12.66 **Halogenated acetonitriles (dichloroacetonitrile, dibromoacetonitrile, bromochloroacetonitrile, trichloroacetonitrile)**

Halogenated acetonitriles are produced during water chlorination or chloramination from naturally occurring substances, including algae, fulvic acid and proteinaceous material. In general, increasing temperature and/or decreasing pH have been associated with increasing concentrations of halogenated acetonitriles. Ambient bromide levels appear to influence, to some degree, the speciation of halogenated acetonitrile compounds. Dichloroacetonitrile is by far the most predominant halogenated acetonitrile species detected in drinking-water.

<table>
<thead>
<tr>
<th>Provisional guideline value for dichloroacetonitrile</th>
<th>0.02 mg/litre</th>
</tr>
</thead>
<tbody>
<tr>
<td>The guideline value for dichloroacetonitrile is provisional due to limitations of the toxicological database.</td>
<td></td>
</tr>
<tr>
<td>Guideline value for dibromoacetonitrile</td>
<td>0.07 mg/litre</td>
</tr>
<tr>
<td>Occurrence</td>
<td>Halogenated acetonitriles have been found in surface water and groundwater distribution systems at concentrations generally below 10 μg/litre and usually below 1 μg/litre.</td>
</tr>
<tr>
<td>TDIs</td>
<td></td>
</tr>
<tr>
<td>Dichloroacetonitrile</td>
<td>2.7 μg/kg of body weight based on a LOAEL of 8 mg/kg of body weight per day for increased relative liver weight in male and female rats in a 90-day study, using an uncertainty factor of 3000 (taking into consideration intra- and interspecies variation, the short duration of the study, the use of a minimal LOAEL and database deficiencies)</td>
</tr>
<tr>
<td>Dibromoacetonitrile</td>
<td>11 μg/kg of body weight, based on a NOAEL of 11.3 mg/kg of body weight per day for decreased body weight in male F344 rats in a 90-day drinking-water study and an uncertainty factor of 1000 (accounting for inter- and intraspecies variation, subchronic to chronic extrapolation and database insufficiencies)</td>
</tr>
<tr>
<td>Limit of detection</td>
<td>0.03 μg/litre by GC with an ECD</td>
</tr>
</tbody>
</table>
Treatment achievability
Concentrations of individual halogenated acetonitriles can exceed 0.01 mg/litre, although levels of 0.002 mg/litre or less are more usual. Trichloroacetonitrile concentrations are likely to be much less than 0.001 mg/litre. Reduction of organic precursors will reduce their formation.

Guideline derivation
- allocation to water: 20% of TDI
- weight: 60-kg adult
- consumption: 2 litres/day

Toxicological review
IARC has concluded that dichloro-, dibromo-, bromochloro- and trichloroacetonitrile are not classifiable as to their carcinogenicity in humans. Dichloroacetonitrile and bromochloroacetonitrile have been shown to be mutagenic in bacterial assays, whereas results for dibromoacetonitrile and trichloroacetonitrile were negative. All four of these halogenated acetonitriles induced sister chromatid exchange and DNA strand breaks and adducts in mammalian cells in vitro but were negative in the mouse micronucleus test.

The majority of reproductive and developmental toxicity studies of the halogenated acetonitriles were conducted using tricaprylin as a vehicle for gavage administration of the compound under study. As tricaprylin was subsequently demonstrated to be a developmental toxicant that potentiated the effects of trichloroacetonitrile and, presumably, other halogenated acetonitriles, results reported for developmental studies using tricaprylin as the gavage vehicle are likely to overestimate the developmental toxicity of these halogenated acetonitriles.

Dichloroacetonitrile
Dichloroacetonitrile induced decreases in body weight and increases in relative liver weight in short-term studies. Although developmental toxicity has been demonstrated, the studies used tricaprylin as the vehicle for gavage administration.

Dibromoacetonitrile
Dibromoacetonitrile is currently under test for chronic toxicity in mice and rats. None of the available reproductive or developmental studies were adequate to use in the quantitative dose–response assessment. The data gap may be particularly relevant since cyanide, a metabolite of dibromoacetonitrile, induces male reproductive system toxicity, and due to uncertainty regarding the significance of the testes effects observed in the 14-day National Toxicology Program (NTP) rat study.

Bromochloroacetonitrile
Available data are insufficient to serve as a basis for derivation of a guideline value for bromochloroacetonitrile.
Trichloroacetonitrile
Available data are also insufficient to serve as a basis for derivation of a guideline value for trichloroacetonitrile. The previous provisional guideline value of 1 μg/litre was based on a developmental toxicity study in which trichloroacetonitrile was administered by gavage in tricaprylin vehicle, and a recent re-evaluation judged this study to be unreliable in light of the finding in a more recent study that tricaprylin potentiates the developmental and teratogenic effects of halogenated acetonitriles and alters the spectrum of malformations in the fetuses of treated dams.

History of guideline development
The 1958, 1963 and 1971 WHO International Standards for Drinking-water and the first edition of the Guidelines for Drinking-water Quality, published in 1984, did not refer to halogenated acetonitriles. The 1993 Guidelines established provisional health-based guideline values of 0.09 mg/litre for dichloroacetonitrile, 0.1 mg/litre for dibromoacetonitrile and 0.001 mg/litre for trichloroacetonitrile. The guideline values were designated as provisional because of the limitations of the databases (i.e., lack of long-term toxicity and carcinogenicity bioassays). Available data were insufficient to serve as a basis for derivation of a guideline value for bromochloroacetonitrile.

Assessment date
The risk assessment was conducted in 2003.

Principal references

12.67 Hardness
Hardness in water is caused by dissolved calcium and, to a lesser extent, magnesium. It is usually expressed as the equivalent quantity of calcium carbonate.

Depending on pH and alkalinity, hardness above about 200 mg/litre can result in scale deposition, particularly on heating. Soft waters with a hardness of less than about 100 mg/litre have a low buffering capacity and may be more corrosive to water pipes.

A number of ecological and analytical epidemiological studies have shown a statistically significant inverse relationship between hardness of drinking-water and cardiovascular disease. There is some indication that very soft waters may have an adverse effect on mineral balance, but detailed studies were not available for evaluation.