N-Nitrosodimethylamine (NDMA)

N-Nitrosodimethylamine, or NDMA, can occur in drinking-water through the degradation of dimethylhydrazine (a component of rocket fuel) as well as from several other industrial processes. It is also a contaminant of certain pesticides. NDMA has recently been identified as a disinfection by-product of chloramination (by the reaction of monochloramine with dimethylamine, a ubiquitous component of waters impacted by wastewater discharges) and, to some extent, chlorination. NDMA can also be formed as a by-product of anion-exchange treatment of water.

Guideline value	0.0001 mg/litre (0.1 µg/litre)
Occurrence	Where chloramination is used, distribution system samples can have much higher levels of NDMA than the finished water at the treatment plant. Levels as high as 0.16 µg/litre have been measured in the distribution system, but concentrations in water at the treatment plant are generally less than 0.01 µg/litre.
Basis of guideline derivation	Hepatic biliary cystadenomas in female rats, the most sensitive carcinogenic end-point, observed in a drinking-water study, using a multistage model
Limit of detection	0.028 ng/litre by capillary column GC and chemical ionization tandem MS; 0.4 ng/litre by capillary column GC and high-resolution MS; 0.7–1.6 ng/litre by GC/MS and ammonia positive chemical ionization detection
Treatment achievability	The most common process for NDMA removal is UV irradiation. A concentration below 0.005 µg/litre should be achievable by UV irradiation provided that the water is not grossly contaminated. NDMA is not removable by air stripping, activated carbon adsorption, reverse osmosis or biodegradation.
Additional comments	Potential methods for reducing the formation of NDMA during disinfection include avoiding the use of chloramination, use of breakpoint chlorination and removal of ammonia prior to chlorination.

Toxicological review

There is conclusive evidence that NDMA is a potent carcinogen in experimental animals by several routes of exposure, including through ingestion of drinking-water. NDMA has been classified by IARC as probably carcinogenic to humans. The mechanism by which NDMA produces cancer is well understood to involve biotransformation by liver microsomal enzymes, generating the methyldiazonium ion. This reactive metabolite forms DNA adducts, with most evidence pointing to O^6-methylguanine as the likely proximal carcinogenic agent. As a consequence of the clear evidence of carcinogenicity, there have been few studies of other possible toxic end-points.

There is also ample evidence that NDMA is genotoxic both *in vivo* and *in vitro*. Activation by liver microsomal S9 fractions is necessary for a positive *in vitro* result. The recent observation that human S9 fractions are much more active in promoting genotoxicity in the Ames test than rat S9 fractions suggests that humans may be especially sensitive to the carcinogenicity of NDMA.

Although there have been several case–control studies and one cohort study of NDMA in humans, none of them can be used to derive a quantitative risk of cancer. The results are supportive of the assumption that NDMA consumption is positively associated with either gastric or colorectal cancer. However, none of the studies focused on drinking-water as the route of exposure; instead, they used estimations of total dietary intake of NDMA.

History of guideline development

N-Nitrosodimethylamine was not considered in the WHO *International Standards for Drinking-water* or in the first or second editions of the WHO *Guidelines for Drinking-water Quality*.

Assessment date

The risk assessment was conducted in 2006.

Principal references

WHO (2002) N-*Nitrosodimethylamine.* Geneva, World Health Organization, International Programme on Chemical Safety (Concise International Chemical Assessment Document No. 38).

WHO (2008) N-*Nitrosodimethylamine in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/HSE/AMR/08.03/8).