

of spills and where there are higher concentrations in industrial areas. Two health-based values are derived based on the limited available information: one for short-term exposure (30 µg/l) and the other for long-term exposure (8–63 µg/l, depending on end-point and approach used). It should be emphasized that the derivation of the long-term health-based values includes large uncertainties because of the dose metric conversion from inhalation studies and the possibility of increased metabolism to aniline in the gastrointestinal tract.

It should be emphasized that nitrobenzene is a potent methaemoglobinaemic agent in humans, which is of particular concern for bottle-fed infants. Currently, data are not adequate to determine a separate health-based value for this end-point.

It should also be noted that the reported odour threshold for nitrobenzene in water is 30–110 µg/l.

N-Nitrosodimethylamine

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 affected 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/l (0.1 µg/l)
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/l have been measured in the distribution system, but concentrations in water at the treatment plant are generally less than 0.01 µg/l
Basis of guideline value 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/l by capillary column GC and chemical ionization tandem MS; 0.4 ng/l by capillary column GC and high-resolution MS; 0.7–1.6 ng/l by GC-MS and ammonia positive chemical ionization detection
Treatment performance	The most common process for NDMA removal is UV irradiation. A concentration below 0.005 µg/l 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.
Assessment date	2006
Principal references	IPCS (2002) <i>N-Nitrosodimethylamine</i> WHO (2008) <i>N-Nitrosodimethylamine in drinking-water</i>

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 O⁶-methylguanine as the likely proximal carcinogenic agent. As a consequence of the clear evidence of carcinogenicity, there have been few studies of other possible toxicity 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.

Parathion

Parathion (CAS No. 56-38-2) is a non-systemic insecticide that is used in many countries throughout the world. It is used as a fumigant and acaricide and as a pre-harvest soil and foliage treatment on a wide variety of crops, both outdoors and in greenhouses. Parathion released to the environment will adsorb strongly to the top layer of soil and is not likely to leach significantly. Parathion disappears from surface waters in about a week. The general population is not usually exposed to parathion from air or water. Parathion residues in food are the main source of exposure.

Reason for not establishing a guideline value	Occurs in drinking-water at concentrations well below those of health concern
Assessment date	2003
Principal references	FAO/WHO (1996) <i>Pesticide residues in food—1995 evaluations</i> WHO (2003) <i>Parathion in drinking-water</i>

Parathion inhibits cholinesterase activity in all species tested. There has been no evidence of carcinogenicity in 2-year rat studies. JMPR concluded that parathion is not genotoxic.

A health-based value of 10 µg/l can be calculated for parathion on the basis of an ADI of 0–0.004 mg/kg body weight based on a NOAEL of 0.4 mg/kg body weight per day in a 2-year study in rats for retinal atrophy and inhibition of brain acetylcholinesterase at the next higher dose, and using an uncertainty factor of 100 for interspecies and intraspecies variation. Lower NOAELs in experimental animals, based only on inhibition of erythrocyte or brain acetylcholinesterase, were not considered relevant