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 for the genotoxicity of chloral hydrate.

A health-based value of 0.1 mg/l (rounded figure) can be calculated on the basis of a TDI of 0.0045 mg/kg body weight derived based on an increased incidence of liver histopathology observed in 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 of health concern, 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.

Chloramines (monochloramine, dichloramine, trichloramine)

Monochloramine, dichloramines and trichloramines are considered by-products of drinking-water chlorination, being formed when chlorine and ammonia are added to water. Monochloramine may also be added to maintain residual disinfection activity in potable water distribution systems. Because higher chloramines are formed only occasionally and cause taste and odour problems at concentrations lower than those at which monochloramine causes taste and odour problems, only monochloramine has been considered for development of a health-based guideline value. Chloramine is rapidly decomposed in the stomach by gastric juice. The use of chloramines for disinfection instead of chlorine reduces the formation of THMs in drinking-water supplies. However, formation of other by-products, such as haloketones, chloropicrin, cyanogen chloride, HAAs, haloacetonitriles, aldehydes and chlorophenols, has been reported. Monochloramine, the most abundant chloramine, is recognized as a less effective disinfectant than chlorine and is used as a secondary disinfectant to maintain a residual in distribution systems.

Guideline value	*Monochloramine:* 3 mg/l (3000 µg/l)
Occurrence	Typical chloramine concentrations of 0.5–2 mg/l are found in drinking-water supplies where chloramine is used as a primary disinfectant or to provide a chlorine residual in the distribution system

TDI	94 µg/kg body weight, based on a NOAEL of 9.4 mg/kg body weight per day, the highest dose administered to male rats in a 2-year United States National Toxicology Program (NTP) drinking-water study (although mean body weights of rats given the highest dose were lower than those of their respective control groups, it is probable that the lower body weights were caused by the unpalatability of the drinking-water)
Limit of detection	10 µg/l by colorimetric methods
Treatment performance	It is possible to reduce the concentration of chloramine effectively to zero (< 0.1 mg/l) by reduction; however, it is normal practice to supply water with a chloramine residual of a few tenths of a milligram per litre to act as a preservative during distribution.
Guideline value derivation	
allocation to water	100% of TDI
weight	60 kg adult
consumption	2 litres/day
Additional comments	An additional uncertainty factor for possible carcinogenicity was not applied because equivocal cancer effects reported in the NTP study in only one species and in only one sex were within the range observed in historical controls.
	Most individuals are able to taste chloramines at concentrations below 5 mg/l, and some at levels as low as 0.3 mg/l.
Assessment date	2003
Principal references	IPCS (2000) *Disinfectants and disinfectant by-products* WHO (2004) *Monochloramine in drinking-water*

Reason for not establishing guideline values	Available data inadequate to permit derivation of health-based guideline values for *dichloramine* and *trichloramine*
Assessment date	1993
Principal references	IPCS (2000) *Disinfectants and disinfectant by-products*

Monochloramine

Although monochloramine has been shown to be mutagenic in some in vitro studies, it has not been found to be genotoxic in vivo. IARC has classified chloramine in Group 3 (not classifiable as to its carcinogenicity to humans). In the NTP bioassay in two species, the incidence of mononuclear cell leukaemias in female rats was increased, but no other increases in tumour incidence were observed. IPCS did not consider the increase in mononuclear cell leukaemia to be treatment related.

Dichloramine and trichloramine

Dichloramine and trichloramine have not been extensively studied, and available data are inadequate to permit derivation of health-based guideline values for either of these chemicals. However, these substances can cause taste and odour problems (see chapter 10) if formation of monochloramine is not controlled adequately.