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)
Guideline value derivation	
• consumption	2 litres/day
Additional comments	Where supplies exceed 30 µg/l, it is important that precipitate action be avoided. Consideration should first be given to exposure from all sources and the availability of alternative safe sources.
	Only chemical, not radiological, aspects of uranium toxicity have been addressed here.
Assessment date	2003, revised in 2011
Principal reference	WHO (2012) *Uranium in drinking-water*

There are insufficient data regarding the carcinogenicity of uranium in humans and experimental animals. Nephritis is the primary chemically induced effect of uranium in humans. Little information is available on the chronic health effects of exposure to environmental uranium in humans. A number of epidemiological studies of populations exposed to uranium in drinking-water have shown a correlation with alkaline phosphatase and β-microglobulin in urine along with modest alterations in proximal tubular function. However, the actual measurements were still within the normal physiological range, and these findings are not consistent between studies.

No clear no-effect concentration has emerged from the human studies to date. This is not surprising, as most of the study populations are quite small, and there is substantial normal variation in the measured parameters in the human population. However, the overall indications are that there is no clear evidence of effects below an exposure concentration of 30 µg/l. In fact, the evidence for effects on the kidney, which appears to be the most sensitive organ, is equivocal until much higher exposure concentrations.

The provisional guideline value of 30 µg/l, which is derived from new epidemiological studies on populations exposed to high uranium concentrations, replaces the previous value derived from experimental animal studies and designated as provisional on the basis of uncertainties regarding the toxicology and epidemiology of uranium as well as difficulties concerning its technical achievability in smaller supplies. It is noted that studies on human populations, when available and of good quality, are

the preferred source of health-related information to be used in deriving guideline values.

Vinyl chloride

Vinyl chloride is used primarily for the production of PVC. Owing to its high volatility, vinyl chloride has rarely been detected in surface waters, except in contaminated areas. Unplasticized PVC is increasingly being used in some countries for water mains supplies. Migration of vinyl chloride monomer from unplasticized PVC is a possible source of vinyl chloride in drinking-water. It appears that inhalation is the most important route of vinyl chloride intake, although drinking-water may contribute a substantial portion of daily intake where PVC piping with a high residual content of vinyl chloride monomer is used in the distribution network. Vinyl chloride has been reported in groundwater as a degradation product of the chlorinated solvents trichloroethene and tetrachloroethene.

Guideline value	0.0003 mg/l (0.3 µg/l)
Occurrence	Rarely detected in surface waters, the concentrations measured generally not exceeding 10 µg/l; much higher concentrations found in groundwater and well water in contaminated areas; concentrations up to 10 µg/l detected in drinking-water
Basis of guideline value derivation	Application of a linear extrapolation by drawing a straight line between the dose, determined using a pharmocokinetic model, resulting in tumours in 10% of animals in rat bioassays involving oral exposure and the origin (zero dose), determining the value associated with the upper-bound risk of 10^{-5} and assuming a doubling of the risk for exposure from birth
Limit of detection	0.01 µg/l by GC-ECD or GC-FID with MS for confirmation
Treatment performance	0.001 mg/l should be achievable using air stripping
Additional comments	The results of the linear extrapolation are nearly identical to those derived using the linearized multistage model.
	As vinyl chloride is a known human carcinogen, exposure to this compound should be avoided as far as practicable, and levels should be kept as low as technically feasible.
	Vinyl chloride is primarily of concern as a potential contaminant from some grades of PVC pipe and is best controlled by specification of material quality.
Assessment date	2003
Principal references	IPCS (1999) *Vinyl chloride* WHO (2004) *Vinyl chloride in drinking-water*

There is sufficient evidence of the carcinogenicity of vinyl chloride in humans from industrial populations exposed to high concentrations via the inhalation route, and IARC has classified vinyl chloride in Group 1 (carcinogenic to humans). Studies of workers employed in the vinyl chloride industry showed a marked exposure–response