Health Canada Santé Canada

Guidelines for Canadian Drinking Water Quality:

Guideline Technical Document

Arsenic

Prepared by the
Federal-Provincial-Territorial Committee on Drinking Water
of the
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Arsenic

1.0 Guideline

The maximum acceptable concentration (MAC) for arsenic in drinking water is 0.010 mg/L (10 µg/L) based on municipal- and residential-scale treatment achievability. Certified residential treatment devices[1] are commercially available to remove arsenic to well below this concentration. Every effort should be made to maintain arsenic levels in drinking water as low as reasonably achievable (or ALARA).

2.0 Executive summary

Arsenic is a natural element that is widely distributed throughout the Earth's crust. It is often found naturally in groundwater, through erosion and weathering of soils, minerals, and ores. Arsenic compounds are used commercially and industrially in the manufacture of a variety of products and may enter drinking water sources directly from industrial effluents and indirectly from atmospheric deposition.

This Guideline Technical Document reviews the health risks associated with arsenic in drinking water, focussing on inorganic forms of arsenic. It assesses all identified health risks, taking into account new studies and approaches, as well as the limitations of available treatment technology. It considers exposure to arsenic through drinking water only from ingestion, as exposure through inhalation and skin contact is not considered to be significant. From this review, the guideline for arsenic in drinking water is established at a maximum acceptable concentration of 0.010 mg/L (10 µg/L), based on municipal- and residential-scale treatment achievability.

2.1 Health effects

Arsenic is classified as a human carcinogen. As arsenic is a natural contaminant of groundwater, its health effects have been widely studied in humans, most notably in Taiwan. This is particularly significant because the toxic effects of arsenic vary significantly between species, making animal studies an unreliable basis on which to develop a guideline.

The maximum acceptable concentration for arsenic in drinking water was established based on the incidence of internal (lung, bladder, and liver) cancers in humans, through the calculation of a lifetime unit risk. This guideline for arsenic has been set at a level that is higher than the level that would be considered to be associated with an "essentially negligible" risk, based on limitations of available treatment technology.

The health effects of arsenic in humans vary depending on the compound and form. Metallic arsenic is not absorbed from the stomach and does not have any adverse health effects.

[1] Treatment devices include point-of-use and point-of-entry devices.

Although it was generally accepted that the inorganic forms of arsenic were responsible for its toxic and carcinogenic effects and that its organic forms were less toxic, recent evidence is now questioning this assumption.

2.2 Exposure

Arsenic can be found in both surface water and groundwater sources, with levels generally higher in groundwater. Most provinces and territories across Canada report some areas where arsenic can be detected in drinking water supplies. Although levels are generally well below the guideline, elevated arsenic concentrations have been found in areas with natural sources.

Drinking water is considered to be the major source of exposure to arsenic only in populations living near a source of arsenic (either a natural geological source or a site of contamination). For most Canadians, the primary source of exposure to arsenic is food, followed by drinking water, soil, and air.

2.3 Treatment

The establishment of a drinking water guideline must take into consideration the ability to both measure the contaminant and remove it from drinking water supplies. Arsenic can be reliably measured at a concentration of 0.005 mg/L. The selection of an appropriate treatment process for a specific water supply will depend on the characteristics of the raw water supply and many other factors. It is important to determine what, if any, pretreatment is required. Because arsenic is a human carcinogen, every effort should be made to maintain levels in drinking water as low as reasonably achievable.

Arsenic can be effectively treated in municipal-scale treatment facilities through a number of well-documented methods, which typically include both a pretreatment step and a final polishing step. Arsenic can be reduced to levels below the guideline of 0.010 mg/L (10 µg/L) in both large and smaller municipal plants.

Arsenic can also be removed by residential-scale drinking water treatment devices to levels below 0.010 mg/L. Certified devices are frequently designed to remove arsenic to well below this concentration, but certification to the standard verifies only that a final concentration of 0.010 mg/L or less is achieved.

Since treatment technology considerations are a limiting factor in establishing a guideline for arsenic in drinking water, Health Canada and the Federal-Provincial-Territorial Committee on Drinking Water will continue to monitor new developments in treatment technologies to revise and update the guideline and the guideline technical document as required.

3.0 Application of the guideline

Note: Specific guidance related to the implementation of drinking water guidelines should be obtained from the appropriate drinking water authority in the affected jurisdiction.

Every effort should be made to maintain arsenic levels in drinking water as low as reasonably achievable. Arsenic is a human carcinogen, which means that exposure to any level

in drinking water may increase the risk of cancer. Subpopulations (such as children and pregnant women) are not at a greater risk of developing health effects from exposure to arsenic than the general population.

The drinking water guideline is based on lifetime exposure to arsenic from drinking water. For drinking water supplies that occasionally experience short-term exceedances above the guideline value, it is suggested that a plan be developed and implemented to address these situations. For more significant, long-term exceedances that cannot be addressed through treatment, then it is suggested that alternative sources of water for drinking and food preparation be considered.

The guideline for a carcinogen is normally established at a level where the increased cancer risk is "essentially negligible" when a person is exposed at that level in drinking water over a lifetime (70 years). In the context of drinking water guidelines, Health Canada has defined this term as a range from one new cancer above background per 100 000 people to one new cancer above background per 1 million people (i.e., 10^{-5} to 10^{-6}). In the case of arsenic, the guideline is higher than the concentration that would present an "essentially negligible" risk of internal organ cancers, since it represents the lowest level of arsenic in drinking water that can be technically achieved at reasonable cost, especially for smaller public systems and private wells.

Table 1 lists the estimated lifetime (70 years) risk of excess internal cancers associated with the ingestion of arsenic in drinking water at various concentrations. The overall risk is is reported as a range, because lifetime exposure to arsenic could be linked to several types of cancer, including liver, bladder, and lung cancers.

Table 1: Estimated lifetime range of risk of excess internal organ cancers (in addition to the background lifetime cancer risk) associated with various concentrations of arsenic in drinking water

Level of Arsenic in Drinking Water (µg/L)	Estimated Lifetime Range of Risk of Excess Internal Organ Cancers[a] ($\times 10^{-5}$)
0.3 ("essentially negligible" risk)	0.09–1
5	2–20
10 (MAC)	3–39
25	8–97

[a] The estimated lifetime risk of internal organ cancers (lung, bladder, and liver) is calculated from the risk range associated with ingesting 1 µg/L of arsenic in drinking water. This risk range is 3.06×10^{-6} to 3.85×10^{-5} (using a 1% increase in risk).

Exposure to the MAC over a lifetime (70 years) may result in an increased risk, as estimated using a population in southwestern Taiwan exposed to very high levels (ranging from 350 to 1140 µg/L) of arsenic in their drinking water; the genetic make-up, health status, arsenic metabolism, and nutritional status of the study population may not be representative of the North

American situation. However, the Taiwanese study population was chosen because it represents long-term exposure to arsenic and follow-up, extensive pathology data, homogeneity between lifestyles of the population, and a large population (approximately 40 000 people).

Most existing studies on the health effects of arsenic in drinking water have reported links between internal organ cancers and very high concentrations of arsenic. Recent studies conducted in the United States have not found a clear association between cancer risks and arsenic in drinking water at levels greater than 10 µg/L (and below 50 µg/L). However, these recent studies cannot be used to derive a guideline until their results are confirmed by further research.

4.0 Identity, use, and sources in the environment

Arsenic is a metalloid with oxidation states of −3, 0, 3, and 5. It is widely distributed throughout the Earth's crust and is a major constituent of at least 245 mineral species. Natural sources of arsenic include volcanically derived sediment, sulphide minerals, and metal oxides. The most common arsenic mineral, globally, is arsenopyrite, which is commonly found in many vein gold deposits, such as those of Yellowknife. The most common source of arsenic in Canada is sulphide minerals. These minerals are typically composed of 0.02–0.5% arsenic; however, certain pyrite minerals may contain up to 5% arsenic (Hindmarsh and McCurdy, 1986; Pellerin, 2003).

Arsenicals are used commercially and industrially as alloying agents in the manufacture of transistors, lasers, and semi-conductors, as well as in the processing of glass, pigments, textiles, paper, metal adhesives, ceramics, wood preservatives, ammunition, and explosives. They are also used in the hide tanning process and, to a limited extent, as pesticides, feed additives, and pharmaceuticals, including veterinary drugs.

The principal sources of arsenic in ambient air are the burning of fossil fuels (especially coal), metal production, agricultural use, and waste incineration. Arsenic is introduced into water through the erosion and weathering of soil, minerals, and ores, from industrial effluents, and via atmospheric deposition (Hindmarsh and McCurdy, 1986; Hutton and Symon, 1986).

In surface water, arsenite (+3 valence) and arsenate (+5 valence) form insoluble salts with cations (usually iron) that are dissolved or suspended in the water. These particles generally settle out in sediments. This cleansing process occurs to a lesser extent in deep groundwater because of higher pH levels and lower iron concentrations (Hindmarsh and McCurdy, 1986).

Arsenic occurs in different forms (organic vs. inorganic) and valences depending upon the pH and oxidation potential of the water. In well-oxygenated surface waters, pentavalent arsenic (arsenate) is generally the most common species present (Irgolic, 1982; Cui and Liu, 1988); under reducing conditions, such as those often found in deep lake sediments or groundwaters, the trivalent species (arsenite) is the predominant form (Lemmo et al., 1983; Welch et al., 1988).

5.0 Exposure

5.1 Water

Levels of inorganic arsenic are generally higher in groundwater sources than in surface water. Where arsenic is found in surface water, some organic forms may be present (U.S. NRC, 1999). Monitoring data for water supplies have been submitted by several Canadian provinces. Arsenic levels ranged from 0.1 to 26.0 µg/L in groundwater supplies in Prince Edward Island between 1986 and 2002; levels in greater than 99% of samples were below 10 µg/L, the average being approximately 1.5 µg/L (Prince Edward Island Department of Fisheries, Aquaculture and Environment, 2003).

In Quebec, arsenic levels ranged from 1.0 to 25.0 µg/L in municipal treated surface water in 523 communities for 1990–2002; levels in more than 99% of samples were less than 10 µg/L, the annual average being 1.6 µg/L. Levels ranged from 1.0 to 60 µg/L in municipal treated groundwater in 562 communities for the same period; approximately 98% of samples contained levels less than 10 µg/L, the annual average being 2.0 µg/L (Ministère de l'Environnement du Québec, 2003).

In Ontario, arsenic levels ranged from 0.1 to 18 µg/L in treated groundwater and surface water in 726 communities for 1997–2002. Levels in more than 99% of samples were less than 10 µg/L, the annual average being less than or equal to 0.7 µg/L (Ontario Ministry of Environment and Energy, 2003). Ontario monitoring data submitted by private laboratories indicated that arsenic levels in treated and raw drinking water ranged from less than 2.5 to 68 µg/L for the period 1999–2002, the average value being less than 2.5 µg/L. The higher values came predominantly from wells (Ontario Ministry of Environment and Energy, 2003).

In Saskatchewan, arsenic levels ranged from 0.5 to 105.0 µg/L in municipal treated water supplies in 539 communities between 1976 and 2002; concentrations in 97% of samples were less than or equal to 10 µg/L, the average being 3.0 µg/L (Saskatchewan Department of Environment and Resource Management, 2003). Arsenic levels ranged from 0.1 to 1000 µg/L in treated groundwater and surface water in 573 Alberta communities for 1980–2002. Approximately 99% of samples contained less than 10 µg/L, the annual average being 1.8 µg/L (Alberta Department of Environment, 2003).

Elevated arsenic concentrations have been reported in areas with natural sources. In Nova Scotia, 9% of well water samples tested for arsenic at the Environmental Chemistry Laboratory in Halifax between 1991 and 1997 exceeded 25 µg/L (Nova Scotia Department of the Environment, 1998). Méranger et al. (1984) reported that levels exceeded 50 µg/L in 33–93% of wells in each of seven communities in Nova Scotia; concentrations were greater than 500 µg/L in 10% of the wells sampled (n = 94). In Newfoundland, maximum arsenic levels ranged from 6 to 288 µg/L in public water supplies (54 wells) in 2002. Public schools (n = 16) with their own water supplies had levels ranging from 1 to 368 µg/L; approximately 19% of school wells had maximum levels above 10 µg/L (Newfoundland Department of Environment and Labour, 2003). In British Columbia, a maximum arsenic concentration of 580 µg/L was reported in groundwater samples taken on Bowen Island (Boyle et al., 1998).

Some western U.S. states with volcanic rock and sulphidic mineral deposits have arsenic levels in groundwater exceeding 3 mg/L (ATSDR, 2000). Elevated levels of arsenic in drinking water from wells in the northern provinces of Argentina have been reported; in Médanos in Buenos Aires Province and La Francia in Córdoba, concentrations as high as 2 mg/L and 12 mg/L, respectively, have been reported. Levels exceeded 1 mg/L at several other locations (Grinspan and Biagini, 1985).

On the basis of results indicating that the concentration of arsenic in drinking water in areas without natural sources is usually less than 5 µg/L and assuming that the average daily intake of drinking water is 1.5 L, the mean daily intake of arsenic from this source (in the predominantly pentavalent inorganic form) for an adult will generally be less than 7.5 µg. A child (0.5–4.0 years) with an average daily intake of 0.7 L of drinking water would consume less than 3.5 µg.

5.2 Food

Food is generally considered the major source of arsenic exposure except in situations where a population is living near a point source (natural geological source or site of contamination). However, it is difficult to compare the intake of arsenic from food with that from drinking water, as the form (organic vs inorganic), valence, and biological availability of arsenic in these two sources vary.

Arsenic is concentrated by many species of fish and shellfish and is used as a feed additive for poultry and livestock; fish and meat are therefore the main sources of dietary intake (78.9%, according to a U.S. survey) (Gartrell et al., 1986). A 1997 British total diet study found that seafood contributed 94% of the total arsenic intake for the general population (U.K. MAFF, 1999). In Canada, arsenic levels ranging from 0.4 to 118 mg/kg have been reported in marine fish sold for human consumption, whereas concentrations in meat and poultry range up to 0.44 mg/kg (Department of National Health and Welfare, 1983). While organic arsenic compounds (e.g., arsenocholine and arsenobetaine) found in most seaweed and other marine foods have been determined to be relatively non-toxic (Sabbioni et al., 1991), toxic inorganic forms have been found in hijiki seaweed (CFIA, 2001). Levels in vegetation are generally an order of magnitude lower than those in fish, whereas concentrations in shellfish are often far higher than those in fish (Subramanian, 1988). Exogenous sources of arsenic in the diet potentially include arsenic-containing fungicides used in fruit production. In North America, however, arsenic-containing pesticides are no longer used on food (ATSDR, 2000; PMRA, 2003).

Recent estimates of the mean daily intake of total arsenic in food for adults are as follows: 42 µg (range 22.5–78.7 µg) for adults 20–65+ years old in Canada (Dabeka et al., 1993), 56 µg (range 27.5–92.1 µg) for adults 25–70+ years old in the United States (Tao and Bolger, 1998), 120 µg in the United Kingdom (U.K. MAFF, 1999), 150 µg in New Zealand (Vannoort et al., 1995), 286 µg in Spain (Urieta et al., 1996), and 182 µg in Japan (Mohri et al., 1990).

In children aged 1–4 and 5–11 years, mean daily intakes of total arsenic in food from six Canadian cities have been reported to be 14.9 µg (range 11.4–18.1 µg) and 29.9 µg (range 25.5–

39.7 µg), respectively (Dabeka et al., 1993). Daily intakes of 2.15 µg, 23.4 µg, 20.3 µg, and 13.3 µg have been reported for children aged 6–11 months, 2 years, 6 years, and 10 years, respectively, in the United States (Tao and Bolger, 1998).

With regard to food preparation, the U.S. Environmental Protection Agency (EPA) estimates that preparing foods with arsenic-containing water may increase arsenic content by as much as 10–30% for most foods; beans and grains that absorb water when cooked may absorb up to 200–250% (Mead, 2005).

5.3 Air

Ambient levels of arsenic in air in 11 Canadian cities and one rural site for the period 1985–1990 ranged from <0.0005 to 0.017 µg/m^3 (24-hour average), the mean for cities being 0.001 µg/m^3 (Dann, 1990). Higher atmospheric concentrations are normally found near metal smelters. In Yellowknife in 1997, concentrations ranged from 0.002 to 0.063 µg/m^3, with an annual average of 0.005 µg/m^3 (Government of the Northwest Territories, 1998).

In the United States, average annual arsenic concentrations in air have been reported to be 0.4 ng/m^3 in rural areas remote from smelting activities, 3 ng/m^3 for all locations, and 30 ng/m^3 in areas within 80 km of non-ferrous smelters (Ball et al., 1983). Concentrations of arsenic in indoor air in the presence of environmental tobacco smoke (ETS) ranged from <0.1 to 1 ng/m^3, while sites that were ETS-free had concentrations below 0.13 ng/m^3 (Landsberger and Wu, 1995).

Based on the Canadian (0.001 µg/m^3) and U.S. (0.003 µg/m^3) ambient air levels, intake of arsenic through inhalation (principally in the inorganic form) is likely to be negligible (<0.1 µg, assuming 16.2 m^3 of air inhaled per day) for adults compared with the amount ingested (mainly in the organic form). Intake of arsenic (inorganic) for a child (1–4 years) based on the same ambient levels and an inhalation rate of 5 m^3 of air per day would be less than 0.05 µg (Health Canada, 1998).

5.4 Soil

Arsenic in soil (predominantly inorganic) originates from underlying materials that form soils, industrial wastes, or the use of arsenical pesticides. In Canada, average concentrations of arsenic in soil range from 4.8 to 13.6 mg/kg (Kabata-Pendias and Pendias, 1984). U.S. background levels are similar, ranging from 1 to 40 mg/kg, with a mean of approximately 5 mg/kg (ATSDR, 2000). Significantly higher concentrations in soil have been found near smelters (means of 50–100 mg/kg), near gold mining operations (means of 60–110 mg/kg), in arsenical-treated soils (means up to 54 mg/kg), and at wood preservation sites (means up to 6000 mg/kg) (Environment Canada and Health and Welfare Canada, 1993). Generally, exposure from soil is potentially significant only in those circumstances where residential neighbourhood areas have been built in contaminated sectors.

While exposure to arsenic via soil is unlikely to be a concern for older children and adults, hand-to-mouth behaviour and intentional ingestion may result in significant exposure for

young children. In unexposed and exposed populations, young children (≤4 years) were estimated to be exposed to 0.02–0.05 and 0.01–1.9 µg/kg bw per day, respectively (Environment Canada and Health and Welfare Canada, 1993).

5.5 Estimates of total exposure to arsenic

It is difficult to compare the intake of arsenic from food with that from drinking water, as the form (organic vs inorganic), valence, and biological availability of arsenic in these two sources vary. For example, a major portion of the organic arsenic in fish is present as highly complexed forms that are biologically unavailable (e.g., arsenobetaine) (Vahter et al., 1983; JECFA, 1988). The remainder is present largely as simple organic complexes, mainly trimethyl arsine, which are rapidly excreted from the body. Seafood contributes much of the daily arsenic intake, even where the consumption of fish is low (Hazell, 1985). On the basis of data on the organic and inorganic arsenic contents of various foodstuffs (Hazell, 1985; U.S. EPA, 1988), it can be estimated that approximately 25% of the intake of arsenic from food is inorganic and 75% is organic. Assuming that the average daily intake of arsenic from food is 42 µg, the daily intake of inorganic arsenic from food would be 10.5 µg. This contrasts with an intake of <7.5 µg of principally the pentavalent inorganic arsenic species in drinking water. Intake of inorganic arsenic for a child (1–4 years) based on an average daily intake of total arsenic from food of 14.9 µg would be approximately 3.7 µg, which is similar to the intake from drinking water for this age group (<3.5 µg).

Based on the above estimates for a typical population, the exposure media may be ranked in the following order of importance in terms of contributing to arsenic intake: food, drinking water, soil, and air. In a situation where a population is living near a point source (natural geological source or site of contamination), drinking water has been calculated to be the most important contributor to overall exposure (Environment Canada and Health and Welfare Canada, 1993).

6.0 Analytical methods

The U.S. EPA has approved several analytical methods, based on spectroscopy, for the analysis of total arsenic in drinking water. Table 2 outlines the various EPA-approved analytical methods, their respective detection limits, and their advantages and disadvantages. Total arsenic is defined as the concentration of arsenic present in the dissolved and suspended fractions of a water sample. In these methodologies, the arsenic is oxidized and analysed without regard to its chemical form (inorganic or organic) or oxidation state (i.e., As(III) or As(V)).

Atomic absorption via gaseous hydride formation (GHAA) is considered to be the most common method for the determination of arsenic in water, with a detection limit of about 0.001 mg/L (1 µg/L). Some of the other methods may have limitations and may not be appropriate for routine monitoring. These include graphite furnace atomic absorption spectroscopy (GFAA), stabilized temperature platform graphite furnace atomic absorption (STP-GFAA), inductively coupled plasma mass spectroscopy (ICP-MS), selective ion monitoring with ICP-MS, and inductively coupled plasma atomic emission spectroscopy (ICP-AES). For

example, ICP-MS analysis may be subject to chloride interference when samples contain high levels of chloride. This method also requires a high level of skill and operator training, and the high initial cost of instrumentation may prevent smaller laboratories from using this method due to operational and financial considerations.

Table 2: Standard U.S. EPA analytical methods for arsenic

Methodology	Reference Method	MDL (µg/L)	Advantages	Disadvantages
Inductively coupled plasma mass spectroscopy (ICP-MS)	200.8 (EPA)	1.4	Multi-analyte Low MDL	High capital cost High level of operator skill required
ICP-MS with selective-ion monitoring	(modification)	0.1	Multi-analyte Low MDL Short analysis time	Interferences from argon-chloride in high-chloride samples
Stabilized temperature platform graphite furnace atomic absorption (STP-GFAA)	200.9 (EPA)	0.5	Widely used Low MDL	Single analyte
Graphite furnace atomic absorption (GFAA)	3113B (SM)	1	Widely used Low MDL	Single analyte
	D-2972-93C (ASTM)	5		
Gaseous hydride atomic absorption (GHAA)	3114B (SM)	0.5	Low MDL	Single analyte
	D-2972-93B (ASTM)	1		

ASTM - American Society for Testing and Materials; EPA - EPA Methods; MDL - Method Detection Limit; SM - Standard Methods (American Public Health Association)

The practical quantitation limit (PQL) for all EPA-approved methods, based on the capability of laboratories to measure arsenic within reasonable limits of precision and accuracy, is 0.003 mg/L (3 µg/L) (U.S. EPA, 1999).

EPA Method 1632 is a GHAA method that provides for direct analysis of drinking water and for speciation of arsenic. The method detection limit is 0.002 µg/L; however, this method requires a high degree of skill (U.S. EPA, 1999). Common methods used for identifying arsenic species include high-performance liquid chromatography or GHAA followed by detection using atomic absorption, atomic fluorescence spectroscopy, or ICP-MS.

7.0 Treatment technology

In water in the pH range of 4–10, the predominant As(III) species are neutral in charge, while As(V) species are negatively charged. The neutral charge on As(III) makes its removal efficiency poor in comparison with that of As(V) (U.S. EPA, 2001a).

As(III) can be converted to As(V) using a pre-oxidation step. Chlorine, ferric chloride, potassium permanganate, ozone, and hydrogen peroxide are effective at oxidizing As(III) to As(V). However, pre-oxidation with chlorine may create undesirable concentrations of chlorinated disinfection by-products (U.S. EPA, 2000).

The selection of an appropriate treatment process for a specific water supply will depend on the characteristics of the raw water supply and many other factors. It is important to determine what, if any, pretreatment is required. Pretreatment may be necessary to remove competing ions such as iron, fluoride, sulphate, and silicate, as well as total dissolved solids; to adjust the pH; and to oxidize As(III) to As(V). Pretreatment is critical for ensuring arsenic removal efficacy with any subsequent treatment technology. Speciation may be performed to assess the species of arsenic present; however, there appears to be limited benefit with respect to time and costs involved. Oxidation of As(III) to As(V) is the preferred method of removing inorganic arsenic, as it ensures that total arsenic is reduced in an efficient manner. Most treatment technology is used in combination with pretreatment and a polishing step, which typically involves polishing the finished water with ion exchange to remove the resulting negative As(V) ion. In addition, contact time, system maintenance, and cost effectiveness are key considerations when selecting a treatment process for arsenic removal. An in-depth review of the various treatment technologies used to remove arsenic from drinking water is beyond the scope of this document. However, detailed information on the effectiveness and application of the various treatment technologies for arsenic removal is available in a review by Thirunavukkarasu and Viraraghavan (2003).

7.1 Municipal-scale

The most practical municipal-scale technologies for the removal of arsenic from drinking water include coagulation/filtration, lime softening, activated alumina, ion exchange, reverse osmosis, and manganese greensand filtration. The U.S. EPA has also identified electrodialysis reversal as a best available technology for arsenic removal. Removal efficiency can be very good (>90%) for some of these technologies; however, manganese greensand filtration and electrodialysis reversal usually achieve lower removal rates (U.S. EPA, 2001a). Recently, adsorption/filtration has also shown promise for arsenic removal.

Although it is difficult to achieve low levels of arsenic using coagulation/filtration alone, when coagulation/filtration is combined with pretreatment (oxidation to convert arsenic to its pentavalent form) and a polishing step (polishing the finished water with ion exchange), the process can reduce total arsenic levels in finished drinking water to concentrations as low as 0.003–0.005 mg/L (U.S. EPA, 2000).

Lime softening is widely used in large utilities and is effective at reducing total arsenic in drinking water to concentrations of 0.001–0.003 mg/L. However, lime softening is an expensive

process and is not recommended unless there is also a need to reduce hardness in the raw water feed (U.S. EPA, 2000). The performance and consistency of lime softening can be improved by pretreating the raw water using oxidation and polishing the finished water with ion exchange.

Currently, the most common arsenic removal process for municipal-scale treatment uses activated alumina adsorption followed by microfiltration. Several studies have demonstrated that activated alumina is an effective treatment for the removal of arsenic (As(V)) from drinking water. Pilot plant studies of arsenic removal using activated alumina achieved effluent arsenic levels of <0.01 mg/L (Simms and Azizian, 1997). The U.S. EPA has identified activated alumina as a best available technology for arsenic removal, with a removal efficiency of 95% (U.S. EPA, 2001a). However, the chemical handling requirements may make this process too complex and potentially dangerous for smaller utilities (U.S. EPA, 2000), and therefore this treatment process is not commonly used for these smaller utilities.

The treatment processes described above are effective, but relatively expensive to build and maintain on a municipal scale, and they may not be appropriate for small water treatment utilities. These systems also create significant quantities of either sludge or brine, which must be disposed of appropriately, thus increasing the cost of these processes (NDWAC, 2001).

Ion exchange processes in combination with an oxidation pretreatment step have been shown to reduce total arsenic in finished drinking water to levels as low as 0.003 mg/L. Laboratory column studies using ion exchange resin achieved effluent concentrations as low as 0.002 mg/L where the influent had an arsenic concentration of 0.021 mg/L (Clifford *et al*., 1999). These systems are recommended for water supplies with low concentrations of total dissolved solids and sulphate (U.S. EPA, 2000).

Reverse osmosis systems, when combined with a pretreatment step, can remove up to 85% of total arsenic from drinking water. These systems are reliable but require large quantities of influent water to obtain the required volume of drinking water, as they reject a significant portion of the influent water as an arsenic-rich brine; as such, they may not be suitable for use in areas where water resources are scarce (U.S. EPA, 2000).

In manganese greensand filtration, the arsenic contained in the water passing through the filter is oxidized and then trapped in the filter. This technology does not achieve a high removal efficiency and is dependent on the presence of iron in the water to remove arsenic. It may be appropriate where the source water has a high iron level and requires only little arsenic removal (U.S. EPA, 2000).

Adsorption/filtration appears to be a promising technology that is applicable to small water treatment utilities. Adsorption using media such as iron, aluminum, and titanium oxide is effective at removing arsenic. Fixed-bed treatment systems, such as adsorption and ion exchange, are becoming increasingly popular for arsenic removal in small water treatment systems because of their simplicity, ease of operation and handling, and regeneration capacity. Several studies that tested the removal of arsenic from drinking water under both laboratory- and pilot-scale conditions showed that adsorptive materials containing various iron oxides are capable of removing As(III) and As(V). More specifically, iron oxide-coated sand and granular ferric hydroxide can remove As(III) and As(V) present in the water to a concentration below

0.005 mg/L (Pierce and Moore, 1980, 1982; Fuller *et al*., 1993; Hsia *et al*., 1994; Wilkie and Hering, 1996; Raven *et al*., 1998; Driehaus *et al*., 1998; Ramaswami *et al*., 2001; Thirunavukkarasu *et al*., 2001, 2003a,b).

A non-treatment option for delivering water with reduced levels of arsenic is water blending. Water blending consists of combining water from a source that has high levels of arsenic with one that has a much lower concentration of arsenic. This ensures that the water being delivered to the consumer has a final concentration of arsenic that meets the guideline.

7.2 Residential-scale

Municipal treatment of drinking water is designed to reduce contaminants to levels at or below guideline value. As a result, the use of residential-scale treatment devices on municipally treated water is generally not necessary but primarily based on individual choice. In cases where an individual household obtains its drinking water from a private well, a private residential drinking water treatment device (treatment device) can be used for reducing arsenic concentrations in drinking water. Residential treatment devices are affordable and can remove arsenic from drinking water to concentrations below 0.010 mg/L. Periodic testing by an accredited laboratory should be conducted on both the water entering a treatment device and the water it produces to verify that the device is effective.

The most common types of treatment devices available for the removal of arsenic from drinking water in residential systems are reverse osmosis and steam distillation. Other types of systems based on alternative technologies such as adsorption are also becoming more common. Filtration systems may be installed at the faucet (point of use) or where water enters the home (point of entry).

Before a treatment device is installed, the well water should be tested to determine general water chemistry and to verify the concentration of arsenic. The testing should also include assessing the presence and concentration of competing ions (e.g., fluoride, iron, sulphate, silicate) and organic matter in the water, which could interfere with arsenic removal.

Given that most technology cannot effectively remove trivalent arsenic, pretreatment with an oxidation step is recommended to convert trivalent (dissolved) arsenic to pentavalent (filterable) arsenic, to ensure good removal by the treatment device (U.S. EPA, 2001a). Individuals should refer to the manufacturer's claims in its literature to obtain information on the amount of arsenic that the treatment device will remove, as well as operational and maintenance requirements.

Residential reverse osmosis systems have been shown to effectively remove total arsenic from drinking water. The amount of arsenic removed depends on the type of membrane filter employed in the system. Reverse osmosis requires larger quantities of influent (incoming) water to obtain the required volume of drinking water, as reverse osmosis systems reject (waste) part of the influent water. A consumer may need to pretreat the influent water to reduce fouling and extend the service life of the membrane. The major advantage of using reverse osmosis systems is that they are widely available, affordable, and easy to service and can remove up to 98% of other dissolved minerals as well as fine colloidal and coarse suspended matter (U.S. EPA, 2000).

Distillation systems can remove virtually all arsenic in drinking water. These systems are more complex than reverse osmosis systems. Although distillation systems are usually installed in commercial applications, more systems are becoming available for residential applications. It should be noted that while there are no known harmful health effects associated with the long-term ingestion of drinking water from distillation or reverse osmosis systems, no specific studies have been conducted on the effects of ingestion of water from these systems. Since beneficial minerals such as calcium and magnesium are removed by both distillation and reverse osmosis processes, it is important to consume a reasonably well-balanced diet to offset the removal of these minerals.

Adsorption/filtration appears to be a promising technology that is applicable to residential-scale treatment. Adsorption using media such as iron, aluminum, and titanium oxide is effective at removing arsenic. Fixed-bed treatment systems, such as adsorption and ion exchange, are becoming increasingly popular for arsenic removal in small water treatment systems because of their simplicity, ease of operation and handling, and regeneration capacity.

Health Canada does not recommend specific brands of treatment devices, but it strongly recommends that consumers use devices that have been certified by an accredited certification body as meeting the appropriate NSF International (NSF)/American National Standards Institute (ANSI) drinking water treatment unit standards. These standards have been designed to safeguard drinking water by helping to ensure material safety and performance of products that come into contact with drinking water. Certification organizations provide assurance that a product conforms to applicable standards and must be accredited by the Standards Council of Canada (SCC). In Canada, the following organizations have been accredited by the SCC to certify treatment devices and materials as meeting NSF/ANSI standards:

- Canadian Standards Association International (www.csa-international.org);
- NSF International (www.nsf.org);
- Water Quality Association (www.wqa.org);
- Underwriters Laboratories Inc. (www.ul.com);
- Quality Auditing Institute (www.qai.org); and
- International Association of Plumbing & Mechanical Officials (www.iapmo.org).

An up-to-date list of accredited certification organizations can be obtained from the SCC (www.scc.ca).

The NSF/ANSI standards for arsenic removal currently test for removal to a concentration of 0.01 mg/L under specific water quality conditions. This underlines the importance of characterizing the raw water to ensure effective removal of arsenic. Certified devices are frequently designed to remove arsenic to well below the 0.010 mg/L concentration, but certification to the standard verifies only that a final concentration of less than 0.010 mg/L is achieved. A qualified professional can design a system to meet residential needs and achieve arsenic concentrations below 0.005 mg/L. For example, a system designed with two or more filters in series will often result in removal of virtually all arsenic. As stated above, the selection of an appropriate treatment process for a specific water supply will depend on the characteristics of the

raw water supply and many other factors. It is important to determine what, if any, pretreatment is required and to have the finished water tested by an accredited laboratory to ensure that any designed system is attaining the desired arsenic removal.

For a drinking water treatment device to be certified to NSF/ANSI Standards 53 (Drinking Water Treatment Units — Health Effects) or 58 (Reverse Osmosis Drinking Water Treatment Systems), or for distillation systems to be certified to NSF/ANSI Standard 62 (Drinking Water Distillation Systems), the device will have to be able to reduce the concentration of arsenic in water from 0.3 to 0.010 mg/L. Devices that can be certified as reducing the concentration of arsenic from 0.3 to 0.010 mg/L are appropriate for treating well water with high concentrations of arsenic. Devices certified as reducing the concentration of arsenic from 0.05 to 0.010 mg/L are intended for treating water with lower initial concentrations (i.e., less than 0.05 mg/L) of arsenic.

8.0 Kinetics and metabolism

8.1 Essentiality

Although the results of available studies indicate that arsenic may be an essential element for several animal species (e.g., goats, minipigs, rats, chicks), there is no evidence that it is essential for humans. A Technical Panel on Arsenic convened by the U.S. EPA was "not aware of case reports describing an arsenic requirement for humans, nor of experimental or epidemiologic-type studies designed to determine whether arsenic is essential." After reviewing the available data, the Technical Panel concluded that "if arsenic is a required nutrient for humans, current environmental arsenic exposures are not known to produce human arsenic deficiency" (U.S. EPA, 1988).

8.2 Absorption, distribution, metabolism, and elimination

Ingested elemental arsenic is poorly absorbed and largely eliminated unchanged. Arsenic oxides are readily absorbed (>80%) from the gastrointestinal tract (Fowler et al., 1979) and, to a lesser extent, through the lungs and skin (Wickström, 1972). On the basis of faecal recovery experiments in human volunteers, soluble As(III) and As(V) and organic arsenic are well absorbed; As(III) tends to accumulate in tissues, but As(V) and organic arsenic are rapidly and almost completely eliminated via the kidneys (Bertolero et al., 1987). Both organic and inorganic arsenic are not well absorbed by the skin. Dermal exposure is reported to be of minor importance compared with ingestion. The National Research Council (U.S. NRC, 1999) and the Agency for Toxic Substances and Disease Registry (ATSDR, 2000) reviewed the available information on dermal absorption of arsenic and indicated that systemic absorption of arsenic via the skin is sufficiently low that this route of exposure is unlikely to be of concern to health.

Following ingestion, inorganic arsenic appears rapidly in the circulation, where it binds primarily to haemoglobin (Axelson, 1980); within 24 hours, it is found mainly in the liver, kidneys, lungs, spleen, and skin (Wickström, 1972). Skin, bone, and muscle represent the major storage organs. The accumulation of arsenic in skin is probably related to the abundance of proteins containing sulphydryl groups, with which arsenic readily reacts (Fowler et al., 1979). In

humans, inorganic arsenic does not appear to cross the blood–brain barrier; however, trans-placental transfer of arsenic in both humans (Gibson and Gage, 1982) and mice (Hood et al., 1987) has been reported.

Pathways for the conversion of one form of arsenic to another have been proposed (U.S. NRC, 2001). Methylation of inorganic arsenic is thought to occur following the reduction of pentavalent arsenic to trivalent arsenic. Methylation of this trivalent form of arsenic is then believed to result from the oxidative addition of a methyl group from S-adenosylmethionine by a methyl transferase. Sequential reduction and methylation of arsenic compounds result in the creation of pentavalent monomethylarsinic acid (MMA^V) and dimethylarsinic acid (DMA^V), as well as the trivalent monomethylarsinous acid (MMA^{III}) and dimethylarsinous acid (DMA^{III}) (U.S. NRC, 2001).

There appear to be two main processes, with different rates, for the elimination of ingested trivalent arsenic (As(III)) from the body (Lovell and Farmer, 1985). The first is the rapid urinary excretion of inorganic arsenic in both the trivalent and pentavalent forms (close to 90% of the total urinary arsenic over the first 12-hour period). The second involves the sequential methylation of As(III) in the liver to the organic forms MMA^{III}, DMA^{III}, MMA^V, and DMA^V (Buchet and Lauwerys, 1985; Lovell and Farmer, 1985). Excretion of the methylated compounds commences approximately 5 hours after ingestion but reaches its maximum level 2–3 days later. Less important routes of elimination of inorganic arsenic include skin, hair, nails, and sweat (ICRP, 1975; Kurttio et al., 1999). The half-life of inorganic arsenic in humans is estimated to be between 2 and 40 days (Pomroy et al., 1980).

The results of a study in which inorganic arsenic (125, 250, 500, or 1000 µg $NaAsO_2$) was administered orally once a day for 5 consecutive days to four volunteers indicate that the arsenic methylation capacity is progressively saturated when daily intake exceeds 0.5 mg (Buchet *et al*., 1981a); it does not, however, appear to be completely saturated even for daily doses as high as 1 mg. Studies with human volunteers indicate that most ingested organic arsenic is rapidly excreted unchanged (>80% of the dose within 4 days) (Buchet et al., 1981b; Luten et al., 1982; Tam et al., 1982).

9.0 Health effects

9.1 Effects in humans

The acute toxicity of the various forms and valences of arsenic in humans is predominantly a function of their rate of removal from the body. Metallic arsenic (0 valence) is not absorbed from the stomach and as such does not have any adverse effect. Some arsenic compounds, such as the volatile arsenine (AsH_3), are not present in food or water. Additionally, some organic arsenic compounds have little or no toxicity or are rapidly eliminated from the body in the urine. Lethal doses for the most common arsenic compounds (AsH_3, As_2O_3, As_2O_5, MMA^V, and DMA^V) in humans range from 1.5 mg/kg bw (As_2O_3) to 500 mg/kg bw (DMA^V) (Buchet and Lauwerys, 1982). AsH_3, As_2O_3, and As_2O_5 are gaseous forms of arsenic found in air, and MMA and DMA are organic forms of arsenic found in water.

Symptoms of acute arsenic intoxication associated with the ingestion of well water containing arsenic at 1.2 and 21.0 mg/L have been reported (Feinglass, 1973; Wagner et al., 1979). Early clinical symptoms of acute arsenic intoxication include abdominal pain and vomiting, diarrhoea, pain to the extremities and muscles, and weakness with flushing of the skin. These symptoms are often followed by numbness and tingling of the extremities, muscular cramping, and the appearance of a papular erythematous rash 2 weeks later (Murphy et al., 1981). A month later, symptoms may include burning paraesthesias of the extremities, palmoplantar hyperkeratosis, Mee's lines on fingernails, and progressive deterioration in motor and sensory responses (Fennell and Stacy, 1981; Murphy et al., 1981; Wesbey and Kunis, 1981).

Signs of chronic arsenicalism, including pigmentation and development of keratoses, peripheral neuropathy, skin cancer, peripheral vascular disease, hypertensive heart disease, cancers of internal organs (bladder, kidney, liver, and lung), alterations in gastrointestinal function (non-cirrhotic hypertension), and an increased risk of mortality resulting from diabetes, have been observed in populations ingesting arsenic-contaminated drinking water in southwestern Taiwan (Chen et al., 1985, 1992; Wu et al., 1989), Bangladesh (Smith et al., 2000), Chile (Borgono and Greiber, 1971; Zaldívar, 1980; Zaldívar and Ghai, 1980), India (Mandal et al., 1998), the United States (Valentine et al., 1982; U.S. NRC, 1999; U.S. EPA, 2001a), Mexico (Cebrian *et al.*, 1983), and Canada (Hindmarsh et al., 1977). Dermal lesions, such as hyperpigmentation, warts, and hyperkeratosis of the palms and soles, are the most commonly observed symptoms in 70-kg adults after 5–15 years of exposure equivalent to 700 µg/day or within 6 months to 3 years at exposures equivalent to 2800 µg/day (U.S. EPA, 2001a).[2]

Numerous adverse effects, particularly among children, have been associated with the consumption of arsenic-contaminated water in Antofagasta, Chile (mean arsenic concentration 0.6 mg/L). Effects on the skin (leukomelanoderma, hyperkeratosis), respiratory system (chronic coryza, cough, bronchopulmonary diseases), cardiovascular system (myocardial infarction, peripheral vascular disorders such as ischaemia of the tongue, Raynaud's phenomenon, acrocyanosis), and digestive system (abdominal pain, chronic diarrhoea) were observed in children under 16 years of age (Zaldívar, 1980; Zaldívar and Ghai, 1980). The prevalence of these symptoms decreased after the installation of a water treatment plant in 1972 (mean arsenic concentration 0.08 mg/L); however, prevalence rates were still higher than those of the control population (Zaldívar and Ghai, 1980). Dermal lesions in young people ingesting drinking water containing high arsenic concentrations have also been reported elsewhere (Tseng et al., 1968; Cebrian et al., 1983).

The largest epidemiological study on arsenic to date was conducted in a limited area of southwestern Taiwan (an area well known for its high incidence of blackfoot disease). This data set has been analysed by numerous authors (e.g., Tseng, 1977; Chen et al. 1985, 1992; Wu et al. 1989; U.S. NRC, 1999, 2001) for assessing the health effects of arsenic through ingestion of

[2] For comparison, the estimated intakes per day at various drinking water exposure levels (assuming consumption of 1.5 L of water per day) and a food contribution of 49 µg/day (total organic and inorganic arsenic) are as follows: at 5 µg/L = 56.5 µg/day ((1.5 L/day × 5 µg/L) + 49 µg/day); at 10 µg/L = 64 µg/day; at 100 µg/L = 199 µg/day; and at 500 µg/L = 799 µg/day.

arsenic-contaminated drinking water. Tseng (1977) divided a population of 40 421 into three groups based on the arsenic content of their well water (high ≥0.60 mg/L, medium 0.30–0.59 mg/L, and low 0.01–0.29 mg/L). There was a clear dose–response relationship between exposure to arsenic and the frequency of dermal lesions, "blackfoot disease" (a severe peripheral vascular disorder) (Yu et al., 1984), and skin cancer. Despite certain methodological weaknesses in this early study, it is now widely accepted that exposure to high concentrations of arsenic is a cause of peripheral vascular disease. Blackfoot disease is now sometimes used as an indicator of exposure to arsenic (U.S. EPA, 2001b).

More epidemiological evidence for an association between the incidence of various cancers of the internal organs and the ingestion of arsenic-contaminated water comes from a study conducted in a limited area of southwest Taiwan. In this study, standardized mortality ratios (SMRs) for cancers of the bladder, kidney, skin, lung, liver, and colon were significantly elevated in the area of arsenic contamination. The SMRs for bladder, kidney, skin, lung, and liver cancer also correlated well with the prevalence rate for blackfoot disease (Chen et al., 1986). In an additional case–control study of 69 bladder, 76 lung, and 59 liver cancer mortality cases as well as 368 community controls matched for age and sex, the odds ratios of developing bladder, lung, and liver cancers for those who had used artesian well water for 40 or more years were 3.90, 3.39, and 2.67, respectively, compared with those who had never used artesian well water. Dose–response relationships were observed for all three cancer types by duration of exposure, and the odds ratios were not changed significantly when several other risk factors were taken into consideration in logistic regression analysis (Chen et al., 1986).

In an ecological analysis in which cancer mortality was examined in relation to arsenic concentrations in drinking water in the villages of the blackfoot disease-endemic areas of southwestern Taiwan, Chen et al. (1985) found an association between high-arsenic artesian well water (ranging from 0.35 to 1.14 mg/L; median level 0.78 mg/L) and cancers of the bladder, kidney, lung, skin, liver, and colon. Both the SMR and cumulative mortality rate were significantly higher for cancers of the bladder, kidney, lung, skin, liver, and colon compared with the general population of southwestern Taiwan. The SMRs for cancers of the bladder, kidney, skin, lung, liver, and colon were 1100, 772, 534, 320, 170, and 160, respectively, for males and 2009, 1119, 652, 413, 229, and 168, respectively, for females. A dose–response relationship was observed between the SMRs of the cancers and blackfoot disease prevalence rate of the villages and townships in the endemic areas. An additional ecological analysis of the same southwestern Taiwanese population by Wu et al. (1989) also found significant dose–response relationships for age-adjusted rates of cancers of the bladder, kidney, skin, and lung in both sexes and cancers of the prostate and liver in men (the total numbers of cancers at each site were 181 cancers of the bladder in both sexes, 59 cancers of the kidney in both sexes, 36 cancers of the skin in both sexes, 9 cancers of the prostate in men, 123 cancers of the liver in men, and 268 lung cancers in both sexes) (Wu et al., 1989). A study examining the ecological correlations between arsenic levels in well water and mortality from various malignant neoplasms in southwestern Taiwan demonstrated a significant association between the arsenic level in well water and cancers of the liver, nasal cavity, lung, skin, bladder, and kidney in both sexes and prostate cancer in men (Chen and Wang, 1990). A later reanalysis by Chen *et al.* (1992) on the same southwestern

Taiwanese study population calculated cancer potency indices for liver, lung, bladder, and kidney. The study population was stratified into four groups according to the median arsenic level of well water in each village. There were 13 villages with median arsenic levels below 0.10 mg/L, eight villages with levels ranging from 0.10 to 0.29 mg/L, 15 villages with levels from 0.30 to 0.59 mg/L, and six villages with levels greater than or equal to 0.60 mg/L. The total numbers of cancer-related deaths observed during the study period were as follows: 140 male and 62 female liver cancer deaths, 169 male and 135 female lung cancer deaths, 97 male and 105 female bladder cancer deaths, and 30 male and 34 female kidney cancer deaths. Mortality rates were found to increase significantly with age for all cancers in both males and females. Significant dose–response relationships were observed between the ingested arsenic level and mortality from cancer of the liver, lung, bladder, and kidney in most age groups of both males and females.

Further support for the increased incidence of lung and bladder cancers from arsenic exposure is provided by Ferreccio *et al.* (2000) and Chiou *et al.* (2001). Both of these studies differed from the southwestern Taiwan ones (Chen et al., 1985; Wu et al., 1989), in that they examined the risk factors for newly diagnosed cases of bladder cancer (Chiou *et al*., 2001) and lung cancer (Ferreccio et al., 2000) rather than deaths. The study by Chiou et al. (2001) established a significant dose–response relationship between risk of urinary cancers and arsenic exposure after adjustment for age, sex, and cigarette smoking. This work was, however, limited in terms of its size. Ferreccio *et al.* (2000) revealed a clear association between the odds ratios for lung cancer and concentrations of arsenic in drinking water. While this work further supports the association of cancer with arsenic in drinking water, it has been deemed limited because of control selection methods used (U.S. NRC, 2001).

In a case–control study of 270 children with congenital heart disease and 665 healthy children, maternal consumption of drinking water containing detectable arsenic concentrations during pregnancy was associated with a threefold increase in the occurrence of coarction of the aorta. The prevalence odds ratio adjusted for all measured contaminants and source of drinking water was 3.4, with a 95% confidence interval of 1.3–8.9 (Zierler et al., 1988). However, there was no adjustment for maternal age, socioeconomic status, or previous reproductive history. Exposure was determined by matching the results of available water analyses for the water supplies serving the mothers to their dates of conception. However, for 101 of the mothers residing in communities served by multiple water supplies, it was necessary to average contaminant concentrations from more than one source in the community; the mean interval from the date of analysis to date of conception for the entire study population was 227 days.

In a case–control study in Massachusetts of 286 women with spontaneous abortions and 1391 women with live births, elevated odds ratios for miscarriages were associated with exposure to arsenic in drinking water (Aschengrau et al., 1989). The odds ratios for spontaneous abortion adjusted for maternal age, educational level, and history of prior spontaneous abortion for women exposed to arsenic in their drinking water at undetectable concentrations, 0.0008–0.0013 mg/L, and 0.0014–0.0019 mg/L were 1.0, 1.1, and 1.5, respectively. Exposure was determined by matching each woman to the results of a tap water sample taken in her city or town during pregnancy. However, the median interval from the date of matched metal analysis sample

to the date of conception was 2.1 years, and it was reported that the variability of concentrations of metals in 20 Massachusetts towns and cities over the 7-year period between 1978 and 1985 was 10- to 100-fold. It would be desirable, however, to follow up these preliminary results in studies designed to more accurately assess exposure.

Although some effects have been observed in children and pregnant women, the U.S. NRC concluded that "there was insufficient scientific information to permit separate cancer risk estimates for potential subpopulations such as pregnant women, lactating women and children and that factors that influence sensitivity to or expression of arsenic-associated cancer and non-cancer effects need to be better characterized" (U.S. EPA, 2001a).

Most studies to date on arsenic exposure through drinking water have reported links between cancer and high concentrations of arsenic. A few recent studies in the United States, however, report no clear association between lung and bladder cancer risks and arsenic levels in drinking water that are lower than those reported in Taiwan (350–1140 µg/L). A historical case–control study by Steinmaus *et al.* (2003) looked at arsenic ingestion and bladder cancer incidence in individuals in seven counties in the western United States exposed to arsenic at concentrations ranging from 0 to greater than 120 µg/L. Cancer incidence was recorded from 1994 to 2000, and individual data on water sources, water consumption patterns, smoking, and other factors were collected for 181 cases and 328 controls. No increased risks of bladder cancer were observed for arsenic intakes greater than 80 µg/day (equivalent to ingesting 1.5 L of water daily containing arsenic at 53 µg/L) lagged over 5 years (odds ratio = 0.94, 95% confidence interval = 0.56–1.57). For similar intakes 40 or more years prior to diagnosis of cancer (i.e., 40 years or more lag period), the odds ratio was greater than 1 (odds ratio = 1.78, 95% confidence interval = 0.89–3.56); however, since the confidence intervals were quite large and include the null hypothesis (odds ratio of 1.0), it was concluded that there was no significant association between bladder cancer and arsenic exposure above 80 µg/day. For smokers with exposures greater than 80 µg/day 40 years prior to diagnosis of cancer, an odds ratio of 3.67 (95% confidence interval = 1.43–9.42) was reported, which provides some evidence that smokers ingesting arsenic at levels above 80 µg/day may be at increased risk of bladder cancer. Results from this study suggest that the latency period for arsenic-mediated carcinogenicity may be 40 years or longer, although conclusions from this study should be made with caution, given a few weaknesses in the authors' statistical analysis. These weaknesses include arbitrarily categorized arsenic levels (which may mask a potential dose–response relationship), very small sample sizes in the categories above 10 µg/L, and the use of odds ratios instead of person-years to calculate cancer incidence rates (odds ratios give only a snapshot of cancer incidence at a given time and dose).

A study by Lamm et al. (2004) reported no arsenic-related increase in bladder cancer mortality in 2.5 million white males (from 1950 to 1979) with exposures ranging from 3 to 60 µg/L in drinking water within 133 U.S. counties in 26 states, with 65% of the counties and 82% of the population exposed to arsenic in the 3–5 µg/L range. However, it should be noted that the analysis of cancer risks using bladder cancer mortality data is limited, since bladder cancer generally does not result in mortality (U.S. EPA and Awwa Research Foundation, 2004).

In a similar study by the U.S. EPA and Awwa Research Foundation (2004), lung and bladder cancer incidence and mortality rates were examined in 32 U.S. counties in 11 states (comprising approximately 1.5 million people) with mean drinking water arsenic levels of 10 µg/L or greater during 1950–1999. No associations were observed between arsenic in drinking water at levels greater than 10 µg/L and incidence of, or mortality from, bladder or lung cancer. The authors cautioned that it is possible for elevated risks of lung and bladder cancer mortality or incidence to be present but not apparent in the analysis, since the analysis of cancer risks from bladder cancer mortality data is limited, given that people with bladder cancer generally do not die from it; the latency period between arsenic exposure and death from cancer is relatively long, so that migration and death from other causes may mask health outcomes from arsenic exposure; and an ecological study relates exposures and outcomes in groups of individuals that may not be representative of individual responses to arsenic exposure. The authors also indicated that further research is being conducted to confirm these results.

9.2 Effects in experimental animals and *in vitro*

Arsenic presents unique problems for quantitative risk assessment because there is no test animal species for studying carcinogenicity. It appears that test animals do not respond to inorganic arsenic exposure in a way that makes them useful as a model for human cancer assessment. Their metabolism of inorganic arsenic is also quantitatively different from that by humans (U.S. EPA, 2001a).

The specific form or valence of arsenic that is responsible for teratogenesis in animals is not known, although there is evidence to suggest that it is arsenite (As(III)) rather than arsenate (As(V)) (Hanlon and Ferm, 1986b).

There were significant reductions in cardiac output and stroke volume in male Wistar rats and female New Zealand rabbits ingesting drinking water containing As(III) at 50 µg/mL for 18 and 10 months, respectively. In contrast, there was no effect on cardiac function in rats following ingestion of the same concentration of As(V) for 18 months (Carmignani et al., 1985).

In a multi-organ tumour initiation–promotion study, Yamamoto et al. (1995) reported positive results in rat bladder, kidney, liver, and thyroid. DMA significantly enhanced tumour induction in the urinary bladder, kidney, liver, and thyroid gland in rats treated with DMA at 400 mg/L in the drinking water. Induction of preneoplastic lesions (glutathione S-transferase placental form-positive foci in the liver and atypical tubules in the kidney) was also significantly increased in DMA-treated rats. Ornithine decarboxylase activity in the kidneys of rats treated with 100 mg DMA/L was significantly increased compared with control values ($P < 0.001$). Subsequent studies have also shown positive results for promotion of carcinogenesis when examined in a single initiator–promoter protocol in the rat liver (Wanibuchi et al., 1997) and bladder (Wanibuchi et al., 1996).

Other studies have shown carcinogenic effects in mice and rats (IPCS, 2001), although many of the studies of carcinogenicity of arsenic in animals have resulted in negative findings (ATSDR, 2000). An extensive review of animal models of arsenic carcinogenicity is presented in U.S. NRC (1999), Kitchin (2001), and Wang et al. (2002).

Arsenic has been known to induce chromosome breakage, chromosomal aberrations, and sister chromatid exchange in a linear, dose-dependent fashion in a variety of cultured cell types, including human cells (Jacobson-Kram and Montalbano, 1985; U.S. EPA, 1988). Most of the chromosomal aberrations are lethal events, so that the cells do not survive more than one or two generations (U.S. EPA, 1988). Trivalent arsenic is approximately an order of magnitude more potent than As(V) in this respect. The clastogenic effect of arsenic appears to be due to interference with DNA synthesis, as arsenic induces sister chromatid exchange and chromosomal aberrations only when present during DNA replication (Crossen, 1983). Arsenic has also been shown to block dividing cells in the S and G_2 phases (Petres et al., 1977). While the mechanism of arsenic genotoxicity remains unknown, mechanisms such as reactive oxygen species and the inhibition of DNA repair have been proposed (IPCS, 2001; WHO, 2003). Several possible modes of action for arsenic carcinogenesis, including chromosomal abnormalities, oxidative stress, altered DNA repair, altered DNA methylation patterns, altered growth factors, enhanced cell proliferation, promotion/progression, gene amplification, and suppression of p53, have been reviewed by Kitchin (2001).

In early studies, teratogenic effects of arsenic in chicks, golden hamsters, and mice were reported (Hood and Bishop, 1972; Zierler *et al*., 1988). Arsenate was found to be teratogenic in the offspring of pregnant hamsters following exposure on days 4–7 of gestation by minipump implantation (Ferm and Hanlon, 1985). The threshold blood level for teratogenesis was 4.3 µmol/kg (Hanlon and Ferm, 1986a). In studies with mice and hamsters, MMA^V and DMA^V have been considerably less teratogenic than As(III) or As(V). However, teratogenicity was not observed in mice or rabbits upon oral administration of arsenic acid at 48 mg/kg bw per day during gestation days 6–15 and at 0–3 mg/kg bw per day during gestation days 6–18 (Nemec et al., 1998).

9.3 Relative toxicity of arsenic compounds in humans

While earlier studies reported organic forms of arsenic (MMA^V, DMA^V, MMA^{III}, and DMA^{III}) to be less toxic than their inorganic counterparts (i.e., As(III) and As(V)) (U.S. NRC, 1999), recent evidence suggests that the conversion of inorganic arsenic into organic arsenic may not represent a detoxification pathway. In humans, MMA^V and DMA^V, as well as MMA^{III} and DMA^{III}, result from the sequential reduction and methylation of inorganic arsenic by the liver (Buchet and Lauwerys, 1985; Lovell and Farmer, 1985). Inorganic arsenic that is not immediately removed from the body undergoes these reduction and methylation steps. Recent isolation of MMA^{III} in urine from humans suggests that, contrary to previous belief, MMA^{III} is actually more toxic to hepatocytes than MMA^V and arsenite (As(III)) (Aposhian et al., 2000; Petrick et al., 2000; Styblo *et al*., 2000; U.S. NRC, 2001). Work on human hepatocytes performed by Petrick et al. (2000) has established a relative order of toxicity: MMA^{III} > arsenite (+3) > arsenate (+5) > MMA^V = DMA^V. A study by Mass *et al.* (2001) provides some evidence that organic arsenic is more effective than inorganic arsenic in altering chromosomal integrity in cultured human lymphocytes and phage DNA. Both MMA^{III} and DMA^{III} were found to be more

effective at inducing DNA damage than As(III). Although these studies provide some initial evidence that organic arsenic may be more toxic than inorganic arsenic, further research is required to confirm these findings.

10.0 Classification and assessment

Arsenic is a documented human carcinogen. It has therefore been classified in Group 1 (carcinogenic to humans) both by Health Canada (as defined in Health Canada (1994)) and by the International Agency for Research on Cancer (IARC). Toxic effects other than cancer have also been observed in populations ingesting arsenic-contaminated water supplies; however, carcinogenicity is considered to be the critical effect for derivation of the guideline.

It is important to note that while animal studies have confirmed the carcinogenicity of arsenic, significant differences concerning the observed toxic effects of arsenic exist between animal species. Hence, human studies remain the most reliable sources to be used in establishing a maximum acceptable concentration (MAC).

While early studies on the southwestern Taiwanese population indicated an association between arsenic in drinking water and cancer of internal organs (Chen et al., 1985; Wu et al., 1989), this information on its own was not deemed to be sufficient for quantitative risk assessment during the development of the 1989 guideline for arsenic in drinking water. As a result, the 1989 guideline was based on the increased incidence of skin cancer observed in the southwestern Taiwanese population (Tseng et al., 1968) and a model devised by the U.S. EPA, which estimated lifetime skin cancer risks associated with the ingestion of arsenic in drinking water using a multistage model modified to take into account incidence stratified by age group. This model was quadratic as well as linear in dose and included an adjustment for the larger water consumption of southwestern Taiwanese compared with North American men. Based on this model, lifetime risks of skin cancer in the general population in Canada for ingestion of 1 µg/L of arsenic in drinking water were estimated to range from 1.3×10^{-5} (based on southwestern Taiwanese women) to 3.6×10^{-5} (based on southwestern Taiwanese men).

New data have become available that suggest that the risk of internal cancers due to ingestion of arsenic in drinking water is greater than previously believed (U.S. NRC, 1999). Chen *et al.* (1992) evaluated cancer potency indices in the liver, lung, bladder, and kidney for cancers induced by the ingestion of inorganic arsenic in drinking water. A comparison of observed number of deaths and mortality rate by age, sex, and arsenic level in drinking water for these various internal cancers indicated that lung and bladder cancer presented the greatest lifetime risks for development at an arsenic level of 10 µg/kg bw per day. Morales et al. (2000) calculated excess lifetime risk estimates in the same population for bladder, liver, and lung cancers resulting from exposure to arsenic in drinking water using several mathematical models (generalized linear model, multistage Weibull model, and several variations of these); results for risk estimates were sensitive to the choice of model used.

In addition, a review of the health assessment concerning the toxicity of arsenic in drinking water based on human data from southwestern Taiwan indicates a positive relationship between internal organ cancers (lung, bladder, liver, and kidney) and the ingestion of arsenic in drinking water. Similar conclusions were also reported by U.S. EPA (2001a), U.S. NRC (1999,

2001), and WHO (2003). It should also be noted that, although lacking in necessary data for risk quantification, other studies support the association of arsenic in drinking water with cancers of internal organs (lung and bladder) (Kurttio et al., 1999; Lewis et al., 1999; Ferreccio et al., 2000; Chiou et al., 2001).

The southwestern Taiwan ecological study, as reported by many authors, including Wu et al. (1989), Chen et al. (1992), and the U.S. NRC (1999), has been recommended for quantitative risk assessment (U.S. EPA, 2001a; U.S. NRC, 2001). This study population has been chosen because it presents sufficiently long-term exposure to arsenic and follow-up, extensive pathology data, homogeny between lifestyles of the population, and a large population size (approximately 40 000 people) (U.S. NRC, 2001). A statistical analysis by Morales et al. (2000) fit nine Poisson-type models and one Weibull model to this data set in estimating the risk of cancer to the bladder, liver, and lung from exposure to arsenic in drinking water. Although the U.S. EPA (2001a) concluded that model 1 from Morales *et al.* (2000), which did not use a comparison population, was more reliable than those models utilizing a comparison population, the U.S. NRC (2001) recommends that an external, unexposed population should be used in the dose–response analysis. The use of an external comparison population is classically used in the analysis of cohort data (Breslow and Day, 1987), since it provides a more accurate estimate of the baseline cancer rates and minimizes the impact of exposure misclassification in the low dose range within the study population. On the basis of a review of the available data, Health Canada used the increased incidence of internal organ cancers observed in the southwestern Taiwanese population for calculating the estimated unit risk of cancer due to arsenic exposure through drinking water instead of the increased incidence of skin cancer that was used in the 1989 guideline. Health Canada (2005) concluded that a Poisson model recommended by the U.S. EPA (2001a) and fit by Morales et al. (2000) with an external unexposed comparison population is the most appropriate for estimating the cancer risks associated with the ingestion of arsenic in drinking water. The population from the southwestern region of Taiwan was chosen over the entire Taiwanese population as an external comparison population since it reduces potential bias and confounding that can be associated with differences in populations (i.e., the urban national population versus the rural southwestern region). In the quantitative risk assessment, Health Canada (2005) adopted assumptions similar to those of the U.S. EPA (2001a) regarding the choice of risk metric and the use of a southwestern Taiwanese to Canadian conversion factor. The Health Canada (2005) model analysed data from Morales *et al*. (2000), who sourced their data from Chen *et al.* (1985) and Wu *et al.* (1989).

Overall, using a 1% increase in risk, the unit risks associated with ingestion of 1 µg/L of arsenic in drinking water are estimated to range from 3.06×10^{-6} to 3.85×10^{-5}, with 95% upper bounds ranging from 6.49×10^{-6} to 4.64×10^{-5}. The most sensitive endpoint for both males and females was lung cancer (Health Canada, 2005). The overall unit risk associated with the ingestion of arsenic in drinking water is reported as a range, given that lifetime exposure to arsenic results in more than one cancer endpoint in different individuals. The above unit risk range has the liver cancer unit risk (3.06×10^{-6}) as its lower bound and the lung cancer unit risk (3.85×10^{-5}) as its upper bound. This range also includes the estimated risks for cancers of bladder and other internal organs.

Epidemiological data are often reported with the 95% upper-bound value. This value quantifies the variability in the unit risk due to the variability in the data from the study population. Sources of variability in these data may be, for example, individual differences in arsenic metabolism, drinking rates, or body weights. The 95% upper bound is often interpreted as a reasonable conservative upper-bound estimate of the unit risk. In other words, in repeated trials of the experiment, 95% of the time, the 95% upper-bound value will be above the true value of the unit risk.

Based on this unit risk calculation, an acceptable concentration of arsenic in drinking water can be established that would present an "essentially negligible" level of risk. This target concentration, which is based solely on health considerations, is calculated as 0.3 µg/L. The upper 95% confidence interval for the lifetime cancer risk associated with this concentration in drinking water is 1.9×10^{-6} to 1.39×10^{-5}, which falls within the range considered to be "essentially negligible." In the context of drinking water guidelines, Health Canada has defined the term "essentially negligible" as a range from one new cancer above background per 100 000 people to one new cancer above background per 1 million people (i.e., 10^{-5} to 10^{-6}) over a lifetime.

11.0 Rationale

Humans are exposed to many forms of arsenic that have different toxicities. The acute toxicity of the various arsenic compounds in humans is predominantly a function of their rate of removal from the body. Metallic arsenic (0 valence) is not absorbed from the stomach and as such does not have any adverse effect. Inorganic arsenic has historically been considered to be the predominant form of arsenic responsible for toxic and carcinogenic effects in humans. Inorganic arsenic that is not immediately removed from the body may enter a methylation pathway, which was believed to be a detoxification process. Although some organic arsenic compounds have little or no toxicity or are rapidly eliminated from the body in the urine, forms such as MMA^{III} and DMA^{III} have recently been found to be more toxic than inorganic arsenite (As(III)); however, further research is required to confirm these findings. There is no evidence that children or other groups such as pregnant women are at a greater risk of developing health effects from exposure to arsenic compared with the general population.

Arsenic can be found in both surface water and groundwater sources, with levels generally higher in groundwater. Most provinces and territories across Canada report some areas where arsenic can be detected in drinking water supplies. Levels of arsenic tend to be higher in groundwater than in surface water. Levels of arsenic naturally found in waters generally range between 0.001 and 0.002 mg/L, but arsenic may occur in much higher concentrations. Data collected indicate that the levels of arsenic in Canadian drinking water are generally less than 0.005 mg/L.

Several advanced municipal-scale treatment processes can remove arsenic from drinking water to levels of 0.001–0.005 mg/L. However, given their complexity and cost, these processes may not be practical for smaller communities. Alternative processes, such as adsorption and membrane systems, are suitable for reduction of arsenic to low concentrations (<0.003 mg/L) in

small to mid-sized communities. At residential scale, drinking water treatment devices available to date have been certified as reducing arsenic concentrations to 0.01 mg/L, although lower levels may be achieved with the use of these devices.

Since arsenic is classified in Group 1 (carcinogenic to humans), the MAC is derived based on the estimated lifetime cancer risk; consideration was also given to available practical treatment technology and the PQL.

A MAC of 0.01 mg/L (10 µg/L) for arsenic is established on the basis of the following considerations:

- The concentration of arsenic in drinking water representing an "essentially negligible" risk is 0.3 µg/L. Levels of arsenic in drinking water should be as close as possible to this level.
- The MAC must be measurable. The PQL, based on the ability of laboratories to measure arsenic within reasonable limits of precision and accuracy, is 0.003 mg/L.
- The MAC must be achievable at reasonable cost. Both municipal-scale and residential-scale treatment options can remove arsenic from drinking water to below the guideline value.

The estimated lifetime cancer risk associated with the ingestion of drinking water containing arsenic at 0.01 mg/L (10 µg/L) is greater than the range that is considered generally to be "essentially negligible" (i.e., between 10^{-5} and 10^{-6}). Based on the incidence of internal (lung, bladder, liver) cancers in individuals in southwestern Taiwan, the estimated lifetime risk associated with ingestion of water containing arsenic at 0.01 mg/L (10 µg/L) is 3.0×10^{-5} to 3.9×10^{-4} (derived by multiplying the unit risk by the MAC).

Although arsenic is a documented human carcinogen, limited data on the mode of action of arsenic do not strongly justify the use of either a linear or non-linear quantitative risk assessment model. The use of a non-linear extrapolation method to estimate the risks of internal organ cancers from exposure to low levels of arsenic as well as confounding factors (e.g., genetic differences, differences in health status, arsenic metabolism, and nutritional status of the southwestern Taiwanese study population) may lead to an overestimate of the risks of internal organ cancers. Although some recent studies in the United States have found no clear association between lung and bladder cancer risks and arsenic levels in drinking water between 0.01 and 0.05 mg/L, the weight of evidence still lies with the southwestern Taiwanese cohort data. Given the current uncertainties, the carcinogenic potential of arsenic, and the different practical difficulties associated with removing arsenic from drinking water at the small municipal and residential levels, every effort should be made to reduce arsenic levels in drinking water to as low as reasonably achievable.

In considering both the treatment costs associated with achieving arsenic concentrations in drinking water at or below the health-based guideline value and the health risks associated with concentrations of arsenic in drinking water above the guideline value, the Federal-Provincial-Territorial Committee on Drinking Water has concluded that a MAC of 0.01 mg/L (10 µg/L) should be adopted. This value is the result of a risk management decision, since it exceeds the health-based guideline value.

As part of its ongoing guideline review process, Health Canada will continue to monitor new research in this area and recommend any change(s) to the guideline that it deems necessary.

12.0 References

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Appendix A: List of acronyms

ALARA	as low as reasonably achievable
ANSI	American National Standards Institute
As	arsenic
ASTM	American Society for Testing and Materials
DMA^{III}	dimethylarsinous acid
DMA^{V}	dimethylarsinic acid
EPA	Environmental Protection Agency (USA)
ETS	environmental tobacco smoke
GFAA	graphite furnace atomic absorption
GHAA	gaseous hydride atomic absorption
IARC	International Agency for Research on Cancer
ICP-AES	inductively coupled plasma atomic emission spectroscopy
ICP-MS	inductively coupled plasma mass spectroscopy
kg bw	kilogram body weight
MAC	maximum acceptable concentration
MDL	method detection limit
MMA^{III}	monomethylarsinous acid
MMA^{V}	monomethylarsinic acid
NRC	National Research Council (USA)
NSF	NSF International
PQL	practical quantitation limit
SCC	Standards Council of Canada
SM	Standard Methods (American Public Health Association)
SMR	standardized mortality ratio
STP-GFAA	stabilized temperature platform graphite furnace atomic absorption