chronic oral uptake of potassium antimony tartrate may not be associated with an additional carcinogenic risk, as antimony after inhalation exposure was carcinogenic only in the lung but not in other organs and is known to cause direct lung damage following chronic inhalation as a consequence of overload with insoluble particulates. Although there is some evidence for the carcinogenicity of certain antimony compounds by inhalation, there are no data to indicate carcinogenicity by the oral route.

Arsenic[1]

Arsenic is found widely in Earth's crust in oxidation states of –3, 0, +3 and +5, often as sulfides or metal arsenides or arsenates. In water, it is mostly present as arsenate (+5), but in anaerobic conditions, it is likely to be present as arsenite (+3). It is usually present in natural waters at concentrations of less than 1–2 µg/l. However, in waters, particularly groundwaters, where there are sulfide mineral deposits and sedimentary deposits deriving from volcanic rocks, the concentrations can be significantly elevated.

Arsenic is found in the diet, particularly in fish and shellfish, in which it is found mainly in the less toxic organic form. There are only limited data on the proportion of inorganic arsenic in food, but these indicate that approximately 25% is present in the inorganic form, depending on the type of food. Apart from occupational exposure, the most important routes of exposure are through food and drinking-water, including beverages that are made from drinking-water. Where the concentration of arsenic in drinking-water is 10 µg/l or greater, this will be the dominant source of intake. In circumstances where soups or similar dishes are a staple part of the diet, the drinking-water contribution through preparation of food will be even greater.

Provisional guideline value	0.01 mg/l (10 µg/l)
	The guideline value is designated as provisional on the basis of treatment performance and analytical achievability.
Occurrence	Levels in natural waters generally range between 1 and 2 µg/l, although concentrations may be elevated (up to 12 mg/l) in areas containing natural sources
Basis of guideline value derivation	There remains considerable uncertainty over the actual risks at low concentrations, and available data on mode of action do not provide a biological basis for using either linear or non-linear extrapolation. In view of the practical difficulties in removing arsenic from drinking-water, as well as the practical quantification limit in the region of 1–10 µg/l, the guideline value of 10 µg/l is retained and designated as provisional.
Limit of detection	0.1 µg/l by ICP-MS; 2 µg/l by hydride generation AAS or flame AAS
Treatment performance	It is technically feasible to achieve arsenic concentrations of 5 µg/l or lower using any of several possible treatment methods. However, this requires careful process optimization and control, and a more reasonable expectation is that 10 µg/l should be achievable by conventional treatment (e.g. coagulation).

[1] As arsenic is one of the chemicals of greatest health concern in some natural waters, its chemical fact sheet has been expanded.

Assessment date	2011
Principal references	FAO/WHO (2011) *Evaluation of certain contaminants in food* IARC (1987) *Overall evaluations of carcinogenicity* IPCS (2001) *Arsenic and arsenic compounds* ISO (1982) *Water quality—determination of total arsenic* USNRC (2001) *Arsenic in drinking water, 2001 update* WHO (2011) *Arsenic in drinking-water*

Both pentavalent and trivalent soluble arsenic compounds are rapidly and extensively absorbed from the gastrointestinal tract. Metabolism is characterized by 1) reduction of pentavalent to trivalent arsenic and 2) oxidative methylation of trivalent arsenic to form monomethylated, dimethylated and trimethylated products. Methylation of inorganic arsenic facilitates the excretion of inorganic arsenic from the body, as the end-products monomethylarsonic acid and dimethylarsinic acid are readily excreted in urine. There are major qualitative and quantitative interspecies differences in methylation, but in humans and most common laboratory animals, inorganic arsenic is extensively methylated, and the metabolites are excreted primarily in the urine. There is large interindividual variation in arsenic methylation in humans, probably due to a wide difference in the activity of methyltransferases and possible polymorphism. Ingested organoarsenicals are much less extensively metabolized and more rapidly eliminated in urine than inorganic arsenic.

Arsenic has not been demonstrated to be essential in humans. The acute toxicity of arsenic compounds in humans is predominantly a function of their rate of removal from the body. Arsine is considered to be the most toxic form, followed by the arsenites, the arsenates and organic arsenic compounds. Acute arsenic intoxication associated with the ingestion of well water containing very high concentrations (21.0 mg/l) of arsenic has been reported.

Signs of chronic arsenicism, including dermal lesions such as hyperpigmentation and hypopigmentation, peripheral neuropathy, skin cancer, bladder and lung cancers and peripheral vascular disease, have been observed in populations ingesting arsenic-contaminated drinking-water. Dermal lesions were the most commonly observed symptom, occurring after minimum exposure periods of approximately 5 years. Effects on the cardiovascular system were observed in children consuming arsenic-contaminated water (mean concentration 0.6 mg/l) for an average of 7 years.

Numerous epidemiological studies have examined the risk of cancers associated with arsenic ingestion through drinking-water. Many are ecological-type studies, and many suffer from methodological flaws, particularly in the measurement of exposure. However, there is overwhelming evidence that consumption of elevated levels of arsenic through drinking-water is causally related to the development of cancer at several sites. Nevertheless, there remain considerable uncertainty and controversy over both the mechanism of carcinogenicity and the shape of the dose–response curve at low intakes. The International Programme on Chemical Safety (IPCS) concluded that long-term exposure to arsenic in drinking-water is causally related to increased risks of cancer in the skin, lungs, bladder and kidney, as well as other skin changes, such

as hyperkeratosis and pigmentation changes. These effects have been demonstrated in many studies using different study designs. Exposure–response relationships and high risks have been observed for each of these end-points. The effects have been most thoroughly studied in Taiwan, China, but there is considerable evidence from studies on populations in other countries as well. Increased risks of lung and bladder cancer and of arsenic-associated skin lesions have been reported to be associated with ingestion of drinking-water at concentrations below 50 µg of arsenic per litre. There is a need for more analytical epidemiological studies to determine the dose–time response for skin lesions, as well as cancer, in order to assist in developing suitable interventions and determining practical intervention policies.

Inorganic arsenic compounds are classified by IARC in Group 1 (carcinogenic to humans) on the basis of sufficient evidence for carcinogenicity in humans and limited evidence for carcinogenicity in animals. Although there is a substantial database on the association between both internal and skin cancers and the consumption of arsenic in drinking-water, there remains considerable uncertainty over the actual risks at low concentrations. In its updated evaluation, the United States National Research Council concluded that "the available mode-of-action data on arsenic do not provide a biological basis for using either a linear or nonlinear extrapolation". The maximum likelihood estimates, using a linear extrapolation, for bladder and lung cancer for populations in the United States of America (USA) exposed to arsenic at concentrations of 10 µg/l in drinking-water are, respectively, 12 and 18 per 10 000 population for females and 23 and 14 per 10 000 population for males. The actual numbers indicated by these estimated risks would be very difficult to detect by current epidemiological methods. There is also uncertainty over the contribution of arsenic in food—a higher intake of inorganic arsenic from food would lead to a lower risk estimate for water—and the impact of factors such as variation in the metabolism of arsenic and nutritional status. Some studies in areas with arsenic concentrations somewhat above 50 µg/l have not detected arsenic-related adverse effects in the residents. It remains possible that the estimates of cancer risk associated with various arsenic intakes are overestimates. The concentration of arsenic in drinking-water below which no effects can be observed remains to be determined, and there is an urgent need for identification of the mechanism by which arsenic causes cancer, which appears to be the most sensitive toxicity end-point.

The practical quantification limit for arsenic is in the region of 1–10 µg/l, and removal of arsenic to concentrations below 10 µg/l is difficult in many circumstances. In view of the practical difficulties in removing arsenic from drinking-water, particularly from small supplies, and the practical quantification limit for arsenic, the guideline value of 10 µg/l is retained as a goal and designated as provisional.

The provisional guideline value of 10 µg/l was previously supported by a JECFA PTWI of 15 µg/kg body weight, assuming an allocation of 20% to drinking-water. However, JECFA recently re-evaluated arsenic and concluded that the existing PTWI was very close to the lower confidence limit on the benchmark dose for a 0.5% response ($BMDL_{0.5}$) calculated from epidemiological studies and was therefore no longer appropriate. The PTWI was therefore withdrawn. Nevertheless, given that, in many countries, even the provisional guideline value may not be attainable, it is retained on

the basis of treatment performance and analytical achievability with the proviso that every effort should be made to keep concentrations as low as reasonably possible.

Practical considerations

A silver diethyldithiocarbamate spectrophotometric method (ISO 6595:1982) is available for the determination of arsenic; the detection limit is about 1 μg/l. Graphite furnace AAS, hydride generation AAS and ICP-MS are more sensitive. HPLC in combination with ICP-MS can also be used to determine various arsenic species.

It is technically feasible to achieve arsenic concentrations of 5 μg/l or lower using any of several possible treatment methods. However, this requires careful process optimization and control, and a more reasonable expectation is that 10 μg/l should be achievable by conventional treatment (e.g. coagulation). For local non-piped water supplies, the first option is often substitution by, or dilution with, microbially safe low-arsenic sources. It may also be appropriate to use alternative sources for drinking and cooking but to use the contaminated sources for purposes such as washing and laundry. There are also an increasing number of effective small-scale treatment techniques, usually based around coagulation and precipitation or adsorption, available at relatively low cost for removal of arsenic from small supplies.

Asbestos

Asbestos is introduced into water by the dissolution of asbestos-containing minerals and ores as well as from industrial effluents, atmospheric pollution and asbestos-cement pipes in the distribution system. Exfoliation of asbestos fibres from asbestos-cement pipes is related to the aggressiveness of the water supply. Limited data indicate that exposure to airborne asbestos released from tap water during showers or humidification is negligible.

Reason for not establishing a guideline value	No consistent evidence that ingested asbestos is hazardous to health
Assessment date	1993
Principal reference	WHO (2003) *Asbestos in drinking-water*

Asbestos is a known human carcinogen by the inhalation route. Although it has been well studied, there is little convincing evidence of the carcinogenicity of ingested asbestos in epidemiological studies of populations with drinking-water supplies containing high concentrations of asbestos. Moreover, in extensive studies in experimental animal species, asbestos has not consistently increased the incidence of tumours of the gastrointestinal tract. There is therefore no consistent evidence that ingested asbestos is hazardous to health, and thus it is concluded that there is no need to establish a health-based guideline value for asbestos in drinking-water. The primary issue surrounding asbestos-cement pipes is for people working on the outside of the pipes (e.g. cutting pipe), because of the risk of inhalation of asbestos dust.