Treatment performance	1 µg/l should be achievable using GAC
Guideline value derivation	
• allocation to water	10% of TDI
• weight	60 kg adult
• consumption	2 litres/day
Additional comments	Authorities should note that some impure technical grades of trifluralin could contain potent carcinogenic compounds and therefore should not be used.
Assessment date	1993
Principal reference	WHO (2003) *Trifluralin in drinking-water*

Trifluralin of high purity does not possess mutagenic properties. Technical trifluralin of low purity may contain nitroso contaminants and has been found to be mutagenic. No evidence of carcinogenicity was demonstrated in a number of long-term toxicity/carcinogenicity studies with pure (99%) test material. IARC has assigned technical-grade trifluralin to Group 3 (not classifiable as to its carcinogenicity to humans).

Trihalomethanes (bromoform, bromodichloromethane, chloroform, dibromochloromethane)

THMs are formed in drinking-water primarily as a result of chlorination of organic matter present naturally in raw water supplies. The rate and degree of THM formation increase as a function of the chlorine and humic acid concentration, temperature, pH and bromide ion concentration. Chloroform is the most common THM and the principal disinfection by-product in chlorinated drinking-water. In the presence of bromides, brominated THMs are formed preferentially, and chloroform concentrations decrease proportionally. It is assumed that most THMs present in water are ultimately transferred to air as a result of their volatility. For chloroform, for example, individuals may be exposed during showering to elevated concentrations from chlorinated tap water. For the volatile THMs, approximately equal contributions to total exposure come from four areas: ingestion of drinking-water, inhalation of indoor air largely due to volatilization from drinking-water, inhalation and dermal exposure during showering or bathing and ingestion of food, with all but food exposure arising primarily from drinking-water. Indoor air exposure to the volatile THMs is particularly important in countries with low rates of ventilation in houses and high rates of showering and bathing.

Guideline values	*Chloroform:* 0.3 mg/l (300 µg/l)
	Bromoform: 0.1 mg/l (100 µg/l)
	Dibromochloromethane (DBCM): 0.1 mg/l (100 µg/l)
	Bromodichloromethane (BDCM): 0.06 mg/l (60 µg/l)

Occurrence	THMs are not expected to be found in raw water (unless near a pollution source), but are usually present in finished or chlorinated water; concentrations are generally below 100 µg/l; in most circumstances, chloroform is the dominant compound
TDIs	*Chloroform:* 15 µg/kg body weight, derived from the lower 95% confidence limit for 5% incidence of hepatic cysts, generated by physiologically based pharmacokinetic modelling, in dogs that ingested chloroform in toothpaste for 7.5 years, using an uncertainty factor of 25 (10 for intraspecies differences in toxicokinetics and toxicodynamics and 2.5 for differences in interspecies toxicodynamics)
	Bromoform: 17.9 µg/kg body weight, based on the absence of histopathological lesions in the liver in a well-conducted and well-documented 90-day study in rats, using an uncertainty factor of 1000 (100 for intraspecies and interspecies variation and 10 for possible carcinogenicity and short duration of exposure)
	DBCM: 21.4 µg/kg body weight, based on the absence of histopathological effects in the liver in a well-conducted and well-documented 90-day study in rats, using an uncertainty factor of 1000 (100 for intraspecies and interspecies variation and 10 for the short duration of the study); an additional uncertainty factor for potential carcinogenicity was not applied because of the questions regarding mouse liver tumours from corn oil vehicles and inconclusive evidence of genotoxicity
Basis of guideline value derivation	*BDCM:* Application of the linearized multistage model for the observed increases in incidence of kidney tumours in male mice observed in an NTP bioassay
Limit of detection	0.1–0.2 µg/l (method detection limits) by purge-and-trap and liquid–liquid extraction and direct aqueous injection in combination with a chromatographic system; 0.1 µg/l by GC-ECD; 2.2 µg/l by GC-MS
Treatment performance	Concentrations can be reduced by changes to disinfection practice (e.g. reducing organic THM precursors) or using air stripping.
Guideline value derivation	
• allocation to water	20% of TDI for bromoform and DBCM 75% of TDI for chloroform
• weight	60 kg adult
• consumption	2 litres/day
Additional comments on THMs	For authorities wishing to establish a total THM standard to account for additive toxicity, the following fractionation approach could be taken: $\frac{C_{bromoform}}{GV_{bromoform}} + \frac{C_{DBCM}}{GV_{DBCM}} + \frac{C_{BDCM}}{GV_{BDCM}} + \frac{C_{chloroform}}{GV_{chloroform}} \leq 1$ where C = concentration and GV = guideline value. Authorities wishing to use a guideline value for total THMs should not simply add up the guideline values for the individual compounds in order to arrive at a standard.
	It is emphasized that adequate disinfection should never be compromised in attempting to meet guidelines for THMs. Nevertheless, in view of the potential link between adverse reproductive outcomes and THMs, particularly brominated THMs, it is recommended that THM levels in drinking-water be kept as low as practicable.

Additional comments on chloroform	In countries with low rates of ventilation in houses and high rates of showering and bathing, the guideline value could be lowered to account for the additional exposures from inhalation of indoor air largely due to volatilization from drinking-water and inhalation and dermal exposure during showering or bathing.
	The guideline value is based on the same study as in the third edition; the increase in value is primarily a result of an increase in the allocation of exposure in drinking-water from 50% to 75% to account for the fact that chloroform is used less now than it was in 1993 when the original guideline was developed.
Additional comments on BDCM	Although a health-based value of 21 µg/l is derived, the previous guideline value of 60 µg/l has been retained for two reasons: 1) both calculations were based on the same study, the only differences being the model and model assumptions used to derive the guideline value; there is therefore no scientific basis on which to justify a change in the guideline value; and 2) BDCM concentrations below 50 µg/l may be difficult to achieve using currently available technology without compromising the effectiveness of disinfection.
	As with chloroform, countries with low rates of ventilation and high rates of showering and bathing may wish to lower the guideline value to account for dermal and inhalation exposures, although, as noted above, concentrations below 50 µg/l may be difficult to achieve using currently available technology without compromising the effectiveness of disinfection.
	As BDCM was negative for carcinogenicity in a recent NTP bioassay in which it was dosed in drinking-water, exceedances of the guideline value are not likely to result in an increased risk of cancer.
Assessment date	2004
Principal references	IPCS (2000) *Disinfectants and disinfectant by-products* IPCS (2004) *Chloroform* WHO (2005) *Trihalomethanes in drinking-water*

Chloroform

The weight of evidence for genotoxicity of chloroform is considered negative. IARC has classified chloroform as possibly carcinogenic to humans (Group 2B) based on limited evidence of carcinogenicity in humans but sufficient evidence of carcinogenicity in experimental animals. The weight of evidence for liver tumours in mice is consistent with a threshold mechanism of induction. Although it is plausible that kidney tumours in rats may similarly be associated with a threshold mechanism, there are some limitations of the database in this regard. The most universally observed toxic effect of chloroform is damage to the centrilobular region of the liver. The severity of these effects per unit dose administered depends on the species, vehicle and method by which the chloroform is administered.

Bromoform

In an NTP bioassay, bromoform induced a small increase in relatively rare tumours of the large intestine in rats of both sexes but did not induce tumours in mice. Data from

a variety of assays on the genotoxicity of bromoform are equivocal. IARC has classified bromoform in Group 3 (not classifiable as to its carcinogenicity to humans).

Dibromochloromethane

In an NTP bioassay, DBCM induced hepatic tumours in female mice and possibly in male mice but not in rats. The genotoxicity of DBCM has been studied in a number of assays, but the available data are considered inconclusive. IARC has classified DBCM in Group 3 (not classifiable as to its carcinogenicity to humans).

Bromodichloromethane

IARC has classified BDCM in Group 2B (possibly carcinogenic to humans). BDCM gave both positive and negative results in a variety of in vitro and in vivo genotoxicity assays. In an NTP bioassay, BDCM induced renal adenomas and adenocarcinomas in both sexes of rats and male mice, rare tumours of the large intestine (adenomatous polyps and adenocarcinomas) in both sexes of rats and hepatocellular adenomas and adenocarcinomas in female mice. However, BDCM was negative for carcinogenicity in a recent NTP bioassay in which it was dosed in drinking-water. Exposure to BDCM has also been linked to a possible increase in reproductive effects (increased risk for spontaneous abortion or stillbirth).

Uranium

Uranium is widespread in nature, occurring in granites and various other mineral deposits. It is used mainly as fuel in nuclear power stations. Uranium is present in the environment as a result of leaching from natural deposits, release in mill tailings, emissions from the nuclear industry, the combustion of coal and other fuels and the use of phosphate fertilizers that contain uranium. Intake of uranium through air is low, and it appears that intake through food is between 1 and 4 µg/day. Intake through drinking-water is normally extremely low; however, in circumstances in which uranium is present in a drinking-water source, the majority of intake can be through drinking-water.

Provisional guideline value	0.03 mg/l (30 µg/l)
	The guideline value is designated as provisional because of scientific uncertainties surrounding uranium toxicity.
Occurrence	Levels in drinking-water are generally less than 1 µg/l, although concentrations as high as 700 µg/l have been measured in private supplies.
TDI	60 µg, derived from the lower 95% confidence limit on the 95th percentile uranium exposure distribution in a study from Finland, using an uncertainty factor of 10 for intraspecies variation
Limit of detection	0.01 µg/l by ICP-MS; 0.1 µg/l by solid fluorimetry with either laser excitation or UV light; 0.2 µg/l by ICP using adsorption with chelating resin
Treatment performance	1 µg/l should be achievable using conventional treatment (e.g. coagulation or ion exchange)