IARC has concluded that dichloroacetonitrile, dibromoacetonitrile, bromochloroacetonitrile 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 analysis 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 because cyanide, a metabolite of dibromoacetonitrile, induces male reproductive system toxicity and because of uncertainty regarding the significance of the testes effects observed in a 14-day 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/l was based on a developmental toxicity study in which trichloroacetonitrile was administered by gavage in tricaprylin vehicle, and a 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.

### *Hardness*

Hardness in water is caused by a variety of dissolved polyvalent metallic ions, predominantly calcium and magnesium cations. It is usually expressed as milligrams of calcium carbonate per litre. Hardness is the traditional measure of the capacity of

water to react with soap, hard water requiring considerably more soap to produce a lather.

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|---|---|
| Reason for not establishing a guideline value | Not of health concern at levels found in drinking-water |
| Additional comments | May affect acceptability of drinking-water |
| Assessment date | 1993, revised in 2011 |
| Principal reference | WHO (2011) *Hardness in drinking-water* |

Natural and treated waters have a wide range of mineral content, from very low levels in rainwater and naturally soft and softened water to higher levels in naturally hard waters. Bottled and packaged waters can be naturally mineralized or naturally soft or demineralized. Thus, the mineral consumption from drinking-water and cooking water will vary widely, depending upon location, treatment and water source.

The degree of hardness of drinking-water is important for aesthetic acceptability by consumers (see chapter 10) and for economic and operational considerations. Many hard waters are softened for those reasons using several applicable technologies. The choice of the most appropriate conditioning technology will depend on local circumstances (e.g. water quality issues, piping materials, corrosion) and will be applied either centrally or in individual homes as a consumer preference.

Consumers should be informed of the mineral composition of their water, whether or not it is modified. The contribution of drinking-water minerals to mineral nutrition should be considered where changes in supply are proposed or where less traditional sources, such as recycled water, seawater or brackish water, are processed and exploited for drinking-water. The treatments used remove most minerals, and stabilization of water is always necessary prior to distribution.

Drinking-water can be a contributor to calcium and magnesium intake and could be important for those who are marginal for calcium and magnesium. Where drinking-water supplies are supplemented with or replaced by demineralized water that requires conditioning, consideration should be given to adding calcium and magnesium salts to achieve concentrations similar to those that the population received from the original supply. Modification of calcium and magnesium concentrations in drinking-water for health reasons should comply with the technical requirements to provide water suitable for distribution.

Although there is evidence from epidemiological studies for a protective effect of magnesium or hardness on cardiovascular mortality, the evidence is being debated and does not prove causality. Further studies are being conducted. There are insufficient data to suggest either minimum or maximum concentrations of minerals at this time, as adequate intake will depend on a range of other factors. Therefore, no guideline values are proposed.

### *Heptachlor and heptachlor epoxide*

Heptachlor (CAS No. 76-44-8) is a broad-spectrum insecticide, the use of which has been banned or restricted in many countries. At present, the major use of heptachlor