

Summary Statement

12.20 Chloral hydrate (trichloroacetaldehyde)

Chloral hydrate can be formed as a by-product of the chlorination of water containing organic precursor material, such as fulvic and humic acids. It has been found in drinking-water at concentrations of up to 100 µg/litre, but concentrations are usually below 10 µg/litre. Concentrations are generally higher in surface water than in groundwater, and concentrations appear to increase during distribution.

Chloral hydrate is used as an intermediate in the production of insecticides, herbicides and hypnotic drugs. It has also been widely used as a sedative or hypnotic drug in humans at oral doses of up to about 750–1000 mg/day. Although intake from clinical use is considerably higher than intake from drinking-water, clinical exposure is of shorter-term duration.

No epidemiological or carcinogenic studies were found in humans that associated exposure to chloral hydrate with cancer, despite the fact that chloral hydrate has been used for many decades (and still is used) as a sedative and hypnotic drug in adults and children (specifically for dental procedures). IARC classified chloral hydrate as not classifiable as to its carcinogenicity to humans (Group 3), based on inadequate evidence in humans and limited evidence in experimental animals. There is equivocal evidence of genotoxicity for chloral hydrate.

A health-based value of 0.1 mg/litre (rounded figure) can be calculated on the basis of a TDI of 0.0045 mg/kg of body weight per day derived based on an increased incidence of liver histopathology observed in B6C3F1 mice in a 2-year drinking-water study, allocating 80% of the TDI to drinking-water (because most exposure to chloral hydrate is from drinking-water) and assuming a 60-kg adult consuming 2 litres of water per day. However, because chloral hydrate usually occurs in drinking-water at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a guideline value.

Chloral hydrate levels in drinking-water can be controlled by changes to disinfection practice (e.g., enhanced coagulation and softening to remove organic precursor compounds, moving the point of disinfection to reduce the reaction between chlorine and precursor compounds and using chloramines for residual disinfection instead of chlorine) and by GAC treatment.

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 chloral hydrate. The 1993 Guidelines established a provisional health-based guideline value of 0.01 mg/litre for chloral hydrate in drinking-water. The guideline value was designated as provisional because of the limitations of the available database, necessitating the use of an uncertainty factor of 10 000. This guideline value was brought forward to the third edition of the Guidelines.

Assessment date

The risk assessment was conducted in 2004.

Principal references

IPCS (2000) *Chloral hydrate*. Geneva, World Health Organization, International Programme on Chemical Safety (Concise International Chemical Assessment Document No. 25).

IPCS (2000) *Disinfectants and disinfectant by-products*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 216).

WHO (2005) *Chloral hydrate in drinking-water. Background document for development of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/05.08/49).