to that of ammonia at higher concentrations.

OT_{50}: 0.000079 mg/m^3 [AEGL (2008); Ruijten (2005)]

LOA = 11.8 * OT_{50} * 1.33 = 0.00124 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is below the VRW; therefore subjects can be aware of the odour below the level where health effects may be expected.

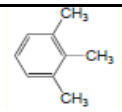
Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **20**	*AEGL-1* 20	*ERPG-1* 0.25		*IDLH*: not derived
AGW level **290**	*AEGL-2* 300	*ERPG-2* 250		
LBW level **940**	*AEGL-3* 930	*ERPG-3* 1200		

Stofdocument deel A

CAS-nr: 526-73-8
C_9H_{12}

1,2,3-Trimethylbenzeen



VN-nr: 3295
GEVI: 30

Synoniemen: hemelliteen (Engels: 1,2,3-trimethylbenzene)

Status: geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarde	**VRW (mg/m³)**	450	450	450	450	450	450
Alarmeringsgrenswaard	**AGW (mg/m³)**	1000	1000	1000	1000	1000	1000
Levensbedreigende	**LBW (mg/m³)**	NA	NA	NA	NA	NA	NA

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,200 ppm; 1 ppm = 5 mg/m³

Explosiegrens:
LEL = 0,8 Vol% ≈ 40.000 mg/m³

Geur: typerende geur
LOA: 188 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,01

Molecuulmassa:	120,2 g/mol
Zuurgraad:	geen data
LogKow:	3,6
Wateroplosbaarheid:	0,006 g/100 ml (zeer slecht)
Verzadigde dampdruk:	1,8 mbar

Overige informatie

Publieke grenswaarde: 100 mg/m³ (8h)

MAK: 100 mg/m³

TLV-TWA: 125 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

***Onder VRW*:** prikkelende ogen en neus.

***VRW → AGW*:** coördinatiestoornissen, rode ogen, hoofdpijn, misselijkheid, keelpijn en hoesten.

***Boven AGW*:** sufheid, duizeligheid, bewusteloosheid, toevallen, ademstilstand

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Blootstelling aan trimethylbenzenen kan leiden tot depressie van het centrale zenuwstelsel.
- Het effect van blootstelling beperkt zich meestal tot sufheid. Bij hoge blootstellingsconcentraties kan dit verergeren tot bewusteloosheid en ademstilstand.
- Irritatie aan de ogen en luchtwegen

Effecten bij blootstelling aan vloeistof

Huidcontact:roodheid, branderig gevoel, pijn

Oogcontact: roodheid, pijn

Carcinogeniteit

IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, en arts raadplegen

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, bij aanhoudende klachten arts raadplegen.

ogen: *uit*spoelen met water (evt. contactlenzen verwijderen), bij aanhoudende irritatieklachten (oog)arts raadplegen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

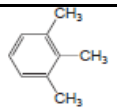
Specifieke behandeling en materialen: *geen*

Neem contact op met het NVIC (Tel:030-2748888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 526-73-8
C_9H_{12}

1,2,3-trimethylbenzene



UN-nr: 3295

Basis for the Dutch Intervention Values

VRW: Same point of departure as for AEGL, but values were flat-lined, 2hr value added

AGW: Same point of departure as for AEGL, but values were flat-lined, 2hr value added

LBW: Not recommended, in accordance with AEGL

Date: 16-10-2018 | AEGL document: final 2013

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	450	450	450	450	450	450	Mild neurotoxic effects in rats and slight ocular irritation
AGW	1000	1000	1000	1000	1000	1000	Ocular and nasal irritation and neurotoxicity in rats
LBW	NR	NR	NR	NR	NR	NR	No adequate data

Derivation of the Dutch Intervention Values

Little difference in toxicity has been observed between the different trimethylbenzene (TMB) isomers (1,2,4-TMB, 1,2,3-TMB, and 1,3,5-TMB). Since data for some individual TMB isomers is insufficient to set adequate limit values, data from all three isomers are used to set the limit values for the individual TMB isomers.

VRW: Repeated exposure of male and female rats to 1,2,4-TMB at 1,000 ppm (5,000 mg/m^3) for 6 h, 5 days a week, 12 exposures resulted in initial signs of slight ocular and nasal irritation (see AGW). Rats exposed to 250-2000 ppm (1250-10,000 mg/m^3) of either 1,2,4-, 1,3,5- or 1,2,3-TMB for four hours, exhibited decreased rotarod performance (mild neurological effect) with an EC_{50} calculated to be 954, 963, and 768 ppm, respectively, corresponding with 4770, 4814, and 3840 mg/m^3. Since the EC_{50} values of individual TMBs are similar, an average EC_{50} for all three trimethylbenzenes of 900 ppm (4500 mg/m^3) was calculated for the trimethylbenzene group and used as point of departure (PoD). Using the specific EC_{50} of 768 ppm (3840 mg/m^3) for 1,2,3 TMB would result in similar VRW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The steady state in blood is reached after 1-2 hours. Therefore, the values for 1-8 hours were flat-lined. Time scaling to 10 and 30 minutes would lead to values conflicting with VRWs derived from slight ocular and nasal irritation observed at 1000 ppm (5000 mg/m^3) in the other rat study (application of total UF of 10). Therefore, the 10 and 30 minute values were also set at 450 mg/m^3.

AGW: The AGW is based on a repeated inhalation toxicity study with rats. Rats (n=4/sex) were exposed to 1000 (5000 mg/m^3) or 2000 ppm (10,000 mg/m^3) 1,2,4-TMB for 6h/d, for 12 days in a 5 days/week dosing regimen. The exposed rats suffered from nasal and ocular irritation, respiratory difficulty, lethargy, tremors, and decreased weight gain. Exposure at 1,000 ppm (5,000 mg/m^3) resulted in initial signs of slight ocular and nasal irritation. All animals survived and no hematology changes or gross or histopathologic lesions were noted after exposure at either 1,000 or 2,000 ppm. There is no adequate data available, specifically with 1,2,3-TMB to derive the AGW. The level of 2,000 ppm (10,0000 mg/m^3) from the study with 1,2,4-TMB was used as point of departure. The PoD is above the criteria for AGW, because the effects could lead to an impaired ability to escape. However, because the key study involved repeated exposures, 2,000 ppm was considered a conservative estimate of effects from a single exposure. Furthermore, no effects were reported in mice exposed to 1,2,4-TMB for up to 2,000 ppm (10,000 mg/m^3) for 12h.The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The effects seen at this PoD include nasal and ocular irritation in the absence of histopathological changes) as well as neurotoxicity. The combination of both effects support flatlining of AGW values over all time points.

LBW: No values for LBW could be derived due to lack of adequate data.

Additional toxicological information (including relevant results of a general literature search, if any)

Little is known about the mechanism of TMB toxicity. At higher concentrations, direct irritation of mucous membranes and narcosis was apparent in some of the animal studies; expected clinical effects include nasal/skin and eye irritation reduced consciousness and tremors.

Substance is not a reproductive toxicant

H332: harmful if inhaled, H315: causes skin irritation, H319: causes serious eye irritation, H335: may cause respiratory irritation

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not evaluated No carcinogenic risk potency (CRP) was derived	Odour: typical scent OT: 12 mg/m^3 (from 1,2,4 TMB as no OT for 1,2,3-TMB is reported) LOA = 11.8 * OT * 1.33 = 188 mg/m^3 (The concentration Level leading to distinct Odour Awareness (l=3) is calculated using the formula: l = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value) The LOA is below all VRW values.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***[73]

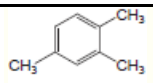
VRW level **450**	*AEGL-1* 690	*ERPG-1* -		*IDLH:* -
AGW level **1000**	*AEGL-2* 1800	*ERPG-2* -		
LBW level **NR**	*AEGL-3* NR	*ERPG-3* -		

[73] Note that the AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL.

Stofdocument deel A

CAS-nr: 95-63-6
C_9H_{12}

1,2,4-Trimethylbenzeen



VN-nr: 3295
GEVI: 30

Synoniemen: pseudocumeen (Engels: 1,2,4-trimethylbenzene)

Status: geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	450	450	450	450	450	450
Alarmeringsgrenswaarden	AGW (mg/m³)	1000	1000	1000	1000	1000	1000
Levensbedreigende waarden	LBW (mg/m³)	NA	NA	NA	NA	NA	NA

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,200 ppm; 1 ppm = 5 mg/m³

Explosiegrens:
LEL = 0,8 Vol% ≈ 40.000 mg/m³

Geur: typerende geur
LOA: 188 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,01

Molecuulmassa:	120,2 g/mol
Zuurgraad:	geen data
LogKow:	3,7
Wateroplosbaarheid:	0,006 g/100 ml (zeer slecht)
Verzadigde dampdruk:	2,1 mbar

Overige informatie

Publieke grenswaarde: 100 mg/m³ (8h)
MAK: 100 mg/m³
TLV-TWA: 125 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

***Onder VRW*:** prikkelende ogen en neus.

***VRW → AGW*:** coördinatiestoornissen, rode ogen, hoofdpijn, misselijkheid, keelpijn en hoesten.

***Boven AGW*:** sufheid, duizeligheid, bewusteloosheid, toevallen, ademstilstand

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Blootstelling aan trimethylbenzenen kan leiden tot depressie van het centrale zenuwstelsel.
- Het effect van blootstelling beperkt zich meestal tot sufheid. Bij hoge blootstellingsconcentraties kan dit verergeren tot bewusteloosheid en ademstilstand.
- Irritatie aan de ogen en luchtwegen

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, branderig gevoel, pijn

Oogcontact: roodheid, pijn

Carcinogeniteit

IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, en arts raadplegen

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, bij aanhoudende klachten arts raadplegen.

ogen: *uit*spoelen met water (evt. contactlenzen verwijderen), bij aanhoudende irritatieklachten (oog)arts raadplegen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

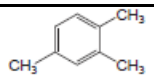
Specifieke behandeling en materialen: *geen*

Neem contact op met het NVIC (Tel:030-2748888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 95-63-6
C_9H_{12}

1,2,4-trimethylbenzene



UN-nr: 3295

Basis for the Dutch Intervention Values

VRW: Same point of departure as for AEGL, but values were flat-lined, 2hr value added

AGW: Same point of departure as for AEGL, but values were flat-lined, 2hr value added

LBW: Not recommended, in accordance with AEGL

Date: 16-10-2018 | AEGL final, 2013

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	450	450	450	450	450	450	Mild neurotoxic effects in rats and slight ocular irritation
AGW	1000	1000	1000	1000	1000	1000	Ocular and nasal irritation and neurotoxicity in rats
LBW	NR	NR	NR	NR	NR	NR	No adequate data

Derivation of the Dutch Intervention Values

Little difference in toxicity has been observed between the different trimethylbenzene (TMB) isomers (1,2,4-TMB, 1,2,3-TMB, and 1,3,5-TMB). Since data for some individual TMB isomers is insufficient to set adequate limit values, data from all three isomers are used to set the limit values for the individual TMB isomers.

VRW: Repeated exposure of male and female rats to 1,2,4-TMB at 1,000 ppm (5,000 mg/m^3) for 6 h, 5 days a week, 12 exposures resulted in initial signs of slight ocular and nasal irritation (see AGW). Rats exposed to 250-2000 ppm (1250-10,000 mg/m^3) of either 1,2,4-, 1,3,5- or 1,2,3-TMB for four hours, exhibited decreased rotarod performance (mild neurological effect) with an EC_{50} calculated to be 954, 963, and 768 ppm, respectively, corresponding with 4770, 4814, and 3840 mg/m^3. Since the EC_{50} values of individual TMBs are similar, an average EC_{50} for all three trimethylbenzenes of 900 ppm (4500 mg/m^3) was calculated for the trimethylbenzene group and used as point of departure (PoD). Using the specific EC_{50} of 768 ppm (3840 mg/m^3) for 1,2,3 TMB would result in similar VRW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The steady state in blood is reached after 1-2 hours. Therefore, the values for 1-8 hours were flat-lined. Time scaling to 10 and 30 minutes would lead to values conflicting with VRWs derived from slight ocular and nasal irritation observed at 1000 ppm (5000 mg/m^3) in the other rat study (application of total UF of 10). Therefore, the 10 and 30 minute values were also set at 450 mg/m^3.

AGW: The AGW is based on a repeated inhalation toxicity study with rats. Rats (n=4/sex) were exposed to 1000 (5000 mg/m^3) or 2000 ppm (10,000 mg/m^3) 1,2,4-TMB for 6h/d, for 12 days in a 5 days/week dosing regimen. The exposed rats suffered from nasal and ocular irritation, respiratory difficulty, lethargy, tremors, and decreased weight gain. Exposure at 1,000 ppm (5,000 mg/m^3) resulted in initial signs of slight ocular and nasal irritation. All animals survived and no hematology changes or gross or histopathologic lesions were noted after exposure at either 1,000 or 2,000 ppm. The level of 2,000 ppm (10,0000 mg/m^3) 1,2,4-TMB was used as point of departure. The PoD is above the criteria for AGW, because the effects could lead to an impaired ability to escape. However, because the key study involved repeated exposures, 2,000 ppm was considered a conservative estimate of effects from a single exposure. Furthermore, no effects were reported in mice exposed to 1,2,4-TMB for up to 2,000 ppm (10,000 mg/m^3) for 12h.The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The effects seen at this PoD include nasal and ocular irritation (in the absence of histopathological changes) as well as neurotoxicity. The combination of both effects support flatlining of AGW values over all time points.

LBW: No values for LBW could be derived due to lack of adequate data.

Additional toxicological information (including relevant results of a general literature search, if any)

Little is known about the mechanism of TMB toxicity. At higher concentrations, direct irritation of mucous membranes and narcosis was apparent in some of the animal studies; expected clinical effects include nasal/skin and eye irritation reduced consciousness and tremors.

Substance is not a reproductive toxicant

H332: harmful if inhaled, H315: causes skin irritation, H319: causes serious eye irritation, H335: may cause

respiratory irritation

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not evaluated No carcinogenic risk potency (CRP) was derived	Odour: typical scent OT: 12 mg/m^3 (AEGL from AIHA, 1995) LOA = 11.8 * OT * 1.33 = 188 mg/m^3 (The concentration Level leading to distinct Odour Awareness (l=3) is calculated using the formula: l = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value) The LOA is below all VRW values.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)[74]

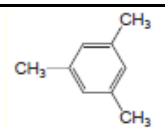
VRW level **450**	*AEGL-1* 690	*ERPG-1* -		*IDLH:* -
AGW level **1000**	*AEGL-2* 1800	*ERPG-2* -		
LBW level **NR**	*AEGL-3* NR	*ERPG-3* -		

[74] Note that the AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL.

Stofdocument deel A

CAS-nr: 108-67-8
C_9H_{12}

1,3,5-Trimethylbenzeen



VN-nr: 2325
GEVI: 30

Synoniemen: mesityleen (Engels: 1,3,5-trimethylbenzene)

Status: geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	450	450	450	450	450	450
Alarmeringsgrenswaarden	VRW (mg/m³)	1000	1000	1000	1000	1000	1000
Levensbedreigende waarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,200 ppm; 1 ppm = 5 mg/m³

Explosiegrens:
LEL = 0,8 Vol% ≈ 40.000 mg/m³

Geur: typerende geur
LOA: 173 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,01

Molecuulmassa:	120,2 g/mol
Zuurgraad:	geen data
LogKow:	3,4
Wateroplosbaarheid:	0,005 g/100 ml (zeer slecht)
Verzadigde dampdruk:	2,7 mbar

Overige informatie

Publieke grenswaarde: 100 mg/m³ (8h)
MAK: 100 mg/m³
TLV-TWA: 125 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

***Onder VRW*:** prikkelende ogen en neus.
***VRW → AGW*:** coördinatiestoornissen, rode ogen, hoofdpijn, misselijkheid, keelpijn en hoesten.
***Boven AGW*:** sufheid, duizeligheid, bewusteloosheid, toevallen, ademstilstand

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Blootstelling aan trimethylbenzenen kan leiden tot depressie van het centrale zenuwstelsel.
- Het effect van blootstelling beperkt zich meestal tot sufheid. Bij hoge blootstellingsconcentraties kan dit verergeren tot bewusteloosheid en ademstilstand.
- Irritatie aan de ogen en luchtwegen

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, branderig gevoel, pijn

Oogcontact: roodheid, pijn

Carcinogeniteit

IARC classificatie: niet geëvalueerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, en arts raadplegen

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, bij aanhoudende klachten arts raadplegen.

ogen: *uit*spoelen met water (evt. contactlenzen verwijderen), bij aanhoudende irritatieklachten (oog)arts raadplegen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

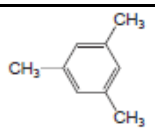
Specifieke behandeling en materialen: *geen*

Neem contact op met het NVIC (Tel:030-2748888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 108-67-8
C_9H_{12}

1,3,5-trimethylbenzene



UN-nr: 2325

Basis for the Dutch Intervention Values

VRW: Same point of departure as for AEGL, but values were flat-lined, 2hr value added

AGW: Same point of departure as for AEGL, but values were flat-lined, 2hr value added

LBW: Not recommended, in accordance with AEGL

Date: 16-10-2018 | AEGL document: final 2013

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	450	450	450	450	450	450	Mild neurotoxic effects in rats and slight ocular irritation
AGW	1000	1000	1000	1000	1000	1000	Ocular and nasal irritation and neurotoxicity in rats
LBW	NR	NR	NR	NR	NR	NR	No adequate data

Derivation of the Dutch Intervention Values

Little difference in toxicity has been observed between the different trimethylbenzene (TMB) isomers (1,2,4-TMB, 1,2,3-TMB, and 1,3,5-TMB). Since data for some individual TMB isomers is insufficient to set adequate limit values, data from all three isomers are used to set the limit values for the individual TMB isomers.

VRW: Repeated exposure of male and female rats to 1,2,4-TMB at 1,000 ppm (5,000 mg/m³) for 6 h, 5 days a week, 12 exposure resulted in initial signs of slight ocular and nasal irritation (see AGW). Rats exposed to 250-2000 ppm (1250-10,000 mg/m³) of either 1,2,4-, 1,3,5- or 1,2,3-TMB for four hours, exhibited decreased rotarod performance (mild neurological effect) with an EC_{50} calculated to be 954, 963, and 768 ppm, respectively, corresponding with 4770, 4814, and 3840 mg/m³. Since the EC_{50} values of individual TMBs are similar, an average EC_{50} for all three trimethylbenzenes of 900 ppm (4500 mg/m³) was calculated for the trimethylbenzene group and used as point of departure (PoD). Using the specific EC_{50} of 768 ppm (3840 mg/m³) for 1,2,3 TMB would result in similar VRW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The steady state in blood is reached after 1-2 hours. Therefore, the values for 1-8 hours were flat-lined. Time scaling to 10 and 30 minutes would lead to values conflicting with VRWs derived from slight ocular and nasal irritation observed at 1000 ppm (5000 mg/m³) in the other rat study (application of total UF of 10). Therefore, the 10 and 30 minute values were also set at 450 mg/m³.

AGW: The AGW is based on a repeated inhalation toxicity study with rats. Rats (n=4/sex) were exposed to 1000 (5000 mg/m³) or 2000 ppm (10,000 mg/m³) 1,2,4-TMB for 6h/d, for 12 days in a 5 days/week dosing regimen. The exposed rats suffered from nasal and ocular irritation, respiratory difficulty, lethargy, tremors, and decreased weight gain. Exposure at 1,000 ppm (5,000 mg/m³) resulted in initial signs of slight ocular and nasal irritation. All animals survived and no hematology changes or gross or histopathologic lesions were noted after exposure at either 1,000 or 2,000 ppm. There is no adequate data available, specifically with 1,3,5-TMB to derive the AGW. The level of 2,000 ppm (10,0000 mg/m³) from the study with 1,2,4-TMB was used as point of departure. The PoD is above the criteria for AGW, because the effects could lead to an impaired ability to escape. However, because the key study involved repeated exposures, 2,000 ppm was considered a conservative estimate of effects from a single exposure. Furthermore, no effects were reported in mice exposed to 1,2,4-TMB for up to 2,000 ppm (10,000 mg/m³) for 12h.The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The effects seen at this PoD include nasal and ocular irritation (in the absence of histopathological changes) as well as neurotoxicity. The combination of both effects support flatlining of AGW values over all time points.

LBW: No values for LBW could be derived due to lack of adequate data.

Additional toxicological information (including relevant results of a general literature search, if any)

Little is known about the mechanism of TMB toxicity. At higher concentrations, direct irritation of mucous membranes and narcosis was apparent in some of the animal studies; expected clinical effects include nasal/skin and eye irritation reduced consciousness and tremors.

Substance is not a reproductive toxicant

H332: harmful if inhaled, H315: causes skin irritation, H319: causes serious eye irritation, H335: may cause respiratory irritation

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not evaluated No carcinogenic risk potency (CRP) was derived	Odour: typical scent OT: 11 mg/m^3 (from AIHA, 1989) LOA = 11.8 * OT * 1.33 = 173 mg/m^3 (The concentration Level leading to distinct Odour Awareness (l=3) is calculated using the formula: l = 2.33 * log (C/OT) + 0.5. A correction factor of 1.33 is applied to this value) The LOA is below all VRW values.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*[75]

VRW level **450**	*AEGL-1* 690	*ERPG-1* -		*IDLH:* -
AGW level **1000**	*AEGL-2* 1800	*ERPG-2* -		
LBW level **NR**	*AEGL-3* NR	*ERPG-3* -		

[75] Note that the AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL.

Stofdocument deel A

CAS-nr: 75-77-4 **Trimethylchloorsilaan** C_3H_9ClSi **VN-nr: 1298**

GEVI: X338

Synoniemen: TMCS, trimethylsiliciumchloride, trimethylsilylchloride (Engels: trimethylchlorosilane) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	8,1	8,1	8,1	8,1	8,1	8,1
Alarmeringsgrenswaarden	AGW (mg/m³)	510	240	150	94	60	60
Levensbedreigende waarden	LBW (mg/m³)	1500	720	450	280	180	180

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,221ppm; 1 ppm = 4,52 mg/m³

Explosiegrens: LEL = 1,2 vol% ≈ 54.000 mg/m³

Geur: scherpe, bijtende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze, rokende vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,7

Molecuulmassa: 108,7 g/mol

Zuurgraad: geen data

LogKow: geen data

Wateroplosbaarheid: reactie

Verzadigde dampdruk: 253 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: irritatie van ogen en luchtwegen, tranenvloed, hoesten, lichte benauwdheid

AGW → LBW: ernstige irritatie van ogen en luchtwegen, pijn op de borst, benauwdheid, longontsteking, longoedeem

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Chloorsilanen reageren zeer snel met water onder vorming van chloorwaterstof (HCl). De acute toxiciteit van difenyldichloorsilaan wordt veroorzaakt door chloorwaterstof.
- Inhalatie van chloorwaterstof veroorzaakt een type I inhalatie intoxicatie.
- Chloorwaterstof veroorzaakt irritatie van de slijmvliezen van ogen en luchtwegen.
- Chloorwaterstof kan bij inhalatie longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, brandwonden

Oogcontact: bijtend, roodheid en pijn, hoornvliesbeschadiging, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: n.v.t.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen, en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen: geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 75-77-4 **Trimethylchlorosilane** **C_3H_9ClSi** **UN-nr: 1298**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same rationale as AEGL (analogy with HCl), 2h value added

LBW: Same rationale as AEGL (analogy with HCl), 2h value added

Date: November 2015 | AEGL document: Final 2012

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	8.1	8.1	8.1	8.1	8.1	8.1	Based on HCl (Threshold of irritation in humans)
AGW	510	240	150	94	60	60	Based on HCl (one-third of LBW)
LBW	1500	720	450	280	180	180	Based on HCl (Calculated threshold for lethality in animals)

Derivation of the Dutch Intervention Values

VRW: Since no appropriate data exist for trimethylchlorosilane, VRW values for hydrogen chloride will be used (on ppm-basis) to derive VRW values for trimethylchlorosilane. The use of hydrogen chloride as a surrogate for trimethylchlorosilane was deemed appropriate since it is believed that the hydrolysis product, HCl, is responsible for the adverse effects. Because one mole of hydrogen chloride are produced for every mole of trimethylchlorosilane, no molar adjustment factor was applied to the hydrogen chloride VRW values.

Derivation of VRW values for HCl

The hydrogen chloride VRW values were based on a no-adverse-effect-level of 1.8 ppm (2.73 mg/m³) in exercising asthmatics with an exposure duration of 45 min. Because the test subjects were considered a sensitive subpopulation and the endpoint was essentially a no-effect level, no uncertainty factor was applied to account for sensitive human subpopulations. The VRW values were held constant for all specified exposure periods since mild irritant effects represent threshold effects and generally do not vary over time.

AGW: Since no appropriate data exist for trimethylchlorosilane, AGW values for hydrogen chloride will be used (on ppm-basis) to derive AGW values for trimethylchlorosilane. Because one mole of hydrogen chloride are produced for every mole of trimethylchlorosilane, no molar adjustment factor was applied to the hydrogen chloride AGW values.

Derivation of AGW values for HCl

The AGW values of HCl for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data. The only study of HCl that addressed effects that meet the definition of an AGW, severe nasal lesions, was a study on hydrogen halides by Stavert et al. (1991). Nevertheless, this study was not considered a suitable basis for derivation of AGW values because 6% of the animals died after exposure to HCl at 1300 ppm (1974 mg/m³), only one concentration was tested and the number of animals tested was inconsistent.

LBW: Since no appropriate data exist for trimethylchlorosilane, LBW values for hydrogen chloride will be used (on ppm-basis) to derive LBW values for trimethylchlorosilane. Because one mole of hydrogen chloride are produced for every mole of trimethylchlorosilane, no molar adjustment factor was applied to the hydrogen chloride LBW values.

Derivation of LBW values for HCl

The LBW values were based on a lethality study in rats. The rat study included six exposure durations and various concentrations. Probit analyses using DoseResp was performed and yielded LC_{01} values for the 10 min, 30 min, 1-, 2-,4-, and 8hrs exposure durations of 3370, 1602, 1002, 627, 393 and 246 ppm (5116, 2433, 1522, 952, 596, and 373 mg/m³), respectively, which were used as point of departure for LBW derivation. The default total uncertainty factor of 10 (3x3) was considered

sufficient to account for inter- and intraspecies differences. The probit analyses yielded an n-value of 1.48, which was supported by the n-value of 1.59 calculated by Arts *et al.* (2000) from the C*t study. To maintain consistency with other hydrogen halogenides, the 8 hour value was set equal to the 4 hour value, as performed for the most potent hydrogen halogenide HF.

Additional toxicological information (including relevant results of a general literature search, if any)

No data concerning lethality and nonlethal toxicity in humans from trimethylchlorosilane exposure were located in the available literature.

Chlorosilanes react violently with water to produce hydrogen chloride gas. Data suggest that the acute toxicity of chlorosilanes is due to the hydrogen chloride hydrolysis product; acute toxicity of the chlorosilanes is both qualitatively (based on clinical signs) and quantitatively (based on molar equivalents of hydrogen chloride) similar to that of HCl.

Although toxicity data are limited for individual chlorosilanes, well-conducted 1-hr inhalation toxicity studies in rats are available for a series of chlorosilanes. In general, LC_{50} values for monochlorosilanes were approximately twice the LC_{50} values for dichlorosilanes and three times the LC_{50} values for trichlorosilanes. Clinical signs were consistent with hydrogen chloride exposure and included lacrimation, salivation, dried material around or on the eyes and/or nose, green staining around the nose and mouth, and perineal urine staining. Labored breathing, rales, hypoactivity, closed or partially closed eyes, prostration, corneal opacity or opaqueness, and swollen and/or necrotic paws were also observed. Hemorrhage, congestion and/or consolidation of the lungs, ectasia of the lungs, gaseous distension of the gastrointestinal tract, absence of body fat, obstruction of nostrils, dried and/or firm nares, alopecia around the eyes and discoloration of hair were observed at necropsy.

No data concerning the developmental or reproductive toxicity of trimethylchlorosilane were identified in the available literature.

No harmonized H-statements for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

No data concerning the carcinogenicity of trimethylchlorosilane in humans or experimental animals were identified in the available literature

Odour and derivation of the LOA value

Odour: sharp, acrid odour

No LOA was derived.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **8.1**	*AEGL-1* 8.1	*ERPG-1* 14		*IDLH:* not derived
AGW level **150**	*AEGL-2* 99	*ERPG-2* 90		
LBW level **450**	*AEGL-3* 450	*ERPG-3* 680		

Stofdocument deel A

CAS-nr: 1344-59-8 **Triuraniumoctaoxide**[76] **U_3O_8** **VN-nr: geen** **GEVI: geen**

Synoniemen: uraniumoctaoxide, uranium(V,VI)oxide (Engels: uranium oxide) ***Status:*** n.v.t.

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	99	68	54	43	28	14
Levensbedreigende waarden	LBW (mg/m³)	NA	NA	NA	NA	NA	NA

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,029 ppm; 1 ppm = 35,0 mg/m³

Explosiegrens: Geen data

Geur: Geen data

LOA: Niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: Olijfgroene tot zwarte vaste stof

Brand: Geen data

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa: 842,1 g/mol

Zuurgraad: Geen data

LogKow: Geen data

Wateroplosbaarheid: Niet oplosbaar

Verzadigde dampdruk: Geen data

Overige informatie

Publieke grenswaarde: Niet afgeleid

MAK: niet afgeleid

TLV-TWA: 0,2 mg U/m³ = 0,24 mg U_3O_8/m³ (8-uurs TGG)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: prikkeling, keelpijn en hoesten

*Boven **AGW***: verstoring van nier- en leverfunctie, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is

Toxiciteit bij eenmalige, inhalatoire blootstelling

- U_3O_8 is voornamelijk mechanisch irriterend, wat leidt tot milde huidirritatie en prikkeling van de slijmvliezen van ogen en bovenste luchtwegen.
- Nierfunctiestoornissen kunnen vertraagd optreden.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid.

Oogcontact: prikkeling, roodheid

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting** **stofdeeltjes

algemeen: frisse lucht, rust.

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep.

ogen: uitspoelen met water (evt. contactlenzen verwijderen)

inslikken: mond laten spoelen (uitspugen!) en onmiddellijk arts raadplegen.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

[76] Dit stofdocument behandelt alléén de chemische effecten van triuraniumoctaoxide. Voor informatie over effecten ten gevolge van straling wordt verwezen naar **International Commission on Radiological Protection (IRCP, 1990):** Recommendations of the International Commission on Radiological Protection. Pergamon Press, Oxford. 1991.

Stofdocument deel B

CAS-nr: 1344-59-8 **Uranium oxide**[77] **U_3O_8** **UN-nr: none**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with ERPG

AGW: Based on UO_2

LBW: Not recommended, in contrast with ERPG

Date: 31-10-2017 | ERPG 2003

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	99	68	54	43	28	14	Set in analogy with UO_2
LBW	NR	NR	NR	NR	NR	NR	Not recommended

Derivation of the Dutch Intervention Values

For the derivation of the Dutch Intervention Values use has been made of studies with depleted uranium. In real life additional effects as a result of radiation exposure cannot be excluded.

VRW: No reliable human or animal data were available to derive VRW values. In absence of appropriate data, the VRW was set to Not Recommended.

AGW: In the absence of suitable acute inhalation toxicity data, the AGW values are set in analogy with uraniumdioxide. Studies in rats and rabbits showed that 6,5 – 8 days of inhalation exposure to aerosols of U_3O_8 or UO_2 lead to similar total uranium content in lung tissue. Further, the pulmonary response in rats (effects on lung weight and gross lung damage) after repeated exposure to U_3O_8 or UO_2 showed similar effects and in rabbits, no effects on urinary protein were noted during the first 4 days of exposure. As U_3O_8 and UO_2 appear to be of similar toxic potency and effects are likely caused by the uranium component, the AGW-values for UO_2 expressed in mg/m³ were directly applied to U_3O_8. These AGW values are supported by the results for the long-term exposure in the studies mentioned above, which showed no changes in liver function in rats after exposure to U_3O_8 dust at a concentration of 14.5 mg U/m³ for 26 weeks, and slight changes in kidney, liver and lung condition in rats and rabbits exposed to 80 mg/m³ U_3O_8 for 6 weeks, 6 hours per day, 5 days per week.

Derivation of the AGW-values for UO_2:

AGW values are derived based on an acute inhalation study in rats (see below under “additional toxicological information”). Rats were exposed nose-only to 190 ± 41 mg/m³ for 30 minutes (n=12), 375 ± 70 mg/m³ for 2 hours (n=9), or 375 ± 70 mg/m³ for 3 hours (n=12). No clinical effects were observed. In addition, in the same study 6 rats were exposed repeatedly to to 190 ± 41 mg/m³ for 30 minutes per day, 4 days per week, for a total duration of 3 weeks. No significant changes in biochemical parameters for kidney and liver function were observed compared to the non-exposed control group. The 3-hour exposure to 375 mg/m³ was taken as a point of departure representing the highest exposure level at which no AGW-related effects are observed. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the default values of n=1 and n=3 when extrapolating to longer and shorter durations, respectively

LBW: No reliable human or animal data were available to derive LBW values. In absence of appropriate data, the LBW was set to Not Recommended.

Additional toxicological information (including relevant results of a general literature search, if any)

This document describes only the chemical effects of U_3O_8. For information about radiation effects, the reader is referred to radiological guidelines (e.g., the International Commission on Radiological Protection (ICRP)).

U_3O_8 belongs to the poorly soluble uranium compounds. Due to its water insolubility, after inhalation the retention time in the lungs my amount to several years. Therefore, the lungs are the primary target organ for U_3O_8, followed

[77] This document describes only the chemical effects of triuraniumoctaoxide. For information about radiation effects, the reader is referred to radiological guidelines (e.g., the International Commission on Radiological Protection (ICRP)).

by the kidneys.

In a ***UO_2*** study investigating the genotoxic and inflammatory effects of UO_2 inhalation (Monleau et al., 2006)[78], rats were exposed nose-only to 190 ± 41 mg/m^3 for 30 minutes (n=12), 375 ± 70 mg/m^3 for 2 hours (n=9), or 375 ± 70 mg/m^3 for 3 hours (n=12). In addition, 6 rats were exposed to 190 ± 41 mg/m^3 for 30 minutes per day, 4 days per week, for a total duration of 3 weeks. All rats survived the exposure. Rats were euthanized at different time points up to 14 days after exposure. No clinical effects were observed except for a momentary decrease in food consumption. In the repeated exposure group, biochemical parameters of kidney (creatinine, urea) and liver function (ALT and AST) were measured in the serum at 1, 3, and 8 days post-exposure. No significant changes in these parameters were found compared with the non-exposed control group. Some positive findings on DNA damage in BAL cells (comet assay) were observed at the highest acute exposure but these were concluded to be a consequence of inflammatory processes. No signs of DNA damage were found in kidney cells.

It has been estimated that soldiers who were exposed to aerosols containing depleted uranium during the 1991 Gulf War, had inhaled up to 79 mg of depleted uranium, 87% of which was expected to be in the form of U_3O_8. In an epidemiologic cohort study a subset of veterans, who were exposed to depleted uranium by inhalation and by having fragments of depleted uranium in their tissues, have been followed. Twenty-five years after exposure, no uranium-related health effects were observed among this cohort (McDiarmid et al 2017).

No reliable data were found regarding reproductive toxicity by inhalation of U_3O_8,

No harmonised H-sentences for human health.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified. No carcinogenic risk potency (CRP) was derived. Because U_3O_8 is radioactive, it could potentially damage DNA and lead to cancer; however, without knowing the precise degree of enrichment, it is difficult to quantitate the potential radiologic hazard.	Odour: No data. No LOA was derived due to lack of data.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **NR**	*AEGL-1* -	*ERPG-1* NR		*IDLH:* 10 mg U/m^3 (30 minutes) = 11.8 mg U_3O_8 / m^3
AGW level **54**	*AEGL-2* -	*ERPG-2* 10		
LBW level **NR**	*AEGL-3* -	*ERPG-3* 50		

[78] M. Monleau, M. De Méo, F. Paquet, V. Chazel, G.Duménil, M. Donnadieu-Claraz; Genotoxic and Inflammatory Effects of Depleted Uranium Particles Inhaled by Rats. *Toxicol Sci* 2006; 89 (1): 287-295. doi: 10.1093/toxsci/kfj010

Stofdocument deel A

CAS-nr: 1344-57-6 **Uraniumdioxide** [79] **O=U=O** **VN-nr: geen** **GEVI: geen**

Synoniemen: uranium(IV)oxide, uranyl(VI), dioxouranium (Engels: uranium dioxide) ***Status:*** n.v.t.

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	100	70	55	43	28	14
Levensbedreigende waarden	LBW (mg/m³)	NA	NA	NA	NA	NA	NA

Datum vaststelling: 31-10-2017 Conversiefactor: 1 mg/m³ = 0,089 ppm; 1 ppm = 11,2 mg/m³

Explosiegrens: geen data

Geur: geen data

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: Bruine tot zwarte kristalvormige vaste stof
Brand: Brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: Geen data

Molecuulmassa: 270,0 g/mol

Zuurgraad: Geen data

LogKow: Geen data

Wateroplosbaarheid: Niet oplosbaar

Verzadigde dampdruk: Geen data

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 0,2 mg/m³ (expressed as U) = 0,23 mg UO_2/m³ (8-uurs TGG)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: prikkeling, keelpijn en hoesten
*Boven **AGW***: verstoring van nier- en leverfunctie, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof is voornamelijk mechanisch irriterend, wat leidt tot milde huidirritatie en prikkeling van de slijmvliezen van ogen en bovenste luchtwegen.
- Nierfunctiestoornissen kunnen vertraagd optreden.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid

Oogcontact: prikkeling, roodheid

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting stofdeeltjes

algemeen: frisse lucht, rust.
huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep.
ogen: *uit*spoelen met water (evt. contactlenzen verwijderen)
inslikken: mond laten spoelen (uitspugen!) en onmiddellijk arts raadplegen.

***Specifieke behandeling en materialen**: geen.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

[79] Dit stofdocument behandelt alléén de chemische effecten van uraniumdioxide. Voor informatie over effecten ten gevolge van straling wordt verwezen naar **International Commission on Radiological Protection (IRCP, 1990):** Recommendations of the International Commission on Radiological Protection. Pergamon Press, Oxford. 1991.

Stofdocument deel B

CAS-nr: 1344-57-6 **Uraniumdioxide** [80] **O=U=O** **UN-nr: none**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with ERPG

AGW: Based on more recent toxicological information than described in the ERPG document

LBW: Not recommended, in contrast to ERPG

Date: 31-10-2017 | ERPG (2006)

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended
AGW	100	70	55	43	28	14	No clinical symptoms in rats
LBW	NR	NR	NR	NR	NR	NR	Not recommended

Derivation of the Dutch Intervention Values

For the derivation of the Dutch Intervention Values use has been made of studies with depleted uranium. In real life additional effects as a result of radiation exposure cannot be excluded.

VRW: No reliable human or animal data were available to derive VRW values. In absence of appropriate data, the VRW was set to Not Recommended.

AGW: AGW values are derived based on an acute inhalation study in rats (see below under "additional toxicological information"). Rats were exposed nose-only to 190 ± 41 mg/m³ for 30 minutes (n=12), 375 ± 70 mg/m³ for 2 hours (n=9), or 375 ± 70 mg/m³ for 3 hours (n=12). No clinical effects were observed. In addition, in the same study 6 rats were exposed repeatedly to to 190 ± 41 mg/m³ for 30 minutes per day, 4 days per week, for a total duration of 3 weeks. No significant changes in biochemical parameters for kidney and liver function were observed compared to the non-exposed control group. The 3-hour exposure to 375 mg/m³ is taken as a point of departure representing the highest exposure level at which no AGW-related effects are observed. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences.. Time scaling was applied using the default values of n=1 and n=3 when extrapolating to longer and shorter durations, respectively.

LBW: No reliable human or animal data were available to derive LBW values. In absence of appropriate data, the LBW was set to Not Recommended.

Additional toxicological information (including relevant results of a general literature search, if any)

UO_2 belongs to the poorly soluble uranium compounds. Due to its water insolubility, after inhalation the retention time in the lungs my amount to several years. Therefore, the lungs are the primary target organ for UO_2, followed by the kidneys.

In a study investigating the genotoxic and inflammatory effects of UO_2 inhalation (Monleau et al., 2006)[81], rats were exposed nose-only to 190 ± 41 mg/m³ for 30 minutes (n=12), 375 ± 70 mg/m³ for 2 hours (n=9), or 375 ± 70 mg/m³ for 3 hours (n=12). In addition, 6 rats were exposed to 190 ± 41 mg/m³ for 30 minutes per day, 4 days per week, for a total duration of 3 weeks. All rats survived the exposure. Rats were euthanized at different time points up to 14 days after exposure. No clinical effects were observed except for a momentary decrease in food consumption. In the repeated exposure group, biochemical parameters of kidney (creatinine, urea) and liver function (ALT and AST) were measured in the serum at 1, 3, and 8 days post-exposure. No significant changes in these parameters were found compared with the non-exposed control group. Some positive findings on DNA damage in BAL cells (comet assay) were observed at the highest acute exposure but these were concluded to

[80] This document describes only the chemical effects of UO_2. For information about radiation effects, the reader is referred to radiological guidelines (e.g., the International Commission on Radiological Protection (ICRP)).

[81] M. Monleau, M. De Méo, F. Paquet, V. Chazel, G.Duménil, M. Donnadieu-Claraz; Genotoxic and Inflammatory Effects of Depleted Uranium Particles Inhaled by Rats. *Toxicol Sci* 2006; 89 (1): 287-295. doi: 10.1093/toxsci/kfj010

be a consequence of inflammatory processes. No signs of DNA damage were found in kidney cells.

No reliable data were found regarding reproductive toxicity by inhalation of UO_2.

No harmonised H-sentences for human health.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived. Because UO_2 is radioactive, it could potentially damage DNA and lead to cancer; however, without knowing the precise degree of enrichment, it is difficult to quantitate the potential radiologic hazard.	Odour: No data. No LOA was derived due to lack of data.

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)*** [82]

VRW level **NR**	*AEGL-1* -	*ERPG-1* NR		*IDLH:* 10 mg U/m³ (30 minutes) = 11.3 mg UO_2 / m³
AGW level **55**	*AEGL-2* -	*ERPG-2* 10		
LBW level **NR**	*AEGL-3* -	*ERPG-3* 30		

[82] Note that the ERPG values as presented here (in mg/m³) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 7783-81-5 **Uraniumhexafluoride** UF_6 **VN-nr: 2977**

GEVI: 78

Synoniemen: uraniumfluoride (Engels: uranium hexafluoride) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	3,6	3,6	3,6	3,6	NA.	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	58	19	9,6	4,8	2,4	1,2
Levensbedreigende waarden	LBW (mg/m³)	219	73	37	18	9,1	4,6

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,068 ppm; 1 ppm = 14,6 mg/m³

Explosiegrens: geen data

Geur: geurloos

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot gele hygroscopische sneeuwachtige vaste stof, aan vochtige lucht rokend
Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa:	352 g/mol
Zuurgraad:	geen data
LogKow:	geen data
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	150 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 0,20 mg/m³ (oplosbare stof als uranium) (UF_6 0,30 mg/m³)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: irritatie aan ogen, huid en luchtwegen, keelpijn, hoesten

AGW → LBW: ernstige irritatie aan ogen, huid en luchtwegen, verlies van gezichtsvermogen, benauwdheid, longoedeem, nierschade

Boven LBW: ademnood , sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De schadelijke effecten van UF_6 worden veroorzaakt door de hydrolyseproducten fluorwaterstof (HF) en uranyl fluoride (UO_2F_2).
- Blootstelling aan HF kan tot longoedeem leiden, waarbij de verschijnselen vertraagd kunnen optreden en versterkt kunnen worden door lichamelijke inspanning.
- HF kan tot diep in de weefsels doordringen.
- Blootstelling aan UO_2F_2 kan nierbeschadiging veroorzaken.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, brandwonden
Oogcontact: bijtend, roodheid en pijn, corneabeschadiging, ernstige brandwonden, verlies van gezichtsvermogen

Carcinogeniteit

IARC classificatie: niet geclassificeerd.
CRP: niet afgeleid.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding, calciumgluconaatoplossing 4% als vernevelde oplossing laten inhaleren en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, afspoelen met water, daarna zo snel mogelijk calciumgluconaatgel 10% op de besmette huid aanbrengen en blijven inwrijven (bij het ontbreken van gel, doorgaan met spoelen met water), direct spoedeisende medische hulp inzetten. Bij het ontbreken van gel, doorgaan met spoelen met water.

ogen: uitspoelen met water (evt. contactlenzen verwijderen), daarna zo snel mogelijk calciumgluconaat oplossing 4% in de ogen druppelen, dan naar oogarts brengen, blijven druppelen tijdens vervoer (bij het ontbreken van gel, doorgaan met spoelen met water).

inslikken: mond laten spoelen (uitspugen!), 200 ml calciumgluconaat 4% laten drinken (indien niet aanwezig melk of water), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 7783-81-5 **Uranium hexafluoride** **UF_6** **UN-nr: 2977**

Basis for the Dutch Intervention Values

VRW: AEGL is adopted, 2h value added

AGW: AEGL is adopted, 2h value added

LBW: AEGL is adopted, 2h value added

Date: 24-09-2009 | AEGL document: Final, 2004

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	3.6	3.6	3.6	3.6	NR	NR	Based on HF (threshold of airway irritation in humans)
AGW	58	19	9.6	4.8	2.4	1.2	Renal pathology in animals
LBW	219	73	37	18	9.1	4.6	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: In the absence of relevant chemical-specific data for the derivation of VRW values, modifications of the VRW values for HF were used to derive the VRW values for UF_6. The use of HF as a surrogate for UF_6 was deemed appropriate for the development of VRW values because it is likely that HF, a hydrolysis product of UF_6, is responsible for the low level irritation effects of UF_6 relevant to the VRW definition. The HF VRW values were based on the threshold for pulmonary inflammation in healthy human adults at exposure of 3 ppm for 1 hour. The default intraspecies factor of 3 was used. Because a maximum of 4 mol of HF are produced for every mole of UF_6 hydrolyzed, a stoichiometric adjustment factor of 4 was applied to the HF VRW values to approximate VRW values for UF_6; the VRW values are constant across time up to 2 h; values were derived for only the 10-min, 30-min, 1-h and 2-h time points, because derivation of the 4- and 8-h VRW values resulted in values greater than the 4- and 8-h AGW for UF_6, which would be inconsistent with the total database.

AGW: Renal pathology observed in dogs was used as the point of departure for AGW values. The lowest concentration (192 mg/m^3) and the shortest exposure time (30 min) were used as point of departure for deriving VRW values. Although only one dog was exposed at each treatment level, the use of this data is supported by a study in which 17 dogs exposed to UO_2F_2 at 200-270 mg/m^3 for 30 min to 2.5 h exhibited similar renal pathology. UO_2F_2 is the hydrolysis product of UF_6 likely responsible for the renal effects. An uncertainty factor of 3 was used to extrapolate from animals to humans, and an uncertainty factor of 3 was also applied to account for sensitive individuals. This total uncertainty factor of 10 is considered sufficient, because the use of a higher factor would yield AGW values below or near VRW values. Time scaling was performed using $C^n \times t = k$, with default an n-value of 1.

LBW An estimated 1-h lethality threshold (one-third of the LC_{50}) in the rat of 365 mg/m^3 UF_6 was used as the point of departure for deriving the LBW values. This approach is considered appropriate due to the steepness (n = 0.66) of the concentration-response curve for lethality in rats exposed to UF_6. An intraspecies uncertainty factor of 3 was applied and is considered sufficient because the steep concentration-response curve for lethality implies little intra-individual variability. An uncertainty factor of 3 was also applied for interspecies variability. Application of higher uncertainty factors would result in LBW values inconsistent with the overall dataset. The value was then scaled to the 10-min, 30-min, 2-h, 4-h, and 8-h time points using $C^1 \times t = k$. An exponent value of n = 0.66 was derived from rat lethality data from experiments ranging in duration from 2 min to 1 h in the key study. The exponent was rounded to 1.0 for extrapolation because the data used to derive the exponent were limited (one study) and the derived n is below the range of a normal dose-response curve.

Additional toxicological information (including relevant results of a general literature search, if any)

People with impaired renal function (chemical toxicity of uranium), fetuses and developing neonates (radiologic hazard), and asthmatic individuals (HF toxicity) might be especially susceptible to UF_6 toxicity.

Case reports from human accidental exposures to UF_6 indicate that acute toxicity is chemical, not radiologic,

in nature and is due to the hydrolysis products, hydrogen fluoride (HF) and uranyl fluoride (UO_2F_2). At high concentrations, death from HF-induced pulmonary edema is observed. Kidney damage attributable to UO_2F_2, was also suggested from urinalysis data.

The available studies indicate that HF is a severe irritant to the skin, eyes, and respiratory tract. It is particularly irritating to the anterior nasal passages where, depending on species and concentration, it appears to be effectively scrubbed from the inhaled air. Effective deposition in the anterior nasal passages may be attributed to the high solubility and reactivity of HF. Penetration into the lungs results in pulmonary hemorrhage and edema and may result in death.

No developmental and reproductive or genotoxicity data of UF_6 in humans or animals were available.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified.

No carcinogenic risk potency (CRP) was derived.

No information concerning carcinogenicity in humans following acute inhalation exposure to UF_6 was located. Because UF6 is radioactive, it could potentially damage DNA and lead to cancer; however, without knowing the precise degree of enrichment, it is difficult to quantitate the potential radiologic hazard. The carcinogenic hazard from radiation exposure is considered to be negligible compared with the chemical toxicity from acute inhalation exposure to UF_6, even in the case of highly enriched UF_6.

Odour and derivation of the LOA value

Odour: odourless

No LOA was derived.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **3.6**	*AEGL-1* 3.6	*ERPG-1* 5		*IDLH* (30 minutes)*:* 10 (soluble compounds as uranium) (UF_6 at 14.8 mg/m³)
AGW level **9.6**	*AEGL-2* 9.6	*ERPG-2* 15		
LBW level **37**	*AEGL-3* 36	*ERPG-3* 30		

Stofdocument deel A

CAS-nr: 108-05-4 **Vinylacetaat** **CH_2=CHOOCH$_3$** **VN-nr: 1301** **GEVI: 339**

Synoniemen: acetoxyetheen, azijnzure vinylester, ethenylethanoaat (Engels: Vinyl acetate) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m^3)	24	24	24	24	24	24
Alarmeringsgrenswaarden	AGW (mg/m^3)	240	160	130	100	82	54
Levensbedreigende waarden	LBW (mg/m^3)	1200	820	650	520	410	270

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m^3 = 0,279 ppm; 1 ppm = 3,58 mg/m^3

Explosiegrens: LEL = 2,3 vol% ≈ 82.000 mg/m^3

Geur: scherpe, irriterende geur

LOA: 0,895 mg/m^3

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,2

Molecuulmassa:	86,1 g/mol
Zuurgraad:	geen data
LogKow:	0,7
Wateroplosbaarheid:	2,3 g/100 ml (matig)
Verzadigde dampdruk:	120 mbar

Overige informatie

Publieke grenswaarde: 18 mg/m^3

MAK: niet afgeleid

TLV-TWA: 36 mg/m^3

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	lichte oog-, neus- en keelirritatie
VRW → AGW:	oog- en bovenste luchtwegirritatie, branderig gevoel, keelpijn en hoesten, hoofdpijn
AGW → LBW:	tranenvloed, irritatie onderste luchtwegen, benauwdheid, verminderde coördinatie, bewustzijnsdaling
Boven LBW:	mogelijk schuimvorming in de luchtpijp en bloedingen in de luchtwegen, bewustzijnsdaling, convulsies, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Vinylacetaat werkt irriterend op de ogen en luchtwegen.
- Beschadiging van cellen in de luchtwegen ontstaat door pH-verlaging als gevolg van de omzetting van vinylacetaat in o.a. azijnzuur.
- Bij hoge concentratie en lange blootstellingsduur kan de stof de onderste luchtwegen bereiken.
- Vinylacetaat kan ook inwerken op het centrale zenuwstelsel met als gevolg bewustzijnsdaling en convulsies.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn, blaren.

De stof kan door de huid worden opgenomen.

Oogcontact: roodheid en pijn, slecht zien.

Carcinogeniteit

IARC classificatie: 2B

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, spoelen met veel water / kleding verwijderen, arts raadplegen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 108-05-4 **Vinyl acetate** **CH_2=CHOOCH$_3$** **UN-nr: 1301**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: November 2015 | AEGL document: Final, 2013

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	24	24	24	24	24	24	No effect level for notable discomfort in humans
AGW	240	160	130	100	82	54	No effect level for serious, long-lasting histopathologic nasal lesions in rats
LBW	1200	820	650	520	410	270	Highest nonlethal concentration in rats or mice

Derivation of the Dutch Intervention Values

VRW: The VRW was based on human data. In a controlled human exposure study, a 2-minute exposure to 4, 8, or 20 ppm (14, 29 or 72 mg/m^3) resulted in minimal eye, nose, and throat irritation in 1-2 of nine exposed individuals. Exposure to 20 ppm (72 mg/m^3) for 4 hours resulted in one of three individuals reporting persistent slight throat irritation. When exposure was increased to 34 ppm (122 mg/m^3) for 2 hours, one of three individuals complained of persistent throat irritation. Exposure to 72 ppm (258 mg/m^3) for 4 hours resulted in eye irritation and slight throat irritation for up to 60 minutes post exposure in all four subjects exposed. The point of departure is 20 ppm (72 mg/m^3), which represents a no-effect level for notable discomfort. An intraspecies uncertainty factor of 3 is applied because the irritation is caused by a local effect of the chemical and the response is not expected to vary greatly among individuals. No time-scaling was applied because irritation is considered a threshold effect and therefore should not vary over time.

AGW: AGW values are based on an animal study in which groups of 6 male rats were exposed to 0, 50, 200, 600, 1000 ppm (0, 179, 716, 2149, 3581 mg/m^3) vinyl acetate for 6 hours/day for a total of one, five or twenty consecutive exposures. Exposure to 200 ppm (716 mg/m^3) was considered to represent a NOAEL for serious long-lasting histopathological nasal lesions in rats exposed for 6 h. This was chosen as point of departure. Human data (2 h exposure to 34 ppm) resulted in persistent throat irritation (n=1/3) and 30 min exposure to 72 ppm (258 mg/m^3) resulted in ocular irritation and slight throat irritation up to 60 minutes after exposure (n=4/4)) were not used for deriving the AGW values, since this does not represent a health endpoint corresponding to the definition of the AGW intervention value and would lead to overly conservative AGWs. Therefore, rat histopathology data were used as basis for the AGW.
A total uncertainty factor of 10 was applied: 3 for interspecies and 3 for intraspecies variability. An interspecies uncertainty factor of 3 was applied on the basis that the mechanism of nasal toxicity appears to depend on the metabolism of vinyl acetate to the metabolites acetic acid and acetaldehyde via carboxylesterase and aldehyde dehydrogenase. Studies investigating the metabolism by the nasal cavity reported little difference among male and female mice, rats and humans in the carboxylesterase-mediated metabolism of vinyl acetate, particularly by olfactory epithelium. Time scaling was performed using $C^n \times t = k$, with the default values of n =1 and n = 3 for extrapolations to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-2 value that was set equal to the 30 minute AEGL-2 value, time scaling was also applied to derive the 10 minute AGW value.

LBW: Because the reported lethality data were not suitable for determining a lethality threshold for vinyl acetate, the LBW values are based on the highest non-lethal concentration in different species (rats, guinea pig, rabbit). A point of departure of 1,000 ppm (3580 mg/m^3) for 6 h was used to derive the LBW values. This was a nonlethal concentration in rats exposed for a single 6-h duration, as well as in both rats and mice exposed repeatedly for 6 h/day, 5 days/week for 4 weeks. A total uncertainty factor of 10 was applied: 3 for interspecies and 3 for intraspecies variability. An interspecies uncertainty factor of 3 was applied on the basis that the mechanism of nasal toxicity appears to depend on the metabolism of vinyl acetate to the metabolites acetic acid and acetaldehyde via carboxylesterase and aldehyde dehydrogenase. Studies investigating the metabolism by the nasal

cavity reported little difference among male and female mice, rats and humans in the carboxylesterase-mediated metabolism of vinyl acetate, particularly by olfactory epithelium. Esterase distribution in the nasal respiratory tissue of humans is believed to be similar to that of rats. An intraspecies uncertainty factor of 10 would normally be applied; however, a total uncertainty factor of 30 would reduce the LBW values to concentrations that did not result in serious health effects in human volunteer studies. Therefore, the intraspecies uncertainty factor was reduced to 3, and the total uncertainty factor is 10. Time scaling was performed using $C^n \times t = k$, with the default values of n =1 and n = 3 for extrapolations to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-3 value that was set equal to the 30 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Metabolism studies have demonstrated that vinyl acetate is metabolized to acetic acid and vinyl alcohol, which rearranges to form acetaldehyde. The acetaldehyde can be further metabolized to acetic acid. The reaction is catalyzed by carboxylesterase. Both acetic acid and acetaldehyde are nasal toxicants, and acetaldehyde has been shown to cause DNA-protein crosslinks in the rat nasal cavity. The metabolic rate of vinyl acetate is determined by the ventilation rate when metabolic saturation has not been reached. A study provided information on the deposition of inhaled vinyl acetate in the rat nasal cavity. The histopathology results demonstrated a strong anterior to posterior gradient, with the response moving anterior to posterior with increasing concentrations. These findings are indicative of a material in which deposition is metabolically dependent. As the concentration increases, fractional deposition decreases, due, in part, to saturation of the metabolism-dependent component of deposition. It appears that olfactory degeneration would be the primary endpoint until metabolic saturation in the nasal cavity is reached. Once metabolic saturation has occurred vinyl acetate would be able to make it further down into the respiratory tract.

No studies were found addressing the potential for inhaled vinyl acetate to cause developmental or reproductive effects in humans. A study in rats showed that inhalation of up to 1000 ppm (3580 mg/m^3) vinyl acetate for 6 hours/day from days 6 through 15 of gestation resulted in maternal and fetal toxicity (delay in growth) at the highest exposure concentration. It was concluded that vinyl acetate was not uniquely toxic to the fetus.

H25: Highly flammable liquid and vapour; H332: Harmful if inhaled; H335: May cause respiratory irritation; H351: Suspected of causing cancer.

Carcinogenicity and derivation of the CRP value

IARC classification: 2B (possibly carcinogenic to humans)

No carcinogenic risk potency (CRP) was derived.

A carcinogenicity assessment was not appropriate for an acute exposure scenario on the basis that the proposed mechanism of carcinogenicity suggests a nonlinear mode of action requiring continued exposure. Therefore, a one-time exposure even to high-concentrations would not be expected to result in tumor development.

Odour and derivation of the LOA value

Odour: immediately pleasant, but quickly becoming sharp and irritating
OT_{50}: 0.016 ppm (0.057 mg/m^3) [Hellman and Small (1974)]
LOA = 11.8 * OT_{50} * 1.33 = 0.895 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)
The LOA is below the VRW; therefore subjects will be aware of the odour below the level where health effects may be expected.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level	*AEGL-1*	*ERPG-1*		*IDLH*: not derived
24	24	18		
AGW level	*AEGL-2*	*ERPG-2*		
130	130	270		
LBW level	*AEGL-3*	*ERPG-3*		
650	640	1800		

Stofdocument deel A

CAS-nr: 75-01-4 **Vinylchloride** **CH_2=CHCl** **VN-nr: 1086** **GEVI: 239**

Synoniemen: chlooretheen, chloorethyleen (Engels: vinyl chloride) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	1.200	810	650	510	370	190
Alarmeringsgrenswaarden	AGW (mg/m³)	7.400	4.200	3.000	2.100	2.100	2.100
Levensbedreigende waarden	LBW (mg/m³)	31.000*	18.000*	13.000*	8.800	8.800	8.800

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,384 ppm; 1 ppm = 2,60 mg/m³

Explosiegrens: LEL = 3,6 vol% ≈ 94.000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

Geur: typerende geur, zoet

LOA: niet afgeleid.

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos onder druk tot vloeistof verdicht gas

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 2,2

Molecuulmassa: 62,5 g/mol

Zuurgraad: Geen data

LogKow: Geen data

Wateroplosbaarheid: 0,3 g/100 ml (slecht)

Verzadigde dampdruk: 3400 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 13 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

VRW → AGW: milde hoofdpijn

AGW → LBW: hoofdpijn, duizeligheid, misselijkheid, bewustzijnsdaling, longoedeem, leverschade

Boven LBW: coma, hartritmestoornissen, ademstilstand, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Vinylchloride heeft een depressieve werking op het centraal zenuwstelsel.
- Hoge concentratie kan de gevoeligheid van het hart voor adrenaline verhogen.
- Blootstelling aan vinylchloride kan leverschade veroorzaken.
- Vinylchloride is een genotoxisch carcinogeen

Effecten bij blootstelling aan vloeistof

Huidcontact: bij bevriezing: roodheid en pijn, blaren

Oogcontact: roodheid en pijn, bij bevriezing: ernstige brandwonden

Carcinogeniteit

IARC classificatie: 1

CRP: 910 mg/m³

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust en onmiddellijk arts raadplegen.

Ontsmetting vloeistof

huid: kleding uittrekken (NIET lostrekken), direct spoelen met veel water (minimaal 20 min.), dan pas eventueel aan de huid vastgevroren kleding verwijderen en verder spoelen,.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer..

inslikken: n.v.t. (gas).

Specifieke behandeling en materialen:.

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 75-01-4 **Vinyl chloride** **CH_2=CHCl** **UN-nr: 1086**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2hr value added.

AGW: AEGL value is adopted, 2hr value added.

LBW: AEGL value is adopted, 2hr value added.

Date: 24-09-2009 | AEGL document, interim 2008

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	1,200	810	650	510	370	190	Mild headache in humans
AGW	7,400	4,200	3,000	2,100	2,100	2,100	Threshold of neurotoxic effects in humans
LBW	31,000 *	18,000 *	13,000 *	8,800	8,800	8,800	Threshold of animal mortality, cardiac sensitization.

* value higher than 10% of LEL

Derivation of the Dutch Intervention Values

VRW: The endpoint "mild headache" can be regarded as a no effect level for notable discomfort (491 ppm (1,277 mg/m^3) for 3.5 h). Occurrence of headache has been reported in two subjects after acute exposure (the time of onset of headaches is not specified and is assumed to have occurred after 3.5 hours of exposure). Headaches observed in occupationally exposed persons at unknown exposure levels of vinyl chloride support the use of headache (the least severe effect) as a VRW type effect. An intraspecies factor of 3 is employed: it is assumed that the effects are due to vinyl chloride itself and not due to a metabolite, so only small interindividual differences are expected. Time scaling was performed using $C^n * t = k$ with the default n-values n=1 and n=3, as the mechanism for the induction of headache is not well understood. The extrapolation to 10 minutes from a 3.5 hour exposure is justified because exposure of human at 4,000 ppm (10,400 mg/m^3) for 5 minutes did not result in headache. However, the resulting VRW values may not provide a sufficient margin of safety to avoid mutational events or malignancies after short-term exposure to vinyl chloride (see CRP below)).

AGW: Dizziness, reeling, swimming head, nausea etc., which can be regarded as early signs of narcosis, have been reported in humans exposed to vinyl chloride in concentrations greater than or equal to 12,000 ppm (31,200 mg/m^3) for 5 min. The effects were only seen in 1 or 2 of 6 persons (one person was unsure of an effect) and do not yet impair the capability to escape, whereas, the effects observed at concentrations greater than or equal to 16,000 ppm (41,600 mg/m^3) (dizziness, nausea, headache, dulling of visual and auditory cues) might possibly impair escape. Therefore, 12,000 ppm (31,200 mg/m^3) is interpreted as the no effect level for impaired ability to escape and is used to derived the AGW values. By analogy to other anaesthetics the effects are assumed to be solely concentration dependent. Thus, after reaching steady state at about 2 hours of exposure, no increase in effect is expected. An intraspecies factor of 3 is applied. The other exposure duration-specific values were derived by time scaling according to the dose-response regression equation $C^n * t = k$, using a factor of n=2, based on experimental data. With this, time extrapolation was performed from 5 to 10, 30, 60 minutes and 2 hours, where the steady state concentration was calculated. However, the resulting AGW values may not provide a sufficient margin of safety to avoid mutational events or malignancies after short-term exposure to vinyl chloride (see CRP below).

LBW: Lethality data provide LBW values that are marginally higher than those derived based on cardiac sensitization. Thus, animal data on cardiac sensitization after exposure for 5 minutes were used to derive the LBW. Severe cardiac sensitization is a life threatening effect, but at 50,000 ppm (130,000 mg/m^3) no animals died in the reported study. Therefore, 50,000 ppm is used to derive LBW values. A total uncertainty factor of 3 is used to account for toxicodynamic differences among individuals. As the challenge with epinephrine and the doses of epinephrine used represent a conservative scenario, no interspecies uncertainty factor was used. As the unmetabolized vinyl chloride is responsible for the effect, no relevant differences in toxicokinetics are assumed. After reaching steady state at about 2 hours of exposure, no increase in effect is expected (see also AGW derivation). The other exposure duration-specific values were derived by time scaling according to the dose-response regression equation $C^n * t = k$, using an n of 2, With this, time extrapolation was performed from 5 to 10, 30, 60 minutes and 2 hours, where the steady state concentration was calculated.

Additional toxicological information (including relevant results of a general literature search, if any)

Acute neurotoxicity by inhalation of high vinyl chloride concentrations is likely dependent upon vinyl chloride concentrations and independent of its metabolism. This assumption is supported by comparison of narcotic concentrations which are similar for the four species guinea pig, mouse, rabbit and rat. Acute toxicity/lethality is mainly accompanied by congestion of all internal organs, pulmonary edema, liver and kidney changes (up to necrosis). The mechanism of action is not elucidated; toxic effects are possibly mediated by reactive metabolites.
Acute exposure of experimental animals towards vinyl chloride results in narcotic effects, cardiac sensitization, and hepatotoxicity. Narcotic effects are characterized by a typical sequence of events from euphoria and dizziness, followed by drowsiness and loss of consciousness. Finally, animals die due to respiratory failure.

No reproductive toxicity or developmental toxicity studies with single exposure were identified. In repeated exposure studies always maternal effects were observed when fetal effects were found.

H350: May cause cancer

Carcinogenicity and derivation of the CRP value

IARC classification: 1 (carcinogenic to humans)

Derivation of the carcinogenic risk potency (CRP):

10^{-4} risk level after inhalation: 33 * 10^{-3} mg/m^3 [Maltoni et al., 1981, assumed 150 weeks exposure]

CRP, 24 hrs = 49 mg/m^3

CRP, 1 hr = 910 mg/m^3

Based on the cancer incidence as evident from a five-weeks animal study assuming that 5 weeks of exposure of an animal is equivalent to about 150 weeks exposure of humans, with linear transformation to a single 24 hour exposure without further correction for potential sensitive stages of tumor development. Exposures of less than 24 hours are derived using a PBPK model, because the model uses human parameters to transform the internal dose of a metabolite of vinyl chloride required for a tumor response (based on animal studies) to an external exposure concentration for humans. This way, the strict C x t protocol is not applied to exposure durations under 24 hours. Tumors observed were angiosarcomas and hepatomas. Note that the CRP is below the 10min-VRW of 1,200 mg/m^3.

Odour and derivation of the LOA value

Odour: sweet odour

No LOA was derived due to lack of reliable data. Odour thresholds were reported in the range from 10 to 25,000 ppm (26 to 65,000 mg/m^3).

Other standards and guidelines *(1h values in mg/m^3, unless otherwise indicated)*

VRW level **650**	*AEGL-1* 650	*ERPG-1* 1,300		*IDLH:* not established
AGW level **3,000**	*AEGL-2* 3,100	*ERPG-2* 13,000		
LBW level **13,000**	*AEGL-3* 12,000	*ERPG-3* 52,000		

Stofdocument deel A

CAS-nr: 75-94-5 **Vinyltrichloorsilaan** $C_2H_3Cl_3Si$ **VN-nr: 1305**

GEVI: X338

Synoniemen: ethenyltrichloorsilaan, trichloorvinylsilaan, VTCS (Engels: vinyl trichlorosilane)

Status: A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	4,0	4,0	4,0	4,0	4,0	4,0
Alarmeringsgrenswaarden	AGW (mg/m³)	250	120	75	47	29	29
Levensbedreigende waarden	LBW (mg/m³)	750	360	220	140	88	88

Datum vaststelling: November 2015

Conversiefactor: 1 mg/m³ = 0,149 ppm; 1 ppm = 6,72 mg/m³

Explosiegrens: LEL = 3,2 vol% ≈ 215.000 mg/m³

Geur: scherpe geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze rokende vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,4

Molecuulmassa:	161,5 g/mol
Zuurgraad:	geen data
LogKow:	geen data
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	65 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW	geen informatie
VRW → AGW:	irritatie van ogen en luchtwegen, tranenvloed, hoesten, lichte benauwdheid
AGW → LBW:	ernstige irritatie van ogen en luchtwegen, pijn op de borst, benauwdheid, longontsteking, longoedeem
Boven LBW:	ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Chloorsilanen reageren zeer snel met water onder vorming van chloorwaterstof (HCl). De acute toxiciteit van vinyltrichloorsilaan wordt veroorzaakt door chloorwaterstof.
- Inhalatie van chloorwaterstof veroorzaakt een type I inhalatie intoxicatie.
- Chloorwaterstof veroorzaakt irritatie van de slijmvliezen van ogen en luchtwegen.
- Chloorwaterstof kan bij inhalatie longontsteking en/of longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, brandwonden.

Oogcontact: bijtend, roodheid en pijn, hoornvliesbeschadiging, ernstige brandwonden.

Carcinogeniteit

IARC classificatie: niet geclassificeerd.

CRP: niet afgeleid.

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust; in geval van rode ogen halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken (voorzichtig i.v.m mogelijk reeds beschadigde huid), minimaal 20 min. spoelen met veel water of douchen, en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen:.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 75-94-5 **Vinyl trichlorosilane** **$C_2H_3Cl_3Si$** **UN-nr: 1305**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same rationale as AEGL (analogy with HCl), 2h value added

LBW: Same rationale as AEGL (analogy with HCl), 2h value added

Date:November 2015 | AEGL document: Final, 2012

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	4.0	4.0	4.0	4.0	4.0	4.0	Based on HCl (Threshold for irritation in humans)
AGW	250	120	75	47	29	29	Based on HCl (one-third of LBW))
LBW	750	360	220	140	88	88	Based on HCl (Calculated threshold for lethality in animals)

Derivation of the Dutch Intervention Values

VRW: Since no appropriate data exist for vinyl trichlorosilane, VRW values for hydrogen chloride will be used (on ppm-basis) to derive VRW values for vinyl trichlorosilane. The use of hydrogen chloride as a surrogate for vinyl trichlorosilane was deemed appropriate since it is believed that the hydrolysis product, HCl, is responsible for the adverse effects. Because three moles of hydrogen chloride are produced for every mole of vinyl trichlorosilane, a molar adjustment factor of 3 was applied to the hydrogen chloride VRW values.

Derivation of VRW values for HCl

The hydrogen chloride VRW values were based on a no-adverse-effect-level of 1.8 ppm (2.73 mg/m³) in exercising asthmatics with an exposure duration of 45 min. Because the test subjects were considered a sensitive subpopulation and the endpoint was essentially a no-effect level, no uncertainty factor was applied to account for sensitive human subpopulations. The VRW values were held constant for all specified exposure periods since mild irritant effects represent threshold effects and generally do not vary over time.

AGW: Since no appropriate data exist for vinyl trichlorosilane, AGW values for hydrogen chloride will be used (on ppm-basis) to derive AGW values for vinyl trichlorosilane. Because three moles of hydrogen chloride are produced for every mole of vinyl trichlorosilane, a molar adjustment factor of 3 was applied to the hydrogen chloride AGW values.

Derivation of AGW values for HCl

The AGW values of HCl for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data. The only study of HCl that addressed effects that meet the definition of an AGW, severe nasal lesions, was a study on hydrogen halides by Stavert et al. (1991). Nevertheless, this study was not considered a suitable basis for derivation of AGW values because 6% of the animals died after exposure to HCl at 1300 ppm (1974 mg/m³), only one concentration was tested and the number of animals tested was inconsistent.

LBW: Since no appropriate data exist for vinyl trichlorosilane, LBW values for hydrogen chloride will be used (on ppm-basis) to derive LBW values for vinyl trichlorosilane. Because three moles of hydrogen chloride are produced for every mole of vinyl trichlorosilane, a molar adjustment factor of 3 was applied to the hydrogen chloride LBW values.

Derivation of LBW values for HCl

The LBW values were based on a lethality study in rats. The rat study included six exposure durations and various concentrations. Probit analyses using DoseResp was performed and yielded LC_{01} values for the 10 min, 30 min, 1-, 2-,4-, and 8hrs exposure durations of 3370, 1602, 1002, 627, 393 and 246 ppm (5116, 2433, 1522, 952, 596, and 373 mg/m³), respectively, which were used as point of departure for LBW derivation. The default total uncertainty factor of 10 (3x3) was considered

sufficient to account for inter- and intraspecies differences. The probit analyses yielded an n-value of 1.48, which was supported by the n-value of 1.59 calculated by Arts *et al.* (2000) from the C*t study. To maintain consistency with other hydrogen halogenides, the 8 hour value was set equal to the 4 hour value, as performed for the most potent hydrogen halogenide HF.

Additional toxicological information (including relevant results of a general literature search, if any)

No data concerning lethality or nonlethal toxicity in humans from vinyl trichlorosilane were located in the available literature.

Chlorosilanes react violently with water to produce hydrogen chloride gas. Data suggest that the acute toxicity of chlorosilanes is due to the hydrogen chloride hydrolysis product; acute toxicity of the chlorosilanes is both qualitatively (based on clinical signs) and quantitatively (based on molar equivalents of hydrogen chloride) similar to that of HCl.

Although toxicity data are limited for individual chlorosilanes, well-conducted 1-hr inhalation toxicity studies in rats are available for a series of chlorosilanes. In general, LC_{50} values for monochlorosilanes were approximately twice the LC_{50} values for dichlorosilanes and three times the LC_{50} values for trichlorosilanes. Clinical signs were consistent with hydrogen chloride exposure and included lacrimation, salivation, dried material around or on the eyes and/or nose, green staining around the nose and mouth, and perineal urine staining. Labored breathing, rales, hypoactivity, closed or partially closed eyes, prostration, corneal opacity or opaqueness, and swollen and/or necrotic paws were also observed. Hemorrhage, congestion and/or consolidation of the lungs, ectasia of the lungs, gaseous distension of the gastrointestinal tract, absence of body fat, obstruction of nostrils, dried and/or firm nares, alopecia around the eyes and discoloration of hair were observed at necropsy.

No data concerning developmental/reproductive toxicity for exposure to vinyl trichlorosilane were located in the available literature.

No harmonized H-statements for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified.

No carcinogenic risk potency (CRP) was derived

No data concerning carcinogenicity for exposure to vinyl trichlorosilane were located in the available literature.

Odour and derivation of the LOA value

Odour: pungent odour

No LOA was derived due to lack of data.

***Other standards and guidelines** (1h values in mg/m³, unless otherwise indicated)*

VRW level **4.0**	*AEGL-1* 4.0	*ERPG-1* 3.4		*IDLH:* not derived
AGW level **75**	*AEGL-2* 49	*ERPG-2* 34		
LBW level **220**	*AEGL-3* 220	*ERPG-3* 340		

Stofdocument deel A

CAS-nr: 50782-69-9 **VX** **$C_{11}H_{25}NO_2PS$** **VN-nr: geen**

GEVI: geen

Synoniemen: Agent VX, Zenuwgas VX, O-ethyl-S-(diisopropylaminoethyl)methylfosfonothiolaat (Engels: agent VX)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,00070	0,00036	0,00020	0,00013	0,00010	$6{,}6x10^{-5}$
Alarmeringsgrenswaarden	AGW (mg/m³)	0,035	0,011	0,005	0,0024	0,0011	0,00052
Levensbedreigende waarden	LBW (mg/m³)	0,099	0,030	0,014	0,0067	0,0032	0,0015

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,09 ppm; 1 ppm = 11,1 mg/m³

Explosiegrens: geen gegevens

Geur: geurloos

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: amberkleurige viskeuze vloeistof

Brand: geen gegevens

Relatieve dichtheid van verzadigd damp-lucht mengsel: 9,2

Molecuulmassa: 266 g/mol

Zuurgraad: Geen data

LogKow: Geen data

Wateroplosbaarheid: Geen data

Verzadigde dampdruk: 0,001 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 1 x 10^{-5} mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: oogpijn, hoofdpijn

VRW → AGW: pupilvernauwing, misselijkheid, braken

AGW → LBW: speekselvloed, tranenvloed, benauwdheid, spiertrillingen, verlammingsverschijnselen, bewustzijnsdaling

Boven LBW: convulsies, coma, verlamming, ademstilstand, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Zenuwgas VX is een zeer potente irreversibele cholinesterase remmer. Hierdoor wordt de afbraak van de neurotransmitter acetylcholine geremd en de zenuwimpuls bij de motorische eindplaat verstoord.
- Doelorganen zijn het centrale en perifere zenuwstelsel.
- De meeste effecten treden zeer snel op, echter neuropathologische effecten zoals verlamming kunnen vertraagd optreden en langdurig van aard zijn.

Effecten bij blootstelling aan vloeistof

Huidcontact: spiertrillingen, zweten, misselijkheid, braken, diarree, zwaktegevoel, bewusteloosheid, toevallen, ademstilstand.

Oogcontact: roodheid en (hevige) pijn, nauwe pupillen, visusklachten, tranenvloed, en verdere systemische effecten

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, specifieke behandeling en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!) , specifieke behandeling en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: benodigde middelen (100% zuurstof, specifieke antidota zoals o.a. atropine) moeten met gebruiksaanwijzing beschikbaar zijn.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 50782-69-9 **Agent VX** **$C_{11}H_{25}NO_2PS$** **UN-nr: none**

Basis for the Dutch Intervention Values

VRW: Based on recent available data of Benton et al., 2006a.

AGW: Based on recent available data of Genovese et al., 2007.

LBW: Based on recent available data of Benton et al., 2006b.

Date: 24-09-2009 | AEGL document Final 2003.

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.00070	0.00036	0.00020	0.00013	0.00010	0.000066	Miosis (pupil constriction) in animals.
AGW	0.035	0.011	0.005	0.0024	0.0011	0.00052	Ataxia, miosis in animals
LBW	0.099	0.030	0.014	0.0067	0.0032	0.0015	Threshold of animal lethality

Derivation of the Dutch Intervention Values

VRW: VRW values can be derived using recent data of Benton *et al.* (2006a), where adult rats were exposed to VX vapour at various concentrations for several exposure durations. In this study, female rats were more sensitive to the miotic effects than males. As point of departure for the VRW values the 10 min, 1-h and 4-h EC_{50} values for miosis in female rats of 0.007, 0.002 and 0.001 mg/m³ were used. An interspecies factor of 1 was considered appropriate as the miosis response to nerve agents is similar across species. An intraspecies factor of 10 was applied, because of human variability of blood cholinesterase and carboxyesterase activity. Subjects with abnormally low blood activity levels are especially susceptible to the effects of cholinesterase inhibitors. Time scaling was performed using $C^n \times t = k$. Based on the miosis data an n-value of 1.65 could be derived, which is used to derive the 30-min (from 10-min data), 2-h (from 1-h data) and 8-h (from 4-h data) VRW values.

The AEGL committee used the sarin database and a relative potency factor to derive the AEGL-1 values for VX. Because relevant data have become available on agent VX itself, it was preferred to use that data instead of the sarin data as point of departure. The sarin database supports the choice of point of departure, because almost similar VRW values are obtained.

Benton BJ, Sommerville DR, Anthony JS et al. (2006a) Low-level effects of VX vapor exposure on pupil size and cholinesterase levels in rats. Inhalation Toxicology (2nd Edition)

AGW: The AGW values were based on data from a recently published study (Genovese et al., 2007). Rats were exposed to 0.016, 0.15, 0.30, 0.45 mg/m³ for 1-h and tested for behavioural effects and cholinesterase activity. At this level, pinpoint pupils (miosis) were observed in the rats. At 0.016 mg/m³ VX exposure, miosis and reduction in cholinesterase activity were observed. At 0.15 and 0.30 mg/m³ exposure to VX no additional toxicity signs were observed, except for one animal in the 0.30 mg/m³ group, which was observed to be ataxic. In the 0.45 mg/m³ group 5/6 animals were observed to be ataxic. Therefore, exposure to 0.15 mg/m³ for 1-hr, considered the NOEL for ataxia, was selected as point of departure. An interspecies factor of 3 was applied to protect against ataxia, instead of the factor of 1 that would suffice for the endpoint miosis, which is considered similar across species. An intraspecies factor of 10 was applied, because of human variability of blood cholinesterase and carboxyesterase activity. Subjects with abnormally low blood activity levels are especially susceptible to the effects of cholinesterase inhibitors. Time scaling was performed using $C^n \times t = k$. Based on ataxia an n-value of 0.92 could be derived to derive the AGW values.

The AEGL committee used the sarin database and a relative potency factor to derive the AEGL-2 values for VX. Because relevant data have become available on agent VX itself, it was preferred to use that data instead of the sarin data as point of departure. The sarin database supports the choice of point of departure, because almost similar AGW values are obtained.

Genovese RF, Benton BJ, Lee EH, Shippee SJ, Jakubowski EM. (2007) Behavioral and biochemical evaluation of sub-lethal inhalation exposure to VX in rats. Toxicology 2007; 232(1-2):109-18.

LBW: As point of departure for the LBW values, the female rat lethality data from a recently performed study (Benton et al., 2006b) were used. The study included three exposure durations, i.e. 10, 60 and 240 minutes) and introduced exposure concentrations ranging from 0.14 to 6.35 mg/m³. The

calculated LC_{01} values for the 10 min, 30 min, 1-, 2-, 4-, and 8-h were 2.98, 0.90, 0.43, 0.20, 0.095, and 0.045 mg/m^3, respectively. The LBW values were derived by dividing the point of departures by the total uncertainty factor of 30. The total uncertainty factor consists of an interspecies factor of 3 and an intraspecies factor of 10. Because the point of departure was determined for each LBW separately, no time scaling was necessary. The lethality data showed an n-value of 0.92 (point of departures and n-value were calculated using DoseResp, ten Berge, 2006).

The AEGL committee used the sarin database and a relative potency factor to derive the AEGL-3 values for VX. Because relevant data have become available on agent VX itself, it was preferred to use that data instead of the sarin data as point of departure. The sarin database supports the choice of point of departure, because almost similar LBW values are obtained.

Benton BJ, McGuire JM, Sommerville DR et al. (2006b) Effects of whole-body VX vapor exposure on lethality in rats. Inhal Toxicol 2006; 18(14):1091-9.

Additional toxicological information (including relevant results of a general literature search, if any)

Nerve agent VX is very potent cholinesterase inhibitor. The warfare agent is structurally related to the agent G-series, amongst which is agent GB (Sarin), and of which agent VX is the most potent (four times more potent than sarin). Their mechanism of action is the same.
Nerve agents exert toxic effects on the central and peripheral nervous system indirectly through acetylcholinesterase inhibition, nerve agents may also affect nerve impulse transmission by additional mechanisms at neuromuscular junctions and at neurotransmitter receptor sites in the CNS. The first symptoms are related to the nerve conduction inhibition by the substance and consist of: pupil constriction (miosis), headache, shortness of breath, tightness of the chest. A runny nose and lacrimation can also be observed. At increasing exposure levels or prolonged exposures sweating, diarrhea, bradycardia, tremors, overall weakness, paralysis, unconsciousness, convulsions, suppression of respiration and death can occur. The dose-response relation is considered very steep and effects may occur rapidly. However, delayed neuropathological effects (such as paralysis) may occur.

No evidence has been found that Agent VX is a reprotoxic or developmental toxic substance.

No harmonized risk phrases were found.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: Odourless

No LOA was derived since agent VX is odourless.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level	*AEGL-1*	*ERPG-1*		*IDLH: not derived*
0.00020	0.00017	Not derived		
AGW level	*AEGL-2*	*ERPG-2*		
0.0050	0.0029	Not derived		
LBW level	*AEGL-3*	*ERPG-3*		
0.014	0.010	Not derived		

Stofdocument deel A

CAS-nr: 7722-84-1 **Waterstofperoxide 90%** H_2O_2 **VN-nr: 2015**
GEVI: 559

Synoniemen: - (Engels: hydrogen peroxide) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarde	VRW (mg/m³)	3,1	3,1	3,1	3,1	3,1	3,1
Alarmeringsgrenswaard	AGW (mg/m³)	70	48	38	30	24	12
Levensbedreigende	LBW (mg/m³)	210	150	120	91	73	36

Datum vaststelling: 31-10-2017

Conversiefactor: 1 mg/m³ = 0,707 ppm; 1 ppm = 1,414 mg/m³

Explosiegrens: -
Kans op explosie door ontleding en vermenging met andere stoffen.

Geur: typerende, scherpe geur
LOA: niet afgeleid

Fysisch-chemische eigenschappen[83]

Uiterlijk: kleurloze oplossing
Brand: niet brandbaar, maar bevordert brand van andere stoffen

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,17 (ERPG 1997)

Molecuulmassa: 34,0 g/mol

Zuurgraad: 4,3
LogKow: -1,1 (berekend)
Wateroplosbaarheid: volledig

Verzadigde dampdruk: 1 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: 0,71 mg/m³
TLV-TWA: 1,4 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: prikkeling ogen en luchtwegen

VRW → AGW: hoesten, keelpijn, kortademigheid

AGW → LBW: hoofdpijn, duizeligheid, ademnood

Boven LBW: hypotensie, convulsies, coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof veroorzaakt vooral irritatie van de ogen en luchtwegen
- Blootstelling aan hoge concentraties (>10%) kan ernstige irritatie en ontsteking van de luchtwegen, dyspnoe en hoesten veroorzaken. Longoedeem kan optreden tot 24-72 uur na blootstelling.
- Na inhalatie van hoge concentraties kan ook een systemische vergiftiging met shock, coma en convulsies optreden. In ernstige gevallen kans op gas-embolieën en dodelijke afloop.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, bleke huidverkleuring, gezwollen huid, roodheid en pijn, brandwonden

Oogcontact: bijtend, roodheid en pijn, hoornvliesbeschadiging, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding, direct spoedeisende medische hulp inzetten

Ontsmetting vloeistof
huid: spoelen met veel water / kleding verwijderen, direct spoedeisende medische hulp inzetten.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.
inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

[83] Deze fysisch-chemische info is gebaseerd op de Chemiekaart van de 50-60% oplossing in water

CAS-nr: 7722-84-1 **Hydrogen peroxide** H_2O_2 **UN-nr: 2015**

Basis for the Dutch Intervention Values

VRW: Based on additional information than described in ERPG-document, other time-points added

AGW: Different rationale than ERPG, other time points added

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017 | ERPG 2010

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	3.1	3.1	3.1	3.1	3.1	3.1	Slight respiratory irritation in humans
AGW	70	48	38	30	24	12	One third of LBW
LBW	210	150	120	91	73	36	Threshold for lethality in mice

Derivation of the Dutch Intervention Values

VRW: The VRW was based on results of a human volunteer study (see for details "additional toxicological information" below). Healthy, adult volunteers (n=11) were exposed in an inhalation chamber to 0, 0.5 and 2.2 ppm hydrogen peroxide (corresponding to 0, 0.71 and 3.1 mg/m³) during 2 hours. Exposure to 3.1 mg/m³ resulted in slight irritation as measured by increased nasal airway resistance. A 2 hour exposure to 3.1 mg/m³ was used as point of departure for the VRW. As it is noted that none of the other irritation parameters are statistically significantly altered and the change in nasal airway resistance is transient, an intraspecies uncertainty factor of 1 was considered sufficient. Time scaling was not applied. This approach was considered appropriate because mild irritant effects are considered concentration-dependent rather than concentration x time-dependent.
Additional human data are also available: A health surveillance of occupational exposure showed Shift mean levels < 1.4 mg/m³, short term concentrations up to 5 mg/m³, some accidental exposures to 10 mg/m³ with no effects on lung function, occasional skin irritation and whitening following accidental hydrogen peroxide exposure at two plants, past reports of hair bleaching at one plant, one case of acute throat irritation. A second health surveillance showed employees with less than 3 years exposure to peak concentrations of 11 mg/m³, and 8 hour TWA concentrations of 2-3 mg/m³ combined with intermittent skin contact, showing irritation of the eyes and airways, headaches, temporary loss of olfaction, effects on skin and bleaching of hair. A subsequent reduction in concentrations was associated with a reduction in symptoms. Finally, a case study included 7 operators of milk packaging machines with long term exposure to 12 mg/m³ and short term exposures to up to 41 mg/m³ (daily exposure over 6 months preceded by exposure 2 days per week for 3 years), with eye and throat irritation and gradual bleaching of the hair in all 7 subjects, though in one single subject progressive dyspnea, bilateral diffuse nodular infiltrates of the lung occurred. The dyspnea in this subject resolved within 1.5 months of exposure ceasing. It should be noted that this individual had smoked 2 packs of cigarettes per day for 25 years.

AGW: The AGW values of hydrogen peroxide for the 10-min, 30-min, 1-, 2-, 4- and 8-hour time points were derived by dividing the LBW values by a factor of 3 due to the absence of suitable data.

LBW: LBW values were based on an acute mouse inhalation toxicity study. Mice (n=10 or 25/group) were exposed whole body for 4 hours to 37.4, 78.1, 113, 194, 226 and 227 ppm hydrogen peroxide (corresponding to 53, 110, 160, 274, 320, 321 mg/m³). Mortality was as follows: 0/10, 0/10, 4/10, 6/10, 5/10, 22/25, respectively. Doseresp was used to calculate the LC_{01} values, i.e. 72.6 mg/m³. The 4 hour LC_{01} value of 72.6 mg/m³ was used as point of departure for deriving the LBW-values. Applying the default uncertainty factor of 10 (3x3) would result in LBW values that are in conflict with human data (see health surveillance studies as described under VRW).
The uncertainty factors for interspecies and interspecies differences were therefore lowered to 1, resulting in a total factor of 1. Time scaling was performed using the equation $C^n \times t = k$ with the default n = 1 and n= 3, to extrapolate to longer and shorter durations, respectively.
It should be noted that data of a Cxt mouse study were available but could not be analyzed, because

no response was observed in most Cxt groups and inconsistent results were observed in the few Cxt groups that showed a response. Further, these data (for example, the highest exposure without mortality, i.e. 2170 mg/m^3 for 1 hour) were in conflict with the data of the abovementioned 4 hour mouse study and with a repeated exposure study (6 hour/day) in mice and rats.

Additional toxicological information (including relevant results of a general literature search, if any)

The main effect of hydrogen peroxide is local irritation.

Reproductive toxicity studies using the inhalation route are not available.

Additional human data were derived from the public scientific literature. In a human volunteer study (Ernstgård et al., 2012)[84], eleven healthy adult volunteers (six women and five men) were exposed in an inhalation chamber to 0, 0.5 and 2.2 ppm hydrogen peroxide (corresponding to 0, 0.71 and 3.1 mg/m^3) for two hours. Symptoms related to irritation and central nervous system effects were rated with Visual Analog Scales. The ratings varied considerably but were generally low and with no significant differences between exposure conditions, although the ratings of smell ($p = 0.09$, Friedman's test), nasal irritation ($p = 0.06$) and throat irritation ($p = 0.06$) showed borderline tendencies to increase at 3.1 but not at 0 and 0.71 mg/m^3. Nasal airway resistance increased after exposure to 3.1 mg/m^3 hydrogen peroxide ($p = 0.04$, paired t-test) but not after 0.71 mg/m^3. No exposure-related effects on pulmonary function, nasal swelling, breathing frequency and blinking frequency were detected. Furthermore, no clear effects were seen on markers of inflammation and coagulation (interleukin-6, C-reactive protein, serum amyloid A, fibrinogen, factor VIII, von Willebrand factor and Clara cell protein in plasma).

H302: Harmful if swallowed, H314: Causes severe skin burns and eye damage, H332: Harmful if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: slightly sharp, irritating

No information on odour thresholds available.

No LOA was derived.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [85]

VRW level **3.1**	*AEGL-1* -	*ERPG-1* 14		*IDLH:* 106 mg/m^3 (30 minutes)
AGW level **38**	*AEGL-2* -	*ERPG-2* 71		
LBW level **120**	*AEGL-3* -	*ERPG-3* 142		

[84] Ernstgard L., Sjogren B., Johanson G. Acute effects of exposure to vapors of hydrogen peroxide in humans. Toxicology Letters (2012) 212, 222-227

[85] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.

Stofdocument deel A

CAS-nr: 1330-20-7 **Xylenen** $C_6H_4-(CH_3)_2$ **VN-nr: 1307**

GEVI: 30

Synoniemen: Xyleen, Dimethylbenzeen (Engels: Xylenes) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	590	590	590	590	590	590
Alarmeringsgrenswaarden	AGW (mg/m³)	11.000*	5.700*	3.900	3.200	2.200	1.800
Levensbedreigende waarden	LBW (mg/m³)	32.000**	16.000*	11.000*	8.400*	5.700*	4.400*

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,226 ppm; 1 ppm = 4,42 mg/m³

Explosiegrens: LEL = 0,9 vol% ≈ 40.000 mg/m³

* berekende interventiewaarde hoger dan 10% LEL

** berekende interventiewaarde hoger dan 50% LEL

Geur: typerende geur van een aromatische koolwaterstof

LOA: 2,8 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof
Brand: brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,03

Molecuulmassa:	106,2 g/mol
Zuurgraad:	Geen data
LogKow:	3,2
Wateroplosbaarheid:	Niet oplosbaar
Verzadigde dampdruk:	Ca. 10 mbar

Overige informatie

Publieke grenswaarde:
210 mg/m³ (H)
MAK: 440 mg/m³ (H)
TLV-TWA: 440 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte oogirritatie

VRW → AGW: irritatie van huid, ogen, neus en keel, lichte benauwdheid, hoofdpijn, misselijkheid, braken, (draai)duizeligheid

AGW → LBW: ernstige irritatie van luchtwegen, benauwdheid, buikpijn, bewustzijnsdaling

Boven LBW: convulsies, coma, ademnood, ademstilstand, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Xylenen komen meestal voor in (verschillende) mengsels van ortho, meta en para-isomeren. Er zijn in de literatuur geen significante verschillen in toxiciteit tussen de verschillende isomeren aangetoond.
- Blootstelling aan xylenen kan leiden tot irritatie aan ogen en luchtwegen en stoornissen van het centrale zenuwstelsel (CZS), welke bij hoge concentraties tot ademnood en overlijden kunnen leiden.
- Blootstelling aan hoge concentraties xylenen kan leiden tot kortdurende CZS excitatie gevolgd door depressie van het CZS.
- Blootstelling aan hoge concentraties xylenen kan acuut longoedeem, ademnood en lever- en nierfunctiestoornissen veroorzaken, gevolgd door sterfte.
- De respiratoire effecten (ademstilstand) voorafgaand aan sterfte zijn zeer waarschijnlijk een secundaire respons op depressie van het ademhalingscentrum in de hersenen.

Effecten bij blootstelling aan vloeistof

Huidcontact: droge huid, roodheid, ruwe huid, prikkeling. De stof kan door de huid worden opgenomen.

Oogcontact: prikkeling, roodheid en pijn, tranenvloed, corneabeschadiging

Carcinogeniteit

IARC classificatie: 3

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen*.

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 1330-20-7 **Xylenes** **C_6H_4-$(CH_3)_2$** **UN-nr: 1307**

Basis for the Dutch Intervention Values

VRW: AEGL values adopted, 2 hr value added

AGW: AEGL values adopted, 2 hr value added

LBW: AEGL values adopted, 2 hr value added

Date: 06-10-2016 | AEGL document: Final 2010

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	590	590	590	590	590	590	Eye irritation in humans
AGW	11,000*	5,700*	3,900	3,200	2,200	1,800	CNS effects: poor coordination in rats
LBW	32,000**	16,000*	11,000*	8,400*	5,700*	4,400	Threshold for lethality and reversible prostration in rats

* value higher than 10% of LEL; ** value higher than 50% of LEL

Derivation of the Dutch Intervention Values

VRW: The VRW levels were based on a study with male human volunteers exposed for 30 minutes to 0, 100, 200, 400 ppm (0, 442, 884, 1767 mg/m³) xylenes. Exposure to the mixed xylenes resulted in a (statistically non-significant) increase in complaints of eye irritation at all concentrations, but no nose or throat irritation. Exposure to 400 ppm (1767 mg/m³) was used as point of departure and is supported by several other studies on human volunteers. The default intraspecies uncertainty factor of 3 was considered sufficient. Eye irritation is considered a threshold effect which should not vary over time. Therefore, the same VRW value was applied across all time points.

AGW: The AGW levels are based upon CNS effects, being the threshold for reversible equilibrium disturbances and the no-effect level for the impaired ability to escape. Groups of 15 or 16 male rats were exposed for 4 hours to 580, 1300, 2800, 6000, 9000 ppm (2562, 5743, 12369, 26505, 39758 mg/m³) mixed xylenes. Poor coordination was observed in rats exposed to mixed xylenes at 1,300 ppm (5,743 mg/m³), 2 hours into a 4-hour exposure period. It is assumed that the CNS effects observed after xylene exposure is directly related to the concentration of the parent material reaching the brain and that venous blood concentrations correlate with brain concentrations. A PBPK model was run for each time point to determine the equivalent external exposure concentration producing the target internal dose producing impaired coordination in rats. The default intraspecies uncertainty factor of 3 was considered sufficient. An interspecies uncertainty factor of 1 was applied. A higher interspecies uncertainty factor was not considered necessary, since kinetic differences were already processed in the PBPK model and application of a factor 3 for the remaining pharmacokinetic differences would drive the AGW for 8 hours to a value that is inconsistent with the human data set.

LBW: Derivation of LBW values was based on the same animal study which was used to derive the AGW values. The LBW is based on a NOAEL for death at 2,800 ppm (12,369 mg/m³) of mixed xylenes for 4 hours. At this concentration all rats were prostrate between 2 and 3.5 hours, but recovered within 1 hour. Although coordination initially remained poor, it returned to normal the following day. This concentration represents a threshold for marked CNS depression which could lead to death. At 6000 ppm (26505 mg/m³) 4 out of 10 animals died and all surviving animals were prostrate within 30 minutes. In other lethality studies in rats LC_{50}-values were reported ranging from 4,330 ppm (19,128 mg/m³; 6 hours) for o-xylene tot 6,700 ppm (29,597 mg/m³; 4 hours) for mixed xylenes. A PBPK model was run for each time point to determine the equivalent external exposure concentration producing the target internal dose producing impaired coordination in rats. The default intraspecies uncertainty factor of 3 was considered sufficient. An interspecies uncertainty factor of 1 was applied. A higher interspecies uncertainty factor was not considered necessary, since kinetic differences were already processed in the PBPK and application of a factor 3 for the remaining pharmacokinetic differences would drive the LBW for 8 hours to a value that is inconsistent with the human data set.

Additional toxicological information (including relevant results of a general literature search, if any)

The two primary effects of xylenes are irritation and central nervous system effects. The CNS effects are attributed to the low molecular weight and the lipophilic nature, which allows the solvent to rapidly cross the blood:brain barrier. The transient nature of CNS induced disturbances is likely due to rapid elimination of xylenes. The precise mechanism is not known. At high atmospheric concentrations the solvent may cause narcosis and death. Respiratory effects (pulmonary failure) preceding death are most likely a secondary response to depression of the respiratory centre of the brain.

No indication of consistent developmental of reproductive signs of toxicity was observed in the available literature. Embryotoxic and foetotoxic effects are possible at maternally toxic dose levels.

Xylenes are generally a mixture of three isomers. Although differences exist between studies, no consistent, significant differences in the toxicological potency of the xylene isomers following or inhalation exposure were identified.

H312: Harmful in contact with skin; H315: Causes skin irritation; H332: Harmful if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to carcinogenicity to humans)

No carcinogenic risk potency (CRP) was derived.

No studies were found in the published literature regarding the carcinogenic potential of inhaled xylenes in animals. Human data were too limited to draw any conclusions.

Odour and derivation of the LOA value

Odour: penetrating aromatic hydrocarbon odour

In contrast to the AEGL a LOA was derived.

ODT: 0.18 mg/m^3 [Nagata2003]
LOA = 11.8 * ODT * 1.33 = 2.8 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: $I = 2.33 * \log (C/OT_{50}) + 0.5$. A correction factor of 1.33 is applied to this value)

The LOA is based on the ODT of m-xylene, which has the lowest threshold. The LOA lies well below all intervention values.

Other standards and guidelines *(1h values in mg/m^3, unless otherwise indicated)*

VRW level **590**	*AEGL-1* 570	*ERPG-1* -		*IDLH:* 4,000 mg/m^3 (30 minutes)
AGW level **3,900**	*AEGL-2* 4,100	*ERPG-2* -		
LBW level **11,000**	*AEGL-3* 11,000	*ERPG-3* -		

Stofdocument deel A

CAS-nr: 1314-84-7 **Zinkfosfide** P_2Zn_3 **VN-nr: 1714**

GEVI: geen

Synoniemen: trizinkdifosfide (Engels: zinc phosphide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	64	21	11	5,4	2,7	1,3
Levensbedreigende waarden	LBW (mg/m³)	120	39	19	9,7	4,8	2,4

Datum vaststelling: 16-10-2018

Conversiefactor: 1 mg/m³ = 0,093 ppm; 1 ppm = 10,736 mg/m³

Explosiegrens: geen data
Kans op explosie door reactie met water of zuren.

Geur: typerende geur (geur als bij fosfine)

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: donkergrijze kristallen, pasta of poeder

Brand: Niet brandbaar. Echter, bij contact met vocht kans op brand en explosie.

Relatieve dichtheid van verzadigd damp-lucht mengsel: geen data

Molecuulmassa: 258,1 g/mol

Zuurgraad: geen data

LogKow: geen data

Wateroplosbaarheid: reactie

Verzadigde dampdruk: geen data

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

(gebaseerd op vrijkomen fosfine)

*Onder **AGW***: irritatie aan ogen, huid, neus en luchtwegen, hoofdpijn, misselijkheid, braken, zwakte, paresthesie, duizeligheid, tremor

AGW → LBW: benauwdheid, longoedeem, bewustzijnsdaling, hartritmestoornissen, nier- en leverfunctiestoornissen

Boven LBW: convulsies, cardiovasculaire collaps, myocardinfarct, ademnood, coma, sterfte

LET OP: De afwezigheid van een VRW betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Zinkfosfide kan bij contact met vocht uit de lucht of luchtwegen omgezet worden in fosfine. De toxiciteit van zinkfosfide wordt bepaald door de vorming van fosfine.
- Fosfine verstoort door effecten op de celademhaling de zuurstofopname en energievoorziening van de cel.
- Fosfine werkt irriterend op de ogen, huid en luchtwegen.
- Blootstelling aan zinkfosfide kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Kinderen zijn mogelijk gevoeliger voor toxiciteit door fosfine.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid

Oogcontact: roodheid, pijn

Carcinogeniteit

IARC classificatie: niet geëvalueerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

ogen: spoelen met water (evt. contactlenzen verwijderen).

Ontsmetting vaste stof

huid: verontreinigde kleding uittrekken, afspoelen met water.

ogen: spoelen met water (evt. contactlenzen verwijderen).

inslikken: mond laten spoelen (uitspugen!), rust, GEEN mond-op-mondbeademing, actieve kool (carbomix) toedienen, en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 1314-84-7 **Zinc phosphide** P_2Zn_3 **UN-nr: 1714**

Basis for the Dutch Intervention Values

VRW: Not recommended, in accordance with AEGL

AGW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

LBW: AEGL value is adopted (except 10 min value for which time scaling was applied), 2h value added

Date: 16-10-2018 AEGL document: Final 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	(insufficient data)
AGW	64	21	11	5.4	2.7	1.3	Irritation nasal mucosa rats (phosphine)
LBW	120	39	19	9.7	4.8	2.4	Lethality rats (phosphine)

Derivation of the Dutch Intervention Values

VRW: No data are available for zinc phosphide. As toxicity of zinc phosphide is due to phosphine, which is formed due to reaction of zinc phosphide with moisture, data on phosphine could be used to derive intervention values. However, no appropriate data were available for derivation of VRW values for phosphine. Therefore VRW values are not recommended. This does not imply that exposure below AGW is without adverse effects.

AGW: Since no appropriate data exist for zinc phosphide, AGW values for phosphine will be used (on ppm-basis) to derive AGW values for zinc phosphide. The use of phosphine as a surrogate for zinc phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because two moles of phosphine are produced for every mole of zinc phosphide, a molar adjustment factor of 2 was applied to the zinc phosphide AGW values.

Derivation of AGW values for phosphine

The phosphine AGW values were based on red mucoid nasal discharge in rats exposed to 10 ppm (14 mg/m3) phosphine for 6 hours, corresponding to 53.7 mg/m³ zinc phosphide. Since this endpoint is less severe than effects defined by AGW, the resulting values should be protective.
The default uncertainty factor of 3 was applied to account for interspecies variability. An uncertainty factor of 10 was applied to account for intraspecies variability since the human data suggest that children may be more sensitive than adults when exposed to presumably similar phosphine concentrations. For example, in two reports, exposed children died, but exposed adults survived. Time scaling was performed using the equation $C^n \times t = k$, and an n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine).

LBW: Since no appropriate data exist for zinc phosphide, LBW values for phosphine will be used (on ppm-basis) to derive LBW values for zinc phosphide. The use of phosphine as a surrogate for zinc phosphide was deemed appropriate since it is believed that the reaction product, phosphine, is responsible for the adverse effects. Because two moles of phosphine are produced for every mole of zinc phosphide, a molar adjustment factor of 2 was applied to the zinc phosphide LBW values.

Derivation of LBW values for phosphine

The highest concentration yielding no deaths in rats (18 ppm = 25 mg/m³) for 6 hours was used as point of departure for the calculation of the LBW values, corresponding to 96.6 mg/m³ zinc phosphide. The default uncertainty factor of 3 for interspecies and an intraspecies factor of 10 were applied for reasons provided above. Time scaling was performed using the equation $C^n \times t = k$ and a chemical specific n-value of 1 (derived from rat lethality data of 1- to 6-hours for phosphine). These values are considered protective since workers were repeatedly exposed for “brief” periods of time to phosphine concentrations up to 35 ppm (49 mg/m³) with no life-threatening effects and workers exposed to >50 ppm (>70 mg/m³) for 2-5 minutes experienced only odour.

Additional toxicological information (including relevant results of a general literature search, if any)

When zinc phosphide reacts with moisture, phosphine gas will be formed. Phosphine is considered to induce acute toxic effects following oral and inhalation exposure. Children are thought to be more vulnerable to phosphine exposure. Common clinical signs after exposure to phosphine are headache, vomiting, coughing, shortness of breath, paresthesia, weakness, tremors and jaundice. Pulmonary congestion, pleural effusion, and congestive heart failure may be observed upon post-mortem examination.

In vitro, phosphine reacts with cytochrome c and cytochrome c oxidase, thereby inhibiting mitochondrial oxygen uptake. In vitro studies have also shown that phosphine can react with the heme moiety of hemoglobin in the presence of oxygen. Cell death and loss of cell membrane integrity accounted for the increased liver enzymes, bronchiolytic effects, cloudy swelling of renal tubular epithelia, and hemorrhagic myocardial lesions.

No reproductive or developmental data were found.

H300: Fatal if swallowed

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not evaluated. No carcinogenic risk potency (CRP) was derived. No data concerning carcinogenicity of zinc phosphide are available. Fumigation workers exposed long-term to phosphine have a higher incidence of both stable and less stable chromosomal aberrations. Molecular analysis of these lesions suggests that the breakpoints are near proto-oncogenes involved in non-Hodgkin's lymphoma, possibly contributing to the increased incidence of lymphomas in pesticide workers.	Odour: no information. Pure phosphine is odourless at concentrations up to 200 ppm. Technical-grade phosphine has a garlic-like odour (may be due to impurities). For phosphine, no LOA was derived due to lack of reliable data. Ruth (1986) reported an odour range of 0.028-3.6 mg/m^3 for phosphine.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)* [86]

VRW level **NR**	*AEGL-1* NR	*ERPG-1* -		*IDLH:* not derived
AGW level **11**	*AEGL-2* 11	*ERPG-2* -		
LBW level **19**	*AEGL-3* 19	*ERPG-3* -		

[86] Note that the AEGL values as presented here (in mg/m^3) are derived using the conversion factors of the AEGL.

Stofdocument deel A

CAS-nr: 10025-67-9 **Zwavelchloride** S_2Cl_2 **VN-nr: 1828**

GEVI: X88

Synoniemen: dizwaveldichloride, zwavelmonochloride (Engels: sulfur chloride) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	19	19	19	19	19	19
Alarmeringsgrenswaarden	AGW (mg/m³)	200	140	110	86	68	34
Levensbedreigende waarden	LBW (mg/m³)	470	320	260	200	160	81

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,178 ppm; 1 ppm = 5,62 mg/m³

Explosiegrens: geen data

Geur: irriterende, doordringende, misselijkmakende, stekende of verstikkende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot rode viskeuze vloeistof
Brand: brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,05

Molecuulmassa:	135,0 g/mol
Zuurgraad:	geen data
LogKow:	geen data
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	13 mbar

Overige informatie

Publieke grenswaarde:
niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid
TLV-Ceiling: 5,6 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	geen effecten
VRW→ AGW:	irritatie (erytheem) van slijmvliezen van ogen, neus en keel, tranenvloed, keelpijn, kortademigheid, hoesten
AGW → LBW:	ernstige (erytheem) oog-, neus- en keelirritatie, benauwdheid, longoedeem, pijn op de borst, ophoesten van bloed
Boven LBW:	ademnood, acute longschade, opzwelling in de hals (pharynx en larynx), sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Effecten op de bovenste luchtwegen worden toegeschreven aan hydrolyseproducten van zwavelchloride (nl. zoutzuur en zwaveldioxide) die ontstaan bij contact met vochtige lucht.
- Niet-gehydrolyseerd zwavelchloride kan de lagere luchtwegen bereiken en daar schade veroorzaken aan de bronchi en alveoli en kan oedeemvorming in de keel optreden (met kans op verstikking).
- Zwavelchloride kan een type I inhalatoire intoxicatie veroorzaken, waarbij in een later stadium longoedeem kan ontstaan. Bij het ontbreken van lokale irritatie-effecten zijn de lagere luchtwegen niet aangedaan en ontwikkelt zich geen longoedeem.

Effecten bij blootstelling aan vloeistof

Huidcontact: *bijtend*, roodheid, pijn, ernstige brandwonden

Oogcontact: *bijtend*, roodheid, pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd.
CRP: niet afgeleid.

Beknopte medische informatie

***Ontsmetting* damp**

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: kleding uittrekken (NIET lostrekken), direct spoelen met veel water (minimaal 20 min.), dan pas eventueel aan de huid vastgeplakte kleding verwijderen en verder spoelen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 10025-67-9 **Sulfur chloride** S_2Cl_2 **UN-nr: 1828**

Basis for the Dutch Intervention Values

VRW: Same point of departure as for AEGL-1 value, different uncertainty factor, 2h value added, no time scaling applied

AGW: Same point of departure as for AEGL-2 value, different uncertainty factor, 2h value added

LBW: Same point of departure as for AEGL-3 value, different uncertainty factor, 2h value added

Date: 24-09-2009 | AEGL document: Interim, 2007

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	19	19	19	19	19	19	Threshold of irritation in animals
AGW	200	140	110	86	68	34	Upper respiratory tract irritation in animals
LBW	470	320	260	200	160	81	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: The point of departure for VRW derivation is 33.3 ppm (187 mg/m³), the highest concentration causing no clinical signs, gross lesions in a 4-hour acute inhalation study in rats. A total uncertainty factor of 10 was applied to the 33.3 ppm (187 mg/m³) exposure concentration; 3 for interspecies sensitivity and 3 for intraspecies variability. Very little is known about the toxicity of sulfur chloride, and no data were available to assess the species differences or the response of sensitive groups in the population to sulfur chloride exposure. Based on irritation as endpoint, no time scaling was applied. The exposure concentration for 4 hours was flatlined for other timepoints.

AGW: The only study available for deriving AGW values is the 4-hour acute inhalation study in rats mentioned above. The point of departure for AGW derivation is 242 ppm (1360 mg/m³) that caused signs of upper respiratory tract irritation, dyspnea and decelerated breathing, and signs of discomfort. A total uncertainty factor of 10 was applied: 3 for interspecies sensitivity because only one animal study was available for deriving AGW values and species sensitivity could not be evaluated and 3 for intraspecies variability. The latter factor differs from the factor that is used for the VRW, because it is anticipated that the decomposition products (hydrogen chloride and sulfur dioxide having a lesser toxic potency) are causing the AGW effects. A modifying factor of 2 also was applied because the effects appeared slightly more severe than described by the definition of AGW and the modifying factor would provide a better estimate of the threshold for the respiratory effects. The exposure concentration for 4 hours was scaled to the pertinent AGW time frames using the equation: $C^n \times t = k$, with the default values of n=1 and n=3 for extrapolation to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-2 value that was set equal to the 30 minute AEGL-2 value, time scaling was also applied for the 10 minute AGW value.

LBW: LBW values were also derived from the 4-hour inhalation study using rats. The lethality threshold (LC_{01}) estimated by probit analysis was 296 ppm (1660 mg/m³) (NCSS, Version 5.5) and the 95% lower confidence limit on the LC_{05} (BMDL) was 288 ppm (1620 mg/m³). The BMDL of 288 ppm (1620 mg/m³) was used to derive LBW values. A total uncertainty factor of 10 (3x3) was used to account for intraspecies and interspecies variability. The exposure concentration for 4 hours was scaled to the pertinent LBW time frames using the equation: $C^n \times t = k$, with the default values of n=1 and n=3 for extrapolation to longer and shorter exposure durations, respectively. In contrast to the 10 minute AEGL-3 value that was set equal to the 30 minute AEGL-3 value, time scaling was also applied for the 10 minute LBW value.

Additional toxicological information (including relevant results of a general literature search, if any)

Sulfur chloride is considered an upper respiratory tract irritant. Secondary information found in the literature showed that exposure to sulfur chloride causes pronounced irritation to the eyes and nose.

Sulfur chloride decomposes to hydrogen chloride and sulfur dioxide in a moist environment; the stoichiometry of decomposition in environments with varying moisture content is not known. Hydrogen chloride and sulfur

dioxide are upper respiratory irritants. The upper respiratory tract irritation after exposure to sulfur chloride has been attributed to the decomposition products. Sulfur chloride is not water soluble and would be poorly scrubbed in the upper respiratory tract. Therefore, any undecomposed sulfur chloride could reach the lower respiratory tract thereby causing damage to the bronchiolar and alveolar regions of the lungs. The proportion of the potentially more toxic parent compound that could reach the lower respiratory tract and cause pulmonary damage would vary with the moisture content of the environment.

Clinical signs in rats exposed for 4 hours to 242 ppm (1360 mg/m^3) included bloody and serous nasal discharge, dyspnea (difficult or labored breathing), decelerated breathing, reduced activity, piloerection, and ungroomed fur. Additional clinical signs observed at 453 ppm (2540 mg/m^3) included extreme bradypnea (slowed breathing), cyanosis, corneal opacity, and necrotic lesions in the nose/muzzle area. Gross observation of animals that died showed emphysema, edema in liver-like areas of the lungs, hydrothorax (fluid in the pleural cavity), pale spleen and liver, bloody, yellowish mucous substance in the gastrointestinal tract, reddening of the glandular stomach, and reddening and necrosis of the nose. Gross observation of some survivors (assumed to include animals at 453 ppm (2540 mg/m^3)) showed emphysema and edema in liver-like or dark-red areas of the lungs. No clinical signs, deaths, or pathologic effects were observed in rats exposed to 1.45 or 33.3 ppm (8.1 or 187 mg/m^3).

No data were found on developmental or reproductive toxicity of sulfur chloride.

H301: Toxic if swallowed; H314: Causes severe skin burns and eye damage; H332: Harmful if inhaled.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified No carcinogenic risk potency (CRP) was derived. No data was found on carcinogenicity of sulfur chloride in humans or experimental animals.	Odour: irritating, penetrating, nauseating, pungent or suffocating odor. No LOA was derived.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **19**	*AEGL-1* 3.0	*ERPG-1* not derived	*IDLH:* 84 (30 minutes)
AGW level **110**	*AEGL-2* 36	*ERPG-2* not derived	
LBW level **260**	*AEGL-3* 84	*ERPG-3* not derived	

Stofdocument deel A

CAS-nr: 7446-09-5 **Zwaveldioxide** **SO_2** **VN-nr: 1079**

GEVI: 268

Synoniemen: geen (Engels: Sulfur dioxide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	2,0	2,0	2,0	2,0	2,0	2,0
Alarmeringsgrenswaarden	AGW (mg/m³)	20	20	20	19	15	7,6
Levensbedreigende waarden	LBW (mg/m³)	440	310	240	190	150	76

Datum vaststelling: 06-10-2016

Conversiefactor: 1 mg/m³ = 0,376 ppm; 1 ppm = 2,66 mg/m³

Explosiegrens: geen data

Geur: stekend, irriterend

LOA: 36 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos, onder druk tot vloeistof verdicht gas

Brand: niet brandbaar

Relatieve dichtheid gas (lucht=1): 2,2

Molecuulmassa:	64,0 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	11,4 g/100 ml (goed)
Verzadigde dampdruk:	3300 mbar

Overige informatie

Publieke grenswaarde: 0,7 mg/m³ (15 min)

MAK: 2,7 mg/m³

TLV-TWA: 5,3 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: irritatie van slijmvliezen van ogen, neus en keel. Astmatici: keelpijn, hoesten, branderig gevoel en slikmoeilijkheden, tranen en longfunctieveranderingen t.g.v. reflectoire bronchoconstrictie

AGW → LBW: bronchiale hyperreactiviteit met luchtwegobstructie en longschade (ernstige bronchospasmen en verlamming van de ademhalingsspieren), long- en glottisoedeem

Boven LBW: glottisoedeem, sterfte door ademstilstand

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Inhalatie van zwaveldioxide veroorzaakt een type-I-inhalatoire intoxicatie. Zwaveldioxide werkt irriterend op de ogen en luchtwegen via de vorming van bisulfiet. Bij een betrekkelijk geringe blootstelling bestaan de verschijnselen vooral uit tranende ogen, neusirritatie, keelpijn, hoesten, een brandend gevoel achter het borstbeen en pijn bij doorzuchten.
- Zwaveldioxide veroorzaakt longfunctie-veranderingen als gevolg van reflectoire bronchoconstrictie.
- Het effect van zwaveldioxide op bronchoconstrictie is groter bij lichamelijke inspanning en voor astmatici
- Bij blootstelling aan zeer hoge concentraties kan glottisoedeem optreden met mogelijk asfyxie tot gevolg.
- De effecten treden snel (binnen enkele minuten) op. Bij langere blootstellingsduur (enkele tot meerdere uren) lijkt de duur van de blootstelling minder invloed te hebben op de bronchiale effecten of nemen deze effecten zelfs af.

Effecten bij blootstelling aan vloeistof

Huidcontact: bevriezingsletsel

Oogcontact: conjunctivitis, branderigheid, roodheid, bevriezingsletsel

Carcinogeniteit

IARC classificatie: 3

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

inademing: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

huid: verontreinigde kleding uittrekken en huid afspoelen met water.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof n.v.t. (gas). ,

huid: *in geval van bevriezingsletsel*: spoelen met veel water, niet-verkleefde kleding verwijderen (adembescherming dragen), onmiddellijk arts raadplegen.

ogen: zie hierboven.

inslikken: n.v.t. (gas > –10°C). In geval van inslikken gekoelde vloeistof: mond spoelen (uitspugen!) en direct spoedeisende hulp inzetten

Specifieke behandeling en materialen*: geen*.

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7446-09-5 **Sulfur dioxide** SO_2 **UN-nr: 1079**

Basis for the Dutch Intervention Values

VRW: Same study but different point of departure as for AEGL, 2 h value added

AGW: Same study but different point of departure and different approach as for AEGL, 2 h value added, time scaling from 2-8 h

LBW: Same point of departure as for AEGL values, but using different uncertainty factors, time scaling from 10 minutes to 8 hour, 2 h value added

Date: 06-10-2016	AEGL Document Volume 8 (Final), 2010

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	2.0	2.0	2.0	2.0	2.0	2.0	LOAEL for moderate bronchoconstriction in exercising asthmatics
AGW	20	20	20	19	15	7.6	10 min - 1 hr VRW × 10, 2 h – 8 h 1/10 x LBW
LBW	440	310	240	190	150	76	Calculated $BMCL_{05}$ for rats

Derivation of the Dutch Intervention Values

VRW: A weight of evidence approach based on exercising human asthmatic data was also used to derive the VRW values. The data suggest that 0.75 ppm (2.0 mg/m^3) induces a moderate respiratory response for exposure durations of 10-minutes to 3 hours, as indicated by an increase in airway resistance (SRaw) of 150%, a decrease in FEF of 22%, and a decrease in FEV_1 of 8% in exercising asthmatics exposed for 10-40 minutes, and an increase in SRaw of 322%, 233%, 26% and 5%, 10 minutes, 20, minutes, 1 hour and 2 hours into exposure, respectively. No uncertainty factors were applied, because the point of departure is a study in humans, using a sensitive population (exercising asthmatics). The role of exposure duration to the magnitude of bronchoconstriction after SO_2 exposure in asthmatics appears to decrease with extended exposure. This can be derived from the findings that during exposure to 0.75 ppm (2.0 mg/m^3), the SRaw increases were 322%, 233%, 26% and 5%, 10 minutes, 20, minutes, 1 hour and 2 hours into exposure, respectively. After 3 hours into exposure even a decrease of 12% was observed. Therefore, the VRW values can be held constant over time.

AGW: No adequate data are available that meet the definition of AGW effects. LBW values are not suitable for derivation of AGW values since deaths in experimental animals start to occur at concentrations that are orders of magnitude higher than for respiratory effects. Nevertheless, AGW values are so important that they are derived from the VRW values by a weight-of-evidence approach. AGW values are thus based on data obtained with exercising asthmatics (see VRW for description). In this population, an exposure concentration of 0.75 ppm (2.0 mg/m^3) induces a moderate respiratory response (*i.e.*, bronchoconstriction). Higher concentrations will result in more severe bronchoconstriction whether or not accompanied by additional effects that lead to a further increase in breathing difficulties. It is assumed that a tenfold higher exposure concentration might lead to respiratory difficulties in asthmatics which may impair their ability to escape from an incident location. With this assumption AGW values are derived by multiplying the VRW values by a factor of 10, but with the restriction that they should not be higher than 1/10 of the LBW to avoid damage to the respiratory epithelium that occurs at higher (lethal) concentrations.

LBW: LBW values are based on a calculated $BMCL_{05}$ of 573 ppm (1500 mg/m^3) in rats exposed to SO_2 for 4-hours. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Because data were not sufficient to ascertain whether a maximal response to SO_2 for a lethal end point is obtained within 10 min, time scaling was applied for the derivation of the LBW values. Time scaling was performed using $C^n * t = k$, with the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Sulfur dioxide is a water-soluble irritant of the upper respiratory tract and eyes, which may induce increased airway resistance via reflex bronchoconstriction. The exact mechanism for this bronchoconstriction is unknown. However, the rapid onset and reversibility of SO_2-induced bronchoconstriction observed in asthmatics is likely due to decreased airway caliber caused by contraction of airway smooth muscle. Sulfur oxide may act either directly on smooth muscle or may cause a release of chemical mediators from this tissue. Asthma and physical exercise increase the bronchoconstrictive effect. With regard to respiratory tract, the effects occur rapid (within several minutes). The influence of exposure duration diminishes over time, showing even a decrease in effect level after several hours.
Conjunctivitis, corneal burns, and corneal opacity may occur from direct contact with high concentrations of sulfur dioxide. Death from respiratory arrest may occur from acute over-exposure, while survivors may develop bronchitis, bronchopneumonia, and fibrosing obliterative bronchiolitis. Bronchoconstriction accompanied by increased pulmonary resistance may be asymptomatic or may occur with high-pitched rales.
Co-exposure to respirable particles may increase the severity of adverse effects caused by sulfur dioxide. Although the main effects of SO2 are on the respiratory tract, much of an inhaled dose may be transferred into systemic circulation. Most inhaled SO2 is detoxified in the liver by the sulfite-oxidase pathway, which forms S-sulfonates that can be found in the plasma and sulfates that are excreted in the urine. The S-sulfonates are long-lived and supply the circulation with bisulfite that may reach many tissues.

The VRW and AGW values are based on effect levels in asthmatics and are expected to have no effect on healthy individuals. This is confirmed by two studies in which healthy volunteers were exposed to 0.5, 1.0 and 2.0 ppm (1.33, 2.66 and 5.32 mg/m^3) for 4 hours, with periods of light to moderate exercise. No effects were found on exhaled nitric oxide (FeNO) and airway inflammation biomarkers measured in exhaled breath condensate and nasal lavage fluid (Raulf-Heimsoth et al., 2010), eye blink frequency, nasal airflow, and lung function measured by spirometry (van Thriel et al., 2010).

Sulfur dioxide was generally not a developmental or reproductive toxicant in animal studies.

H314: Causes severe skin burns and eye damage; H331: Toxic if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to carcinogenicity to humans)

No carcinogenic risk potency (CRP) was derived.

Genotoxic studies regarding exposure to SO_2 are equivocal and the carcinogenicity study, although suggesting a possible increase in pulmonary tumors, is of poor quality and thus of limited use. No information suggesting an increased cancer incidence from SO_2 exposure in humans was located.

Odour and derivation of the LOA value

Odor: foul, pungent, irritating odor

ODT: 2.3 mg/m^3 [Nagata, 2003]
LOA = 11.8 * ODT * 1.33 = 36 mg/m^3

(The concentration Level leading to distinct Odor Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies between the AGW and the LBW.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **2.0**	*AEGL-1* 0.53	*ERPG-1* 0.30		*IDLH:* 270 mg/m^3 (10 min)
AGW level **20**	*AEGL-2* 2.0	*ERPG-2* 3.0		
LBW level **240**	*AEGL-3* 80	*ERPG-3* 25		

Stofdocument deel A

CAS-nr: 75-15-0 **Zwavelkoolstof** **CS_2** **VN-nr: 1131**

GEVI: 336

Synoniemen: kooldisulfide, koolstofdisulfide (Engels: carbon disulfide) ***Status:*** A-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	77	53	42	34	27	21
Alarmeringsgrenswaarden	AGW (mg/m³)	910	630	500	400	320	160
Levensbedreigende waarden	LBW (mg/m³)	2.700*	1.900*	1.500	1.200	950	480

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,316 ppm; 1 ppm = 3,17 mg/m³

Explosiegrens: LEL = 0,60 vol % ≈ 19.000

* berekende interventiewaarde hoger dan 10% LEL

Geur: zoete, ether-achtige geur, in pure vorm chloroformachtige en in verdunde vorm rotte radijs/gekookte bloemkoolgeur

LOA: 10 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot lichtgele vloeistof

Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,6

Molecuulmassa:	76,1 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	0,22 g/100 ml (slecht)
Verzadigde dampdruk:	400 mbar

Overige informatie

Publieke grenswaarde: 15 mg/m³ (8 uur)

MAK: 16 mg/m³

TLV-TWA: 32 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: misselijkheid, braken, hoofdpijn, duizeligheid, apathie, tranenvloed, oogirritatie, agitatie, keelpijn, hoesten, benauwdheid, pijn op de borst

AGW → LBW: verwardheid, tremoren, convulsies, bewustzijnsdaling

Boven LBW: coma en sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling aan damp

- Zwavelkoolstof kan effecten op het centraal zenuwstelsel veroorzaken.
- Bij hoge concentraties kan irritatie van ogen en slijmvliezen optreden.
- Gebruik van alcoholische dranken versterkt de schadelijke werking van zwavelkoolstof.
- Verhoogde gevoeligheid kan voorkomen bij alcoholisten, mensen met neuropsychiatrische aandoeningen en mensen met B6-deficiëntie.
- De stof heeft een steile concentratie-respons relatie.

Effecten bij blootstelling aan vloeistof

Huidcontact: droge huid, bijtend, roodheid en pijn, brandwonden.
Stof kan door de huid worden opgenomen!

Oogcontact: bijtend, roodheid en pijn, slecht zien

Carcinogeniteit

IARC classificatie: niet geclassificeerd

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en arts raadplegen.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.

***Specifieke behandeling en materialen**: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 75-15-0 **Carbon disulfide** **CS_2** **UN-nr: 1131**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, (except 10 min value for which time scaling was applied), 2 h value added

AGW: AEGL value is adopted, (except 10 min value for which time scaling was applied), 2 h value added

LBW: AEGL value is adopted, (except 10 min value for which time scaling was applied), 2 h value added

Date: 24-09-2009 | AEGL document: final 2009

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	77	53	42	34	27	21	Elevated acetaldehyde blood level in humans (precursor of Disulfiram effect)
AGW	910	630	500	400	320	160	CNS effects in rats
LBW	2,700*	1,900*	1,500	1,200	950	480	Threshold for lethality in rats

* value higher than 10% of LEL

Derivation of the Dutch Intervention Values

VRW: The VRW is based on an increase of acetaldehyde blood level in a controlled study with human volunteers, indicative for inhibition of ethanol metabolism. Exposure to 20 ppm (63 mg/m³) CS_2 for 8 hours caused a 50-100% increase in these levels when subjects simultaneously or afterwards had taken in moderate amounts of alcohol. The observed effect was not accompanied by a "disulfiram-effect" (=alcohol intolerance/alcohol flush/red and warm face) in healthy subjects. An uncertainty factor of 3 was applied to be protective to sensitive population subgroups (heterozygous in acetaldehyde dehydrogenase (ALDH), i.e. normal ALDH2= more active acetaldehyde dehydrogenase and atypical ALDH2=less active acetaldehyde dehydrogenase). It is noted that the homozygous atypical ALDH2 subpopulation is not accounted for with this uncertainty factor, because they are hyper susceptible to ethanol and tend to avoid drinking alcoholic beverages at all. Time scaling was done using the equation $C^n \times t = k$, using the default value n=3 to extrapolate to shorter exposure periods. In contrast to the 10 min AEGL-1, time scaling was performed for the 10 min VRW.

AGW: The point of departure of the derivation of the AGW is the 1,000 ppm (3,200 mg/m³) no effect level from a 4-hour inhalation neurobehavioral study in rats. In this study groups of 8-10 rats were exposed to 4 hours/day, 5d/w for 2 weeks to 250, 500, 1,000 and 2,000 ppm (790, 1,600, 3,200 and 6,300 mg/m³). At 2,000 ppm (6,300 mg/m³) the rats exhibited inhibition of escape and avoidance response in a pole climbing test. It is likely that this inhibition of response is related to the narcotic effects of CS_2 which are described in other studies following acute exposure at similar and lower concentrations (longer time points). A total uncertainty factor of 10 was applied. An intraspecies factor of 3 was considered sufficient because the threshold for CNS effects is not expected to vary much among individuals. For interspecies a factor 3 is considered sufficient because the use of a higher uncertainty factor to account for interspecies differences would result in AGW values, which would conflict with the results of the human volunteer study. Time scaling was done using the equation $C^n \times t = k$, using the default values n=3 and n=1 to extrapolate to shorter and longer exposure periods, respectively. In contrast to the 10 min AEGL-1, time scaling was performed for the 10 min AGW. It is noted that a human volunteer study could have been used for the derivation of the AGW, but because the study consisted of only two volunteers, it was decided to use this study as supporting data rather than as point of departure. In this study CNS-symptoms and irritation of eyes and throat occurred at 260-420 ppm (820-1,330 mg/m³) up to 4 hours of exposure. Furthermore in the volunteer study used as starting point for the derivation of the VRW, 6-8 hours of exposure to 80 ppm (250 mg/m³) did not result in serious or escape-impairing effects.

LBW: The derivation of the LBW is based on an acute inhalation toxicity study in rats, in which a 4-hour exposure to 3,000 ppm (9,500 mg/m³) did not result in mortality (0/6 animals). In the same study a 4 hour exposure at 3,500 ppm (11,000mg/m³) resulted in the death of all animals (6/6). A total uncertainty factor of 10 was used. An interspecies factor of 3 was used based on the similarity of

acute effects seen in rodents compared to humans for CNS-affecting agents and because a higher factor would lead to levels that are not in agreement with the human data. An intraspecies factor of 3 was applied to account for sensitive individuals, because the threshold for CNS impairment is not expected to vary greatly among individuals. Time scaling was done using the equation $C^n \times t = k$, using the default values n=3 and n=1 to extrapolate to shorter and longer exposure periods, respectively. In contrast to the 10 min AEGL3, time scaling was performed for the 10 min LBW. The obtained values are supported by the data from a controlled human study in which exposure for up to 1 hour to concentrations of 1850-2140 ppm (5860-6770 mg/m^3) caused intoxication with moderate to severe neurological effects (i.e. rapidly developing headache, pressure in the head, feeling of heat in the face, irritation of pharynx progressing to cough, nausea; persistent hiccups; anxiety, increased pulse, increasing dizziness, beginning central paralysis, mental capabilities highly impaired, difficulty to perform tasks. After end of exposure: staggered gait, strong dazed feeling, sudden salivation with increased pulse; vomiting, headaches persisting until next morning, disturbed sleep, 2 days of feeling ill), but no life-threatening symptoms.

Additional toxicological information (including relevant results of a general literature search, if any)

The observed acute toxicity is mainly focused on the CNS. Irritation of eyes and/or mucuous membranes occurs at concentrations that already have effects on the CNS. For lethality there is a steep concentration-response curve. Concomitant use of alcoholic beverages can enhance the toxic effects of acute carbon disulfide exposure.
Alcoholics, people with neuropsychiatric disorders and people with a vitamin B_6 deficiency are more at risk. CS_2 lowers vitamin B_6-levels. This causes a disturbance in hydrocarbon metabolism specifically in the cerebral carbohydrates.

There are no relevant data found regarding the reproductive of developmental toxicity of carbon disulfide after single exposure.

H315: Causes skin irritation; H319: Causes serious eye irritation; H351fd: Suspected of damaging fertility. Suspected of damaging the unborn child; H372: Causes damage to organs.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

The available mutagenicity tests are negative, but the overall database is insufficient for evaluation and no adequate carcinogenicity studies in animals are available.

Odour and derivation of the LOA value

Odour: sweet ether-like odor, similar to chloroform, when diluted the smell changes to boiled cauliflower.

ODT: 0.208 ppm (0.66 mg/m^3)
[Nagata (2003)]
LOA = 11.8 * OT_{50} * 1.33 = 10 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/ODT) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is lower than all the derived intervention values for carbon disulfide.

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **42**	*AEGL-1* 41	*ERPG-1* 3.2		*IDLH:* 1,580 mg/m^3 (30 minutes)
AGW level **500**	*AEGL-2* 506	*ERPG-2* 160		
LBW level **1,500**	*AEGL-3* 1,500*	*ERPG-3* 1,600		* ppm to mg/m^3 conversions in AEGL document are incorrect for the AEGL-3 10 min, 30 min and 1 hour values and are recalculated on the basis of AEGL conversion factor (3.114).

Stofdocument deel A

CAS-nr: 505-60-2 **Zwavelmosterd** **$C_4H_8Cl_2S$** **VN-nr: geen**

GEVI: --

Synoniemen: Bis (2-chloroethyl) sulfide, 1,1'-thiobis (2-chloroethaan), mosterdgas (Engels: Sulfur mustard, mustard gas)

Status: B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,40	0,13	0,067	0,033	0,017	0,0083
Alarmeringsgrenswaarden	AGW (mg/m³)	2,0	0,67	0,33	0,17	0,083	0,042
Levensbedreigende waarden	LBW (mg/m³)	3,9	2,7	2,1	1,1	0,53	0,27

Datum vaststelling: 24-09-2009

Conversiefactor: 1 mg/m³ = 0,151 ppm; 1 ppm = 6,62 mg/m³

Explosiegrens: geen data

Geur: vrijwel geurloos (pure stof) tot knoflook/mosterd-achtig (technisch product)

LOA: 2,35 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos tot gelig olieachtige vloeistof

Brand: zeer slecht brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,0

Molecuulmassa:	159,1 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	0,048 g/100 ml (niet)
Verzadigde dampdruk:	0,087 mbar

Overige informatie

Publieke grenswaarde:
niet afgeleid
MAK: niet afgeleid
TLV-TWA: 0,003 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: mogelijk milde oogirritatie

VRW → AGW: oogirritatie

AGW → LBW: ernstige oogirritatie, luchtwegirritatie, benauwdheid, druk op de borst (mogelijk vertraagd)

Boven LBW: ademnood, ernstige longschade, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Sulfur mosterd is een alkalische stof die epitheelcellen aantast (blaartrekkend). De ogen zijn hierbij het meest gevoelig, maar ook de huid en luchtwegen zijn gevoelig.
- Effecten kunnen mogelijk vertraagd optreden.
- Longschade veroorzaakt door aangetast epitheel zorgt voor moeizame ademhaling met mogelijk overlijden als gevolg. Effecten kunnen blijvend zijn.
- De stof reageert met DNA, RNA en eiwitten en is carcinogeen.
- De stof onderdrukt het immuunsysteem.

Effecten bij blootstelling aan vloeistof

Huidcontact: pijn, roodheid, blaren, ernstige brandwonden

Oogcontact: roodheid, tranenvloed, pijn, ernstige brandwonden, hoornvliesbeschadiging, tijdelijk verlies gezichtsvermogen

Carcinogeniteit

IARC classificatie: 1 (humaan carcinogeen)

CRP: 5,48 mg/m³

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!) , GEEN braken opwekken, en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 505-60-2 **Sulfur Mustard** $C_4H_8Cl_2S$ **UN-nr:** none

Basis for the Dutch Intervention Values

VRW: AEGL-1 value adopted, 2hr value added.

AGW: AEGL-2 point of departure adopted, no modifying factor was applied. 2hr value added

LBW: AEGL-3 value adopted, 2hr value added.

Date: 24-09-2009 | AEGL document final, 2003

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.40	0.13	0.067	0.033	0.017	0.0083	Minor eye irritation in humans
AGW	2.0	0.67	0.33	0.17	0.083	0.042	Severe eye irritation in humans
LBW	3.9	2.7	2.1	1.1	0.53	0.27	Threshold for animal mortality

Derivation of the Dutch Intervention Values

VRW: The VRW is based on a human volunteer study where three to four subjects were exposed to sulfur mustard at varying concentration-time regimens. An exposure concentration-time product of 30 mg x min/m³ represented the upper range for mild effects (conjunctival injection and minor discomfort with no functional decrement) and that 12 mg x min/m³ (minor conjunctival injection and no sensation of irritation) represented a threshold for such effects. The 12 mg x min/m³ is considered the point of departure for deriving the VRW values. Ocular effects appear to be the most sensitive indicator of sulfur mustard exposure and toxicity, thereby justifying ocular irritation as an appropriate end point for development of VRW values. An intraspecies uncertainty factor of 3 was applied and considered appropriate for acute exposures to chemicals whose mechanism of action primarily involves surface contact irritation of ocular and/or respiratory tract tissue. No interspecies uncertainty factor was necessary since effects were observed in humans. Time scaling was performed using $C^n \times t = k$, with an empirically derived n = 1 (several studies showed an n-value in the range of 0.96-1.1). The derivation of the exponent (n) utilized human response data where 75-100% of the responders showed a mild response that would be consistent with the definition of VRW effects. Holding the VRW levels constant across time was not considered appropriate in view of the data, which showed an increase in the severity of the effects as exposure was prolonged at the same exposure levels.

AGW: The AGW is based on a human volunteer study where three or four human volunteers were exposed to varying concentrations of sulfur mustard (0.25-2.4 ppm; 1.7-15.6 mg/m³) for time periods varying from 2 to 33 min. The 60 mg x min/m³ exposure was used as the basis for developing the AGW values, because it is representative of an acute exposure causing an effect severe enough to impair normal visual function and, although not irreversible, would certainly result in potential for additional injury. Effects included irritation, soreness, and widespread conjunctivitis, frequently accompanied by chemosis and photophobia. The ocular irritation and damage were also considered appropriate as a threshold estimate for AGW effects, because the eyes are generally considered the most sensitive indicator of sulfur mustard exposure, and irritation would likely occur in the absence of vesication effects and severe pulmonary effects. The fact that the AGW is based on human data precludes the use of an interspecies uncertainty factor. A factor of 3 was applied for intraspecies variability and considered appropriate for acute exposures to chemicals whose mechanism of action primarily involves surface contact irritation of ocular and/or respiratory tract tissue. A modifying factor of 3 was *not* applied, in contrast with the AEGL-2 value, because the effects were reversible. Adjusting for long term damage, therefore, does not seem appropriate. Time scaling was performed using $C^n \times t = k$, with an empirically derived n = 1 (several studies showed an n-value in the range of 0.96-1.1 for the endpoint eye irritation).

LBW: In an inhalation toxicity study, mice were exposed (head only) for 1-hr to sulfur mustard at concentrations of 0, 1.3, 2.6, 3.2, 4.1, 6.4, or 13 ppm (0, 8.5, 16.9, 21.3, 26.8, 42.3 or 84.7 mg/m³, respectively). The study investigator derived a 1-hr LC_{50} of 6.4 ppm (42.5 mg/m³) based on lethality at 14 d postexposure (95% confidence interval: 2-20 ppm; 13.5-133.4 mg/m³). In a follow-up study, there was no mortality in mice exposed at half the LC_{50} value (42.5/2 = 21.2 mg/m³). Therefore, the 1-hr exposure at 3.2 ppm (21.2 mg/m³) was selected as an estimate of the lethality threshold in mice. When compared with the human exposure-effect data, the 21.2 mg/m³ concentration is not an exposure that has been associated with lethality in humans. An intraspecies uncertainty factor of 3

was applied for protection of sensitive individuals. An interspecies uncertainty factor was limited to 3 because available data do not suggest that humans are notably more sensitive than animals regarding lethality from inhalation exposure to sulfur mustard. In the absence of chemical-specific lethality data, time scaling was performed using exponential extrapolation (n = 3) for shorter time periods and linear extrapolation (n = 1) for longer time periods.

Additional toxicological information (including relevant results of a general literature search, if any)

Sulfur mustard (agent HD) is an alkylating chemical vesicant that affects any epithelial surface it comes in contact with. The eye appears to be the most frequently affected and most sensitive organ and also has one of the shortest latency periods. The skin and respiratory tract are also primary targets of the substance. Sulfur mustard binds with DNA, RNA and proteins leading to cytotoxicity. Sulfur mustard agent is a known immunosuppressant.
Sulfur mustard did not induce reprotoxic effects in the rat after one week exposure during a three week gestation period.

No harmonized H-statements for human health.

Carcinogenicity and derivation of the CRP value

IARC classification: 1 (carcinogenic to humans)

Derivation of the carcinogenic risk potency (CRP):

10^{-4} risk level after inhalation: 2.5 x 10^{-5} mg/m^3 [AEGL]

CRP = (10^{-4} risk level * average life span in hours)/DRCF

= (2.5 x 10^{-5} * 613,200) /2.8 = 5.48 mg/m^3

Evidence for sulfur mustard related carcinogenicity in humans was studied in war veterans, workers at chemical warfare plants or ammunition depots. Tumors were most often located in the respiratory tract. The latency period was generally over 20 years. The CRP is above the LBW values, however carcinogenic effects (genotoxic effect) might result from exposures to sulfur mustard in the range of the intervention values.

Odour and derivation of the LOA value

Odour: Odourless (pure form) to a garlic/mustard-like odor (technical grade).

Odour thresholds ranging from 0.15 to 1.0 mg/m^3 were reported. Using the lowest reported odour threshold to derive the LOA gives:

OT_{50}: 0.023 ppm (0.15 mg/m^3) [AEGL (2003)]
LOA = 11.8 * OT_{50} * 1.33 = 2.35 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies in the order of the LBW values.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **0.067**	*AEGL-1* 0.066	*ERPG-1* Not derived		*IDLH: Not derived*
AGW level **0.33**	*AEGL-2* 0.13	*ERPG-2* Not derived		
LBW level **2.1**	*AEGL-3* 2.1	*ERPG-3* Not derived		

Stofdocument deel A

CAS-nr: 7446-11-9 **Zwaveltrioxide** **SO_3** **VN-nr: 1829**

GEVI: X88

Synoniemen: oleum (vast), triosul, zwavelzuuranhydride (Engels: γ-sulfur trioxide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,20	0,20	0,20	0,20	0,20	0,20
Alarmeringsgrenswaarden	AGW (mg/m³)	25	18	15	13	10	8,7
Levensbedreigende waarden	LBW (mg/m³)	270	200	160	140	110	93

Datum vaststelling: 13-05-2009 — Conversie niet van toepassing

Explosiegrens: geen data

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze, hygroscopische rokende vloeistof of ijs-achtige hygroscopische kristallen
Brand: niet brandbaar, bevordert brand van andere stoffen

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,5

Molecuulmassa: 80,1 g/mol
Zuurgraad: Geen data
LogKow: Geen data
Wateroplosbaarheid: reactie

Verzadigde dampdruk: 260 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: niet afgeleid
TLV-TWA: 1 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: lichte oog- en luchtwegirritatie, hoesten

AGW → LBW: benauwdheid, longoedeem

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Zwaveltrioxide reageert met water onder vorming van zwavelzuur.
- Zwavelzuur is irriterend en corrosief.
- Primaire effecten zijn irritatie en schade aan de luchtwegen
- Zwavelzuur kan longoedeem veroorzaken waarbij de verschijnselen vertraagd kunnen optreden.
- Astmapatiënten zijn gevoeliger voor de effecten van zwavelzuur.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, roodheid en pijn, blaren, brandwonden

Oogcontact: bijtend, roodheid en pijn, slecht zien, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd.
Zwavelzuur in sterke anorganische mist wordt beschouwd als carcinogeen (groep 1)(IARC monograph 54, 1992).

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding, specifieke behandeling en direct spoedeisende medische hulp inzetten.

ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof

huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen, arts raadplegen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen: geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7446-11-9 **Sulfur trioxide** SO_3 **UN-nr: 1829**

Basis for the Dutch Intervention Values

VRW: AEGL value of sulfuric acid adopted, 2hr value added. In accordance with AEGL.

AGW: Same point of departure as for AGEL, but using time-scaling to derive values for other time points.

LBW: AEGL value of sulfuric acid adopted, 2hr value added. In accordance with AEGL.

Date: 13-05-2009 AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.20	0.20	0.20	0.20	0.20	0.20	Nondisabling irritation in humans
AGW	25	18	15	13	10	8.7	Absence of AGW effects in humans
LBW	270	200	160	140	110	93	Threshold in animal lethality

Derivation of the Dutch Intervention Values

VRW: VRW values are based on the decomposition product sulfuric acid, because after accidents with sulfur trioxide the ambient exposure will be to sulfuric acid mist.
The results of various studies clearly indicate that the first signs of respiratory irritation that can be characterized as notable discomfort occur in humans at concentrations higher than 0.2 mg/m³. It is therefore concluded that the concentration of 0.2 mg/m³ can be used as the point of departure for VRW. Since the test subjects included exercising asthmatics, the most sensitive subpopulation, an intraspecies uncertainty factor of 1 is considered sufficient. There are no good data to establish a time-concentration effect (there are no data beyond 120 minutes where concentrations higher than 0.39 mg/m³ were tested). Considering the data up to 120 minutes of exposure and the type of effect (local irritation) the value of 0.2 mg/m³ was flat-lined across the 10- and 30-minute, and the 1-, 2-, 4-, and 8-hour exposure time points. This approach was considered appropriate because mild irritant effects generally do not vary greatly with time, and is in line with the derivation of VRW values for other respiratory irritants.

AGW: AGW values are based on sulfuric acid, which is present and can be formed after contact of sulfur trioxide with moist, because the ambient exposure will be to sulfuric acid mist (containing aerosols) after accidents.
Occupational studies indicate that no irreversible or other serious health effects or an impaired ability to escape are to be expected from single exposures to concentrations of up to 35 mg/m³. The concentration of 26.0 mg/m³ (8-hour exposure) was used as the point of departure for AGW. Under these exposure conditions workers were perfectly able to complete their work shift. An intraspecies uncertainty factor of 3 is needed to account for sensitive subpopulations. This results in an 8-hour AGW value of 8.7 mg/m³. This AGW level is considered to be rather conservative because no irreversible or disabling effects were observed following acute exposure to sulfuric acid in any of the relevant human volunteer studies. Time scaling was performed, with n=3.7 (see LBW). This approach is in contrast with the AEGL approach, which flat-lined the level of 8.7 mg/m³ across time.

LBW: LBW values are based on sulfuric acid, which is present and can be formed after contact of sulfur trioxide with moist, because the ambient exposure will be to sulfuric acid mist after accidents.
The calculated LC_{01} values (796, 592, 491, 338, 280 mg/m³ for 10 min, 30 min, 1-, 4-, and 8 hrs, respectively) for mice were used as a point of departure for the LBW. The probit method was used to derive the LC_{01} for the various exposure durations, because it allows to determine the combined effect of both concentration and time with all data included in the analysis simultaneously. Based on these data, the n-value appears to be 3.7. Using this n-value the 2 hr LBW was derived. No uncertainty factor is applied for the extrapolation from animals to humans, considering that (1) monkeys did not die and showed no serious effects up to 502 mg/m³ for an unknown exposure duration per day for 7 days, and (2) occupational concentrations up to 35 mg/m³ were tolerated during work shifts without significant acute health effects. An uncertainty factor of 3 is applied to account for variation in sensitivity among humans.

Additional toxicological information (including relevant results of a general literature search, if any)

Sulfur trioxide reacts with water in mucous membranes and ambient air to form sulfuric acid (mist) and thus adverse health effects are expected to result from sulfuric acid exposure. Effects will occur rapidly, consisting of irritation and corrosive effects on the lungs primarily. May cause lung edema possibly resulting in death. Effect may be delayed. Asthmatics may have an enhanced risk to health effects.

No data were available on reprotoxic or developmental toxic effects resulting from sulfur trioxide exposure.

No harmonized H-statements for human health.

Carcinogenicity and derivation of the CRP value	***Odour and derivation of the LOA value***
IARC classification: not classified Strong-inorganic-acid mists containing sulfuric acid are carcinogenic to humans (group 1) (IARC monograph 54, 1992). No carcinogenic risk potency (CRP) was calculated, because no chemical specific data on carcinogenicity were available.	Odour: pungent odour. LOA could not be determined due to lack of data.

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)***

VRW level **0.20**	*AEGL-1* 0.20	*ERPG-1* 1		*IDLH:*15 (30 min)
AGW level **15**	*AEGL-2* 8.7	*ERPG-2* 10		
LBW level **160**	*AEGL-3* 160	*ERPG-3* 83		

Stofdocument deel A

CAS-nr: 7783-06-4 **Zwavelwaterstof** **H_2S** **VN-nr: 1053** **GEVI: 263**

Synoniemen: hydrogeensulfide, waterstofsulfide (Engels: hydrogen sulfide) ***Status:*** B-stof

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	3,6	2,8	2,4	2,1	1,8	1,5
Alarmeringsgrenswaarden	AGW (mg/m³)	58	46	39	33	28	24
Levensbedreigende waarden	LBW (mg/m³)	110	84	72	61	52	45

Datum vaststelling: 24-09-2009 Conversiefactor 1 mg/m³ = 0,705 ppm; 1 ppm = 1,42 mg/m³

Explosiegrens: LEL = 4,3 vol% ≈ 61.000 mg/m³

Geur: typerende geur (rotte eieren)
LOA: 0,01 mg/m³

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos onder druk tot vloeistof verdikt gas
Brand: zeer brandgevaarlijk

Relatieve dichtheid gas: 1,2

Molecuulmassa:	34,1 g/mol
Zuurgraad:	geen data
LogKow:	0,5
Wateroplosbaarheid:	0,3 g/100 ml (slecht)
Verzadigde dampdruk:	18.800 mbar

Overige informatie

Publieke grenswaarde:
2,3 mg/m³ (8 uur)

MAK: 7,1 mg/m³

TLV-TWA: 14 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte oogirritatie, misselijkheid

VRW → AGW: hoofdpijn, oogirritatie, tranenvloed, rode ogen, lichte irritatie van de luchtwegen

AGW → LBW: benauwdheid, longoedeem, ophoesten bloed, hyperventilatie, hoornvliesbeschadiging, oogsidderingen, fotofobie, misselijkheid en braken, hoofdpijn, duizeligheid, verwarring/opwinding, pijn op borst, bewustzijnsdaling

Boven LBW: ademstilstand, convulsies, collaps, coma en sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Zwavelwaterstof blokkeert de ademhalingsketen in de cel. Hierdoor wordt de energiehuishouding verstoord en kan lactaatacidose ontstaan.
- Primaire doelorganen zijn het centrale zenuwstelsel en het cardiovasculaire systeem.
- Zwavelwaterstof werkt in lage concentraties irriterend op de ogen en luchtwegen.
- De stof kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Verlamming van de geurzenuw kan optreden bij hoge concentraties, waardoor de geurwaarneming en geurwaarschuwing achterwege blijft.

Effecten bij blootstelling aan vloeistof

Huidcontact: ernstige bevriezingsverschijnselen zoals pijn, blaren, wonden.

Oogcontact: roodheid en pijn, tranenvloed, lichtgevoeligheid, ernstige brandwonden, hoornvliesbeschadiging, bij bevriezing: bijtend.

Carcinogeniteit

IARC classificatie: niet geclassificeerd.

CRP: niet afgeleid.

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust, 100% zuurstof, halfzittende houding, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: in geval van bevriezingswonden: aan de huid vastgevroren kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas).

Specifieke behandeling en materialen*:* Bij vergiftiging door deze stof is specifieke eerste hulp noodzakelijk; specifieke antidota (o.a. 100% zuurstof) moeten met gebruiksaanwijzing ter plekke beschikbaar zijn. Zuurstof 100% moet onmiddellijk worden toegediend, zo nodig via hyperbare zuurstoftherapie (daarvoor is opname in een ziekenhuis noodzakelijk). Voor aanwijzingen over verdere behandeling zo nodig het NVIC (+31(0)30-274 88 88) bellen.

Stofdocument deel B

CAS-nr: 7783-06-4 **Hydrogen sulfide** H_2S **UN-nr: 1053**

Basis for the Dutch Intervention Values

VRW: Same point of departure as for AEGL-1, no modifying factor, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 24-09-2009 | AEGL document: Final, 2010

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	3.6	2.8	2.4	2.1	1.8	1.5	Headache in humans
AGW	58	46	39	33	28	24	Lung edema in animals
LBW	110	84	72	61	52	45	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: Human data were used to derive VRW values. Three of ten asthmatic volunteers exposed to 2 ppm (2.8 mg/m³) H_2S for 30 minutes complained of headache and eight of ten experienced (non-significant) increased airway resistance. Since there were no clinical symptoms of respiratory difficulty and there were no changes in FVC or FEV_1, the VRW was based exclusively upon increased complaints of headache. The values were scaled across time using $C^n \times t = k$, using the empirically-derived chemical specific value of 4.4 (derived from pooled rat lethality data ranging from 10 minutes to 6 hours exposure duration) for n. It was noted that the derivation of the value of n=4.4 is based on data derived from three different studies, which is not in line with the procedures of the Dutch expert panel on probits. However, using the data of a single rat study (Zwart et al., 1990) would result in an n with a very broad confidentiality range (-3.16-25) or would be either 2.8 or 7.8 based on two different mice studies (Zwart et al 1990 or Clanachan 1979.) both based on a very short time range (10 to 30 or 60 minutes, respectively). The third alternative, using the default values for n (n=1, n=3) would lead to unrealistically low VRW-values. Therefore, the n-value of 4.4, as used by AEGL, is adopted for derivation of VRW-values.

AGW: The focal areas of perivascular edema in rats exposed to 200 ppm (280 mg/m³) hydrogen sulfide for 4 hours were used as the point of departure for AGW values. An uncertainty factor of 3 was used to extrapolate from animals to humans since rat and mouse data suggest little interspecies variability. An uncertainty factor of 3 was also applied to account for sensitive individuals. Application of a higher uncertainty factor would yield AGW values inconsistent with the total database. The values were scaled across time using $C^n \times t = k$, using the empirically-derived chemical specific value of 4.4 (derived from pooled rat lethality data ranging from 10 minutes to 6 hours exposure duration) for n (due to a lack of a better alternative, see above) .

LBW: The highest hydrogen sulfide concentration causing no mortality in the rat after a 1 hour exposure (504 ppm; 715 mg/m³), was used as point of departure for LBW values. Lethality was observed in this study in rats exposed for 1 hour to concentrations of 635 and 800 ppm (900 and 1100 mg/m³). An uncertainty factor of 3 was used to extrapolate from animals to humans since rat and mouse data suggest little interspecies variability. An uncertainty factor of 3 was also applied to account for sensitive individuals. The intraspecies uncertainty factor of 3 was considered sufficient because application of a higher uncertainty factor would yield LBW values inconsistent with the total database. The values were scaled across time using $C^n \times t = k$, using the empirically-derived chemical specific value of 4.4 (derived from pooled rat lethality data ranging from 10 minutes to 6 hours exposure duration) for n (due to a lack of a better alternative, see above).

Additional toxicological information (including relevant results of a general literature search, if any)

Hydrogen sulfide is both an irritant and asphyxiant. In humans at relatively low concentrations (<10 ppm; 14 mg/m³), minor ocular and respiratory irritation occur, while at higher concentrations (hundreds to thousands of ppm), the central nervous system is affected and paralysis of the respiratory center may lead to rapid death.

Ocular effects described after inhalation of hydrogen sulfide include acute conjunctivitis ("gas eye") at concentrations of 50-100 ppm (70-140 mg/m^3) and are believed to be the result of direct contact of hydrogen sulfide with the eye. The threshold for eye irritation is reported to be 6-20 ppm (8.5-28 mg/m^3). There are numerous reports of accidental poisonings with hydrogen sulfide; however, neither reliable concentration nor duration parameters are described for lethal or nonlethal endpoints. Several reports suggest that neurological effects may persist in survivors of severe hydrogen sulfide poisonings. Some reports hypothesize that odors, such as the rotten egg smell associated with hydrogen sulfide, may trigger asthma attacks and other health effects; however, it is uncertain if a toxicological mechanism or a non-toxicologic odor-related mechanism is involved.

An association between spontaneous abortion and occupational exposure to hydrogen sulfide was identified in a cohort of female petroleum plant workers; however, no hydrogen sulfide concentrations were provided.

Data suggesting that hydrogen sulfide exposure can impair prenatal neurological development in rats are equivocal.

H330: Fatal if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No information concerning the carcinogenic potential of hydrogen sulfide in humans or experimental animals is available.

Odour and derivation of the LOA value

Odour: similar to rotten eggs

OT_{50}: 0.0006 ppm (0.0009 mg/m^3) [AEGL (2010]

LOA = 11.8 * OT_{50} * 1.33 = 0.01 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is lower than the VRW values

Other standards and guidelines ***(1h values in mg/m^3, unless otherwise indicated)***

VRW level **2.4**	*AEGL-1* 0.72	*ERPG-1* 0.14		*IDLH:* 142 (10 minutes)
AGW level **39**	*AEGL-2* 38	*ERPG-2* 43		
LBW level **72**	*AEGL-3* 71	*ERPG-3* 140		

Stofdocument deel A

CAS-nr: 7664-93-9 **Zwavelzuur** H_2SO_4 **VN-nr: 1830**

GEVI: 80

Synoniemen: dihydrosulfaat, monothionzuur (Engels: sulfuric acid) ***Status:*** geen

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	0,20	0,20	0,20	0,20	0,20	0,20
Alarmeringsgrenswaarden	AGW (mg/m³)	25	18	15	13	10	8,7
Levensbedreigende waarden	LBW (mg/m³)	270	200	160	140	110	93

Datum vaststelling: 13-05-2009 Conversie niet van toepassing

Explosiegrens: geen data

Geur: stekende geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze olieachtige vloeistof (hygroscopisch)

Brand: niet brandbaar, bevordert brand van andere stoffen

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,00

Molecuulmassa: 98,1 g/mol

Zuurgraad: Geen data

LogKow: Geen data

Wateroplosbaarheid: volledig

Verzadigde dampdruk: 0,001 mbar

Overige informatie

Publieke grenswaarde: 0,05 mg/m³ (8 uur)

MAK: 0,1 mg/m³

TLV-TWA: 1 mg/m³

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen informatie

VRW → AGW: lichte oog- en luchtwegirritatie, hoesten

AGW → LBW: benauwdheid, longoedeem

Boven LBW: ademnood, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Zwavelzuur is irriterend en corrosief.
- Primaire effecten zijn irritatie en schade aan de luchtwegen.
- Zwavelzuur kan longoedeem veroorzaken waarbij de verschijnselen vertraagd kunnen optreden.
- Astmapatiënten zijn gevoeliger voor de effecten van zwavelzuur.

Effecten bij blootstelling aan vloeistof

Huidcontact: bijtend, blaren, brandwonden

Oogcontact: bijtend, roodheid en pijn, hoornvliesbeschadiging, slecht zien, ernstige brandwonden

Carcinogeniteit

IARC classificatie: niet geclassificeerd.
Zwavelzuur in sterke anorganische mist wordt beschouwd als carcinogeen (groep 1)(IARC monograph 54, 1992).

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding, specifieke behandeling en direct spoedeisende medische hulp inzetten.

ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof

huid: bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen, arts raadplegen en direct spoedeisende medische hulp inzetten.

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: mond laten spoelen (uitspugen!), rust, GEEN braken opwekken, niet laten drinken en direct spoedeisende medische hulp inzetten.

Ontsmetting bij inademen/inslikken

Inademing/inslikken van sterke zuren kan tevens leiden tot larynx- en glottisoedeem, met risico op verstikking (asfyxie) door zwellingen in de keel. Intubatie (borgen van vrije luchtwegen), eventueel gevolgd door beademing moeten in ernstige gevallen z.s.m. worden uitgevoerd (door specialisten). Zet derhalve direct spoedeisende medische hulp in.

Specifieke behandeling en materialen: geen.

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 7664-93-9 **Sulfuric acid** **H_2SO_4** **UN-nr: 1830**

Basis for the Dutch Intervention Values

VRW: AEGL value adopted, 2hr value added.

AGW: Same point of departure as for AEGL, but using time-scaling to derive values for other time points

LBW: AEGL value adopted, 2hr value added.

Date: 13-05-2009 | AEGL document: Interim, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.20	0.20	0.20	0.20	0.20	0.20	Nondisabling irritation in humans
AGW	25	18	15	13	10	8.7	Absence of AGW effects in humans
LBW	270	200	160	140	110	93	Threshold of animal lethality

Derivation of the Dutch Intervention Values

VRW: The results of various studies clearly indicate that the first signs of respiratory irritation that can be characterized as notable discomfort occur at concentrations higher than 0.05 ppm (0.2 mg/m³) in humans. It is therefore concluded that the concentration of 0.05 ppm (0.2 mg/m³) can be used as the point of departure for VRW. Since the test subjects included exercising asthmatics, the most sensitive subpopulation, an intraspecies uncertainty factor of 1 is considered sufficient. There are no good data to establish a time-concentration effect (there are no data beyond 120 minutes where concentrations higher than 0.096 ppm (0.39 mg/m³) were tested). Considering the data up to 120 minutes of exposure and the type of effect (local irritation) the value of 0.2 mg/m³ was flat-lined across the 10- and 30-minute, and the 1-, 2-, 4-, and 8-hour exposure time points. This approach was considered appropriate because mild irritant effects generally do not vary greatly with time, and is in line with the derivation of VRW values for other respiratory irritants.

AGW: Occupational studies indicate that no irreversible or other serious health effects or an impaired ability to escape are to be expected from single exposures to concentrations of up to 9 ppm (35 mg/m³). The concentration of 6 ppm (26.0 mg/m³) (8-hour exposure) was used as the point of departure for AGW. Under these exposure conditions workers were perfectly able to complete their work shift. An intraspecies uncertainty factor of 3 is needed to account for sensitive subpopulations. This results in an 8-hour AGW value of 2 ppm (8.7 mg/m³). This AGW level is considered to be rather conservative because no irreversible or disabling effects were observed following acute exposure to sulfuric acid in any of the relevant human volunteer studies. Time scaling was performed, with n=3.7 (see LBW). This approach is in contrast with the AEGL approach, which flat-lined the level of 8.7 mg/m³ across time.

LBW: The calculated LC_{01} values (195, 145, 120, 83, 69 ppm; 796, 592, 491, 338, 280 mg/m³ for 10 min, 30 min, 1-, 4-, and 8 hrs, respectively) for mice were used as a point of departure for the LBW. The probit method was used to derive the LC_{01} for the various exposure durations, because it allows determining the combined effect of both concentration and time with all data included in the analysis simultaneously. Based on these data, the n-value appears to be 3.7. Using this n-value the 2 hr LBW was derived. No uncertainty factor is applied for the extrapolation from animals to humans, considering that (1) monkeys did not die and showed no serious effects up to 123 ppm (502 mg/m³) for unknown exposure duration per day for 7 days, and (2) occupational concentrations up to 35 mg/m³ were tolerated during work shifts without significant acute health effects. An uncertainty factor of 3 is applied to account for variation in sensitivity among humans.

Additional toxicological information (including relevant results of a general literature search, if any)

Effects will occur rapidly, consisting of irritation and corrosive effects on the lungs primarily. May cause lung edema possibly resulting in death. Effects may be delayed. Asthmatics may have an enhanced risk to health effects. In mists the effects will occur sooner.

No data are available on reprotoxic or developmental toxic effects of sulfuric acid.

H314: Causes severe skin burns and eye damage.

Carcinogenicity and derivation of the CRP value
IARC classification: not classified Strong-inorganic-acid mists containing sulfuric acid are carcinogenic to humans (group 1) (IARC monograph 54, 1992). No carcinogenic risk potency was calculated, because no chemical specific data on carcinogenicity were available.

Odour and derivation of the LOA value
Odour: pungent odour. LOA could not be determined, due to lack of data.

Other standards and guidelines ***(1h values in mg/m³, unless otherwise indicated)***				
VRW level **0.20**	*AEGL-1* 0.20	*ERPG-1* 2		*IDLH:*15 (30 min)
AGW level **15**	*AEGL-2* 8.7	*ERPG-2* 10		
LBW level **160**	*AEGL-3* 160	*ERPG-3* 120		

Overzicht van stoffen met 'oude' interventiewaarden

Wanneer een stofdocument nog niet herzien is, gelden nog de interventiewaarden uit 2007 waarbij alleen 1-uurs waarden zijn afgeleid. Hieronder wordt een handreiking gegeven hoe de 1-uurs waarden naar andere tijdsduren kunnen worden geschaald.

LEGENDA
VRW: Voorlichtingsrichtwaarde
AGW: Alarmeringsgrenswaarde
LBW: Levensbedreigende waarde

A/B-status: Uitgaande van de fysisch-chemische eigenschappen en toxiciteit van stoffen is een classificering ontwikkeld die de Adviseur Gevaarlijke Stoffen (AGS) van de brandweer direct inzicht geeft in de noodzaak om bij incidenten al dan niet op te schalen. Er worden drie klassen onderscheiden: 1) Geen; 2) A-stof; 3) B-stof. De classificering wordt uitgevoerd door de Veiligheidsregio Rotterdam-Rijnmond.

n.v.t.: Deze stoffen kunnen ernstige acute gezondheidsschade veroorzaken bij een blootstelling van één uur zonder dat daar een sensorische waarneming aan voorafgaat. Deze stoffen hebben dan ook geen VRW onder het niveau van de AGW.
?: Er waren onvoldoende gegevens om deze interventiewaarde vast te stellen.
(getal): Getallen tussen haakjes zijn concentraties gebaseerd op percentages van de onderste explosiegrens (Lower Explosive Limit, LEL). Voor stoffen met explosiegevaar als het kritische effect voor de LBW of AGW is de LBW vastgesteld op 100% van de LEL, en de AGW op 10% van de LEL

Extrapolatie naar andere tijdsduren
Alle oude interventiewaarden zijn afgeleid voor een blootstellingsduur van één uur. Het kan zinvol zijn om een oude interventiewaarde te gebruiken voor een andere blootstellingsduur. Daarvoor is in het verleden na overleg met het GAGS platform besloten de waarde voor een andere duur dan de opgegeven 1 uur als volgt vast te stellen:

1. Voor een blootstelling korter dan 1 uur geldt dezelfde waarde als voor 1 uur blootstelling.
2. Voor een blootstelling van 1 uur geldt de opgegeven waarde.
3. Voor een blootstelling langer dan 1 uur kan volgens onderstaande systematiek een waarde uit de standaard reeks …- 500 – 200 – 100 – 50 – 20 – 10 – 5 – 2 – 1 – 0,5 – 0,2 – 0,1… worden gekozen. Voor de eenvoud en in lijn met de nieuwe methodiek worden alleen waarden voorgesteld voor 2, 4 en 8 uur: voor 2 uur één waarde lager uit de reeks, voor 4 uur twee waarden lager, en voor 8 uur drie waarden lager.

De strategie is onafhankelijk van de interventiewaarde (VRW, AGW of LBW).

Het kan nog voorkomen dat voor sommige oude stoffen de interventiewaarden destijds gebaseerd zijn op structuuranalogie met een stof die op dit moment reeds herzien is.

STOF	CAS nr	VN nr	1-uurs interventiewaarden (mg/m³)			A/B-status
			VRW	AGW	LBW	
Acetylchloride	75-36-5	1717	1	20	200	B
Acetyleen	74-86-2	1001	1.000	(2.500)	(25.000)	B
Allylbromide	106-95-6	1099	10	100	500	A
Allylglycidylether	106-92-3	2219	50	100	500	A
Amylmercaptanen	110-66-7	1111	0,005	100	500	A
Boriumtrichloride	10294-34-5	1741	2	50	100	B
Broomchloormethaan	74-97-5	1887	2.000	5.000	10.000	A
Broomcyanide	506-68-3	1889	0,2	2	20	B
Butaandion	431-03-8	2346	0,1	100	500	A
n-Butaanthiol	109-79-5	2347	0,01	100	500	A
n-Butanol	71-36-3	1120	10	500	5.000	geen
1-Buteen	106-98-9	1012	20	(3.750)	(37.500)	A
2-Buteen	107-01-7	1012	10	(3.750)	(37.500)	A
n-Butylamine	109-73-9	1125	2	20	200	B
sec-Butylamine	13952-84-6	2733	2	20	1.000	B
tert-Butylhydroperoxide	75-91-2	2093	1	50	200	A
Chinon	106-51-4	2587	0,2	2	100	A
Chloortoluenen	25169-05-2	2238	0,5	1.000	5.000	geen
Chloortrifluormethaan	75-72-9	1022	?	100.000	1.000.000	A
Chloraal	75-87-6	2075	1	200	2.000	A
2-Chloropreen	126-99-8	1991	10	100	1.000	A
Collodium	9004-70-0	2059	20	1.000	10.000	A
o-Cresol	95-48-7	3455	0,02	100	1.000	geen
Cumeenhydroperoxide	80-15-9	3109	2	20	100	A
Cyclohexanon	108-94-1	1915	20	200	2.000	geen
Diallylamine	124-02-7	2359	20	100	1.000	A
Dichloordifluormethaan	75-71-8	1028	?	50.000	100.000	A
1,1-Dichloorethaan	75-34-3	2362	1.000	10.000	20.000	geen
Dichloormonofluormethaan	75-43-4	1029	?	2.000	20.000	A
1,2-Dichloorpropaan	78-87-5	1279	20	500	5.000	A
1,3-Dichloorpropeen	542-75-6	2047	20	500	1.000	A
1,2-Dichloor-1,1,2,2-tetrafluorethaan	76-14-2	1958	n.v.t.	5.000	20.000	A
Diethylamine	109-89-7	1154	1	100	1.000	A
Diethylsulfide	352-93-2	2375	0,1	2.000	5.000	geen
Difenyloxide	101-84-8	3077	1	50	2.000	geen
1,1-Difluorethyleen	75-38-7	1959	?	(6.100)	(61.000)	B
Diisodecylftalaat	26761-40-0	nvt	20	200	2.000	geen
Dimethylether	115-10-6	1033	n.v.t.	(6.500)	(65.000)	A
2,4-Dinitroaniline	97-02-9	1596	?	1	200	geen
Etheen	74-85-1	1962	1.000	(3.160)	(31.600)	A
Ether	60-29-7	1155	20	1.000	10.000	A
Ethylacetaat	141-78-6	1173	200	1.000	10.000	A

STOF	CAS nr	VN nr	1-uurs interventiewaarden (mg/m³)			A/B-status
			VRW	AGW	LBW	
Ethylbromide	74-96-4	1891	50	1.000	5.000	A
Ethylbroomacetaat	105-36-2	1603	0,2	2	10	B
Ethylchloride	75-00-3	1037	50	(9.650)	50.000	A
Ethyleenglycolmono-ethyleter	110-80-5	1171	50	500	2.000	geen
Ethyleenglycolmono-ethylether acetaat	111-15-9	1172	2	500	5.000	geen
Ethyleenglycolmono-methylether	109-86-4	1188	20	100	1.000	geen
Ethylformiaat	109-94-4	1190	200	2.000	5.000	A
Fosforpentasulfide	1314-80-3	1340	0,2	20	100	geen
Fosfortribromide	7789-60-8	1808	10	50	500	A
Gasolie	64741-44-2	1202	2	20	200	A
Heptaan	142-82-5	1206	1.000	2.000	10.000	geen
Hexachloorcyclopentadieen	77-47-4	2646	0,1	1	10	A
Hexanol	111-27-3	nvt	2	50	500	geen
Isobutaan	75-28-5	1969	500	(3.850)	(38.500)	A
Isobutanol	78-83-1	1212	50	1.000	5.000	geen
Isobutylacetaat	110-19-0	1213	50	2.000	10.000	geen
Isobutylacrylaat	106-63-8	2527	?	100	1.000	A
Isobutylamine	78-81-9	1214	2	20	200	B
Isobutyleen	115-11-7	1055	100	1.000	(42.000)	A
Isobutylisocyanaat	1873-29-6	2486	0,05	0,2	5	B
Isobutylmethacrylaat	97-86-9	2283	?	500	10.000	geen
Isoforon	78-59-1	nvt	5	50	500	geen
Isopentaan	78-78-4	1265	2000	(3.900)	(39.000)	A
Isopropylacetaat	108-21-4	1220	100	1.000	10.000	A
Isopropylalcohol	67-63-0	1219	200	1.000	10.000	geen
Isopropylamine	75-31-0	1221	2	50	2.000	A
Isopropylchloride	75-29-6	2356	?	(9.200)	50.000	A
Isopropylether	108-20-3	1159	1	2.000	20.000	A
Isopropylnitraat	1712-64-7	1222	?	500	5.000	A
Kooldioxide	124-38-9	1013	n.v.t.	50.000	100.000	A
Koolwaterstof-oplosmiddelen	8052-41-3	1202	200	2.000	10.000	geen
Lachgas	10024-97-2	1070	n.v.t.	10.000	500.000	A
LPG	68476-85-7	1965	?	(2.630)	(26.300)	A
Methylacetaat	79-20-9	1231	500	5.000	20.000	geen
Methylacetyleen/propadieen gasmengsel	59355-75-8	1060	500	(3.600)	(36.000)	A
Methylacrylaat	96-33-3	1919	1	200	1.000	A
Methylal	109-87-5	1234	?	(6.950)	10.000	A
n-Methylethylamine	624-78-2	2924	2	200	1.000	A
Methylformiaat	107-31-3	1243	1.000	2.000	5.000	A
Methylisobutylcarbinol	108-11-2	2053	20	200	2.000	geen
a-Methylstyreen	98-83-9	2303	5	1.000	5.000	geen
Monochloordifluormethaan	75-45-6	1018	2.000	20.000	100.000	A

STOF	CAS nr	VN nr	1-uurs interventiewaarden (mg/m³)			A/B-status
			VRW	AGW	LBW	
Nicotine	54-11-5	1654	?	1	10	A
Nitrobenzeen	98-95-3	1662	10	100	500	geen
Nitromethaan	75-52-5	1261	500	1.000	5.000	geen
2-Nitropropaan	79-46-9	2608	n.v.t.	200	1.000	A
Nitrosylchloride	2696-92-6	1069	5	20	200	B
Octaan	111-65-9	1262	500	(3.800)	20.000	geen
Ozon	10028-15-6	nvt	0,2	0,5	5	B
n-Pentaan	109-66-0	1265	500	(4.200)	(42.000)	geen
Piperazine	110-85-0	2579	?	20	500	geen
n-Propanol	71-23-8	1274	100	1.000	5.000	geen
Propeen	115-07-1	1077	200	(3.500)	(35.000)	A
Propionylchloride	79-03-8	1815	10	50	500	A
Propionzuur	79-09-4	1848	1	1.000	10.000	geen
Propylacetaat	109-60-4	1276	10	1.000	5.000	geen
Propylamine	107-10-8	1277	0,1	50	500	B
Propylbromide	106-94-5	2344	50	1.000	5.000	A
1,2-Propyleenglycol	57-55-6	nvt	200	2.000	20.000	geen
Propyleenglycolethylether	1569-02-4	1987	100	1.000	10.000	geen
Propylmercaptaan	107-03-9	nvt	0,02	200	2.000	A
n-Propylnitraat	627-13-4	1865	n.v.t.	500	5.000	A
Pyridine	110-86-1	1282	2	100	2.000	A
Terpentijn	8006-64-2	1299	100	1.000	2.000	geen
Tetrahydrothiofeen	110-01-0	2412	0,01	1.000	5.000	geen
Tetramethyllood	75-74-1	1649	?	2	200	B
Tintetrachloride	7646-78-8	1827	2	10	100	B
Triethylaluminium	97-93-8	3394	5	50	500	geen
Triethylamine	121-44-8	1296	2	50	500	A
Trifluorazijnzuur	76-05-1	2699	10	100	200	A
Trifluorbroommethaan	75-63-8	1009	n.v.t.	100.000	1.000.000	A
Valeriaanaldehyde	590-86-3	2058	0,05	2.000	10.000	geen
Vinylbromide	593-60-2	1085	?	2.000	50.000	A
Vinylethylether	109-92-2	1302	?	1.000	10.000	A
Vinyltrimethoxisilaan	2768-02-7	nvt	100	1.000	5.000	A
Waterstof	1333-74-0	1049	n.v.t	(330)	(3.300)	A
Xylidine	1300-73-8	1711	0,2	100	1.000	geen
Zwaveldichloride	10545-99-0	1828	0,02	10	50	B
Zwaveltetrafluoride	7783-60-0	2418	0,5	5	20	B

K. Mahieu | L. Geraets | P. Bos

Dit is een uitgave van:

Rijksinstituut voor Volksgezondheid en Milieu
Postbus 1 | 3720 BA Bilthoven
Nederland
www.rivm.nl

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