**WHO/SDE/WSH/03.04/75/Rev/1**

# Arsenic in Drinking-water

Background document for development of
WHO *Guidelines for Drinking-water Quality*

Rev/1: Revisions indicated with a vertical line in the left margin.

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## Preface

One of the primary goals of the World Health Organization (WHO) and its Member States is that "all people, whatever their stage of development and their social and economic conditions, have the right to have access to an adequate supply of safe drinking water". A major WHO function to achieve such goals is the responsibility "to propose ... regulations, and to make recommendations with respect to international health matters ...."

The first WHO document dealing specifically with public drinking-water quality was published in 1958 as *International Standards for Drinking-water*. It was subsequently revised in 1963 and in 1971 under the same title. In 1984–1985, the first edition of the WHO *Guidelines for Drinking-water Quality* (GDWQ) was published in three volumes: Volume 1, Recommendations; Volume 2, Health criteria and other supporting information; and Volume 3, Surveillance and control of community supplies. Second editions of these volumes were published in 1993, 1996 and 1997, respectively. Addenda to Volumes 1 and 2 of the second edition were published in 1998, addressing selected chemicals. An addendum on microbiological aspects reviewing selected microorganisms was published in 2002. The third edition of the GDWQ was published in 2004, the first addendum to the third edition was published in 2006 and the second addendum to the third edition was published in 2008. The fourth edition will be published in 2011.

The GDWQ are subject to a rolling revision process. Through this process, microbial, chemical and radiological aspects of drinking-water are subject to periodic review, and documentation related to aspects of protection and control of public drinking-water quality is accordingly prepared and updated.

Since the first edition of the GDWQ, WHO has published information on health criteria and other supporting information to the GDWQ, describing the approaches used in deriving guideline values and presenting critical reviews and evaluations of the effects on human health of the substances or contaminants of potential health concern in drinking-water. In the first and second editions, these constituted Volume 2 of the GDWQ. Since publication of the third edition, they comprise a series of free-standing monographs, including this one.

For each chemical contaminant or substance considered, a lead institution prepared a background document evaluating the risks for human health from exposure to the particular chemical in drinking-water. Institutions from Canada, Japan, the United Kingdom and the United States of America (USA) prepared the documents for the fourth edition.

Under the oversight of a group of coordinators, each of whom was responsible for a group of chemicals considered in the GDWQ, the draft health criteria documents were submitted to a number of scientific institutions and selected experts for peer review. Comments were taken into consideration by the coordinators and authors. The draft documents were also released to the public domain for comment and submitted for final evaluation by expert meetings.

During the preparation of background documents and at expert meetings, careful consideration was given to information available in previous risk assessments carried out by the International Programme on Chemical Safety, in its Environmental Health Criteria monographs and Concise International Chemical Assessment Documents, the International Agency for Research on Cancer, the Joint FAO/WHO Meeting on Pesticide Residues and the Joint FAO/WHO Expert Committee on Food Additives (which evaluates contaminants such as lead, cadmium, nitrate and nitrite, in addition to food additives).

Further up-to-date information on the GDWQ and the process of their development is available on the WHO Internet site and in the current edition of the GDWQ.

**Acknowledgements**

The current version of Arsenic in Drinking-water, Background document for development of WHO *Guidelines for Drinking-water Quality*, is an update of the background document published in the third edition of the Guidelines, which was prepared by Mr J.K. Fawell and Mr R. Mascarenhas, United Kingdom.

The work of the following working group coordinators was crucial in the development of this document and others contributing to the fourth edition:

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The draft text was discussed at the Expert Consultation for the fourth edition of the GDWQ, held in December 2011. The final version of the document takes into consideration comments from both peer reviewers and the public. The input of those who provided comments and of participants at the meeting is gratefully acknowledged.

The WHO coordinators were Mr R. Bos and Mr B. Gordon, WHO Headquarters. Ms C. Vickers provided a liaison with the International Programme on Chemical Safety, WHO Headquarters. Mr M. Zaim, Public Health and the Environment Programme, WHO Headquarters, provided input on pesticides added to drinking-water for public health purposes.

Ms P. Ward provided invaluable administrative support throughout the review and publication process. Ms M. Sheffer of Ottawa, Canada, was responsible for the scientific editing of the document.

Many individuals from various countries contributed to the development of the GDWQ. The efforts of all who contributed to the preparation of this document and in particular those who provided peer or public domain review comments are greatly appreciated.

## Acronyms and abbreviations used in the text

| | |
|---|---|
| $BMDL_{0.5}$ | lower confidence limit on the benchmark dose for a 0.5% response |
| DMA | dimethylarsinic acid |
| DNA | deoxyribonucleic acid |
| FAO | Food and Agriculture Organization of the United Nations |
| IARC | International Agency for Research on Cancer |
| ICP-MS | inductively coupled plasma mass spectrometry |
| JECFA | Joint FAO/WHO Expert Committee on Food Additives |
| MMA | monomethylarsonic acid |
| PTWI | provisional tolerable weekly intake |
| WHO | World Health Organization |

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## *1. GENERAL DESCRIPTION*

### *1.1 Identity*

Arsenic exists in oxidation states of −3, 0, 3 and 5. It is widely distributed throughout Earth's crust, most often as arsenic sulfide or as metal arsenates and arsenides. In water, it is most likely to be present as arsenate, with an oxidation state of 5, if the water is oxygenated. However, under reducing conditions (<200 mV), it is more likely to be present as arsenite, with an oxidation state of 3 (IPCS, 2001).

| *Compound* | *Chemical Abstracts Service No.* | *Molecular formula* |
|---|---|---|
| Arsenic | 7440-38-2 | As |
| Arsenic trioxide | 1327-53-3 | $As_2O_3$ |
| Arsenic pentoxide | 1303-28-2 | $As_2O_5$ |
| Arsenic sulfide | 1303-33-9 | $As_2S_3$ |
| Dimethylarsinic acid (DMA) | 75-60-5 | $(CH_3)_2AsO(OH)$ |
| Monomethylarsonic acid (MMA) | 124-58-3 | $(CH_3)AsO(OH)_2$ |
| Lead arsenate | 10102-48-4 | $PbHAsO_4$ |
| Potassium arsenate | 7784-41-0 | $KH_2AsO_4$ |
| Potassium arsenite | 10124-50-2 | $KAsO_2HAsO_2$ |

### *1.2 Physicochemical properties (IARC, 1980; Lide, 1992–1993)*

| *Compound* | *Melting point (°C)* | *Boiling point (°C)* | *Density (g/cm$^3$)* | *Water solubility (g/l)* |
|---|---|---|---|---|
| As | 613 | – | 5.727 at 14 °C | insoluble |
| $As_2O_3$ | 312.3 | 465 | 3.738 | 37 at 20 °C |
| $As_2O_5$ | 315 (decomposes) | – | 4.32 | 1500 at 16 °C |
| $As_2S_3$ | 300 | 707 | 3.43 | $5 \times 10^{-4}$ at 18 °C |
| $(CH_3)_2AsO(OH)$ | 200 | – | – | 829 at 22 °C |
| $CH_3AsO(OH)_2$ | – | – | – | – |
| $PbHAsO_4$ | 720 (decomposes) | – | 5.79 | very slightly soluble |
| $KH_2AsO_4$ | 288 | – | 2.867 | 190 at 6 °C |
| $KAsO_2HAsO_2$ | – | – | – | soluble |

### *1.3 Major uses*

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

### *1.4 Environmental fate*

Arsenic is introduced into water through the dissolution of rocks, minerals and ores, from industrial effluents, including mining wastes, and via atmospheric deposition (IPCS, 1981; Nadakavukaren et al., 1984; Hindmarsh & McCurdy, 1986). In well oxygenated surface waters, arsenic(V) is generally the most common arsenic species present (Irgolic, 1982; Cui & Liu, 1988); under reducing conditions, such as those often found in deep lake sediments or groundwater, the predominant form is arsenic(III) (Lemmo et al., 1983; Welch et al., 1988). An increase in pH may increase the concentration of dissolved arsenic in water (Slooff et al., 1990).

## *2. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE*

### *2.1 Air*

Arsenic concentrations measured in remote or rural areas range from 0.02 to 4 ng/$m^3$ (USNRC, 1999). In urban areas, arsenic concentrations of 3–200 ng/$m^3$ have been measured. Much higher concentrations (>1000 ng/$m^3$) are present in the vicinity of industrial sources (Ball et al., 1983; WHO, 1987; USNRC, 1999).

### *2.2 Water*

The level of arsenic in natural waters, including open ocean seawater, generally ranges between 1 and 2 µg/l (Hindmarsh & McCurdy, 1986; USNRC, 1999). Concentrations may be elevated, however, in areas with volcanic rock and sulfide mineral deposits (Hindmarsh & McCurdy, 1986); in areas containing natural sources, where levels as high as 12 mg/l have been reported (Grinspan & Biagini, 1985); near anthropogenic sources, such as mining and agrochemical manufacture (USNRC, 1999); and in geothermal waters (mean 500 µg/l, maximum 25 mg/l) (USNRC, 1999). Mean arsenic concentrations in sediment range from 5 to 3000 mg/kg; the higher levels occur in areas of contamination (USNRC, 1999) but are generally unrelated to arsenic concentrations in water.

### *2.3 Food*

The total estimated daily dietary intake of arsenic may vary widely, mainly because of wide variations in the consumption of fish and shellfish. Most data reported are for total arsenic intake and do not reflect the possible variation in intake of the more toxic inorganic arsenic species. Limited data indicate that approximately 25% of the arsenic present in food is inorganic, but this is highly dependent upon the type of food (Hazell, 1985; USEPA, 1988; IPCS, 2001).

Fish and meat are the main sources of dietary intake of arsenic (Gartrell et al., 1986a); levels ranging from 0.4 to 118 mg/kg have been reported in marine fish sold for human consumption, and concentrations in meat and poultry can be as high as 0.44 mg/kg (Health and Welfare Canada, 1983).

The mean daily intake of arsenic in food for adults has been estimated to range from 16.7 to 129 μg (Hazell, 1985; Gartrell et al., 1986a; Dabeka et al., 1987; Zimmerli et al., 1989); the corresponding range for infants and children is 1.26–15.5 μg (Nabrzyski et al., 1985; Gartrell et al., 1986b). In preliminary studies in North America, the estimated daily intake of arsenic from the diet was 12–14 μg of inorganic arsenic (Yost et al., 1998).

### *2.4 Estimated total exposure and relative contribution of drinking-water*

Except for individuals who are occupationally exposed to arsenic, the most important route of exposure is through the oral intake of food and drinking-water, including beverages made from drinking-water. The mean daily intake of arsenic from drinking-water will generally be less than 10 μg; however, in those areas in which drinking-water contains elevated concentrations of arsenic, this source will make an increasingly significant contribution to the total intake of inorganic arsenic as the concentration of arsenic in drinking-water increases. As the estimated daily intake of arsenic from food in preliminary studies of diets in North America is 12–14 μg of inorganic arsenic (Yost et al., 1998), consumption of 2 litres of drinking-water containing 10 μg/l would make drinking-water the dominant source of intake. In circumstances where rice, soups or similar dishes are a staple part of the diet, the drinking-water contribution through preparation of food will be even greater. The estimated intake from air is generally less than 1 μg.

## *3. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS*

Ingested elemental arsenic is poorly absorbed and largely eliminated unchanged. Soluble arsenic compounds are rapidly absorbed from the gastrointestinal tract (Hindmarsh & McCurdy, 1986); arsenic(V) and organic arsenic are rapidly and almost completely eliminated via the kidneys (Buchet et al., 1981a; Luten et al., 1982; Tam et al., 1982). Inorganic arsenic may accumulate in skin, bone, liver, kidney and muscle (Ishinishi et al., 1986); its half-life in humans is between 2 and 40 days (Pomroy et al., 1980). Inorganic arsenic is eliminated from the body by the rapid urinary excretion of unchanged arsenic in both the trivalent and pentavalent forms and by sequential methylation to MMA and DMA in both 3 and 5 valence states (Buchet & Lauwerys, 1985; Lovell & Farmer, 1985). Limited short-term studies on humans indicate that the capacity to methylate inorganic arsenic is progressively, but not completely, saturated when daily intake exceeds 0.5 mg (Buchet et al., 1981b).

The internal dose of inorganic arsenic in individuals can be determined by measuring the arsenic species in urine. The concentrations of metabolites of inorganic arsenic in urine from individuals with no known exposure to arsenic are reported to be generally below 10 μg/l in European countries; however, in West Bengal, India, and Bangladesh, urinary arsenic concentrations above 1 mg/l have frequently been observed (IPCS, 2001).

In humans, inorganic arsenic does not appear to cross the blood–brain barrier; however, transplacental transfer of arsenic in humans has been reported (Gibson & Gage, 1982).

## *4. EFFECTS ON LABORATORY ANIMALS AND IN VITRO TEST SYSTEMS*

### *4.1 Long-term exposure*

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

### *4.2 Reproductive and developmental toxicity*

Teratogenic effects of arsenic in chicks, golden hamsters and mice have been reported (Hood & Bishop, 1972; Zierler et al., 1988). Arsenate was teratogenic in the offspring of pregnant hamsters following exposure on days 4–7 of gestation by minipump implantation (Ferm & Hanlon, 1985). The specific form of arsenic responsible for teratogenesis is not known, but it may be arsenite (Hanlon & Ferm, 1986). Other workers did not observe teratogenicity in studies in which mice or rabbits were orally administered arsenic acid at 0–48 mg/kg of body weight per day on gestation days 6–15 and at 0–3 mg/kg of body weight per day on gestation days 6–18, respectively (Nemec et al., 1998). The above data indicate that although arsenic is teratogenic when given by parenteral routes, it is considerably less potent when given by the oral route.

### *4.3 Mutagenicity and related end-points*

Arsenic does not appear to induce point mutations in bacterial and mammalian assays, although it can 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 & Montalbano, 1985; USEPA, 1988). Arsenic(III) is about an order of magnitude more potent than arsenic(V) in this respect (USEPA, 1988). Methylated trivalent arsenic metabolites have also been reported to be genotoxic in vitro and to show significantly greater potency than arsenic(III) (Mass et al., 2001). Arsenic has been shown to be capable of causing chromosome damage in bone marrow cells of mice in in vivo assays (Deknudt et al., 1986; Tinwell et al., 1991; Das et al., 1993; Choudhury et al., 1996). The mechanism of arsenic genotoxicity is not clear, although several mechanisms have been proposed, including reactive oxygen species and the inhibition of deoxyribonucleic acid (DNA) repair (IPCS, 2001).

### *4.4 Carcinogenicity*

Arsenic has not been found to be carcinogenic in traditional animal bioassays. In a study of the potential of arsenic compounds to act as promoters, a significant increase in the incidence of kidney tumours was observed in male Wistar rats injected intraperitoneally with a single dose of diethylnitrosamine (30 mg/kg of body weight) and, from day 7, given the maximum tolerated dose (160 mg/l) of arsenic(III) in drinking-water for 25 weeks (Shirachi et al., 1986). Other studies using mice with specific genetic characteristics have shown carcinogenic effects (IPCS, 2001), and these may be of value in studying the potential mechanism by which arsenic causes cancer. Animal models of arsenic carcinogenicity have been extensively reviewed by Wang et al. (2002).

## *5. EFFECTS ON HUMANS*

A number of studies have attempted to show that arsenic is an essential element, but a biological role has not been demonstrated so far (USNRC, 1999, 2001). Arsenic has not been demonstrated to be essential in humans (IPCS, 2001).

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 (arsenic(III)), the arsenates (arsenic(V)) and organic arsenic compounds. Lethal doses in humans range from 1.5 mg/kg of body weight (diarsenic trioxide) to 500 mg/kg of body weight (DMA) (Buchet & Lauwerys, 1982). Acute arsenic intoxication associated with the ingestion of well water containing 1.2 and 21.0 mg of arsenic per litre has been reported (Feinglass, 1973; Wagner et al., 1979). MMA(III) and DMA(III) are more toxic than arsenate in vivo and in vitro.

Early clinical symptoms of acute intoxication include abdominal pain, vomiting, diarrhoea, muscular pain 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 (Murphy et al., 1981). Within a month, symptoms may include burning paraesthesias of the extremities, palmoplantar hyperkeratosis, Mee's lines on fingernails and progressive deterioration in motor and sensory responses (Fennell & Stacy, 1981; Murphy et al., 1981; Wesbey & Kunis, 1981).

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 (Tseng et al., 1968; Borgońo & Greiber, 1972; Hindmarsh et al., 1977; Tseng, 1977; Zaldivar, 1980; Zaldivar & Ghai, 1980; Valentine et al., 1982; Cebrian et al., 1983). 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 (Zaldivar, 1980; Zaldivar & Ghai, 1980).

In a large study conducted in Taiwan, China, a population of 40 421 was divided 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, <0.29 mg/l) (Tseng, 1977). There was a clear dose–response relationship between exposure to arsenic and the frequency of dermal lesions, "blackfoot disease" (a peripheral vascular disorder) and skin cancer. However, several methodological weaknesses (e.g. investigators were not "blinded") complicate the interpretation of the results. In addition, the possibility of other causes of blackfoot disease (e.g. humic acids in artesian well water) were not considered (Lu, 1990).

In Taiwan, China, the prevalence and mortality rates of diabetes mellitus were higher among the population of the blackfoot disease endemic area. There was also an exposure–response relationship between cumulative arsenic exposure and the prevalence of diabetes mellitus. A similar exposure–response pattern was observed in a study in Bangladesh, where prevalence of keratosis was used as a surrogate for arsenic exposure (USNRC, 1999, 2001; IPCS, 2001).

There have been numerous epidemiological studies that have examined the risk of various cancers associated with arsenic ingestion through drinking-water. Many of these studies 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, particularly skin, bladder and lung. In several parts of the world, arsenic-induced disease, including cancer, is a significant public health problem. The studies have been reviewed in detail (USNRC, 1999, 2001; ATSDR, 2000; IPCS, 2001). Because trivalent inorganic arsenic has greater reactivity and toxicity than pentavalent inorganic arsenic, it is generally believed that the trivalent form is the carcinogen. However, there remain considerable uncertainty and controversy over both the mechanism of carcinogenicity and the shape of the dose–response curve at low intakes. Recently, the trivalent methylated metabolites, MMA(III) and DMA(III), have been found to be more genotoxic than inorganic arsenic. The role of these metabolites with regard to arsenic carcinogenicity remains unknown.

IPCS (2001) 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 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 ≤50 µg arsenic/litre.

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) recently evaluated arsenic (FAO/WHO, 2011a,b). Their evaluation[1] of the effects of arsenic on humans was summarized as follows:

> The main adverse effects reported to be associated with long-term ingestion of inorganic arsenic by humans are cancer, skin lesions, developmental effects, cardiovascular disease, neurotoxicity and diabetes.
>
> The classification of arsenic as a carcinogen was originally based on evidence of skin cancers. Studies in Taiwan, China, and other regions where high exposures to arsenic in drinking-water occurred have confirmed the relationship. Significant associations between exposure to high levels of ingested arsenic in drinking-water and bladder cancer have been observed in ecological studies from Chile, Argentina and Taiwan, China, and cohort studies in Taiwan, China. Some of the studies showed an association only in smokers. In studies from Chile, Argentina and Taiwan, China, exposure to arsenic at high concentrations in drinking-water has been shown to be associated with lung cancer. Again, when smokers and non-smokers were compared, the associations were stronger in the smokers. Nutritional status of exposed populations has been observed to influence cancer risk. Thus, compromised nutrition (e.g. low protein intake) is likely to be associated with significantly higher risk. The evidence for an association with cancers at other sites, including prostate, liver and kidney, is less conclusive.
>
> Epidemiological studies in different regions of the world have consistently demonstrated a strong association between long-term inorganic arsenic ingestion and skin lesions, typically in the form of hyperkeratosis, hyperpigmentation or hypopigmentation. Observations of skin lesions following low chronic exposure have suggested that these characteristic dermal changes are sensitive indications of the toxic effects of inorganic arsenic.
>
> Available epidemiological studies indicate a positive relationship between high concentrations of inorganic arsenic in drinking-water and sensitive end-points for peripheral and central neurotoxicity. There is some evidence that exposure of children to inorganic arsenic in areas with elevated arsenic concentrations (>50 µg/l) in drinking-water produces effects on cognitive performance, but so far this is not conclusive.
>
> The cardiovascular outcomes that have been associated with chronic exposure to arsenic through drinking-water include blackfoot disease, increased mortality or prevalence of coronary heart disease, peripheral arterial disease, myocardial infarction and stroke, and other cardiovascular end-points, such as increased blood pressure and prolonged QT interval of the electrocardiogram. The association between blackfoot disease and inorganic arsenic exposure has been confirmed by many studies, but blackfoot disease has been reported primarily in an area along the south-western coast of Taiwan, China, where arsenic contamination in well water is very high (170–880 µg/l). Except for blackfoot disease, the reported associations between inorganic arsenic exposure and cardiovascular disease prevalence/mortality and other cardiovascular end-points currently do not provide sufficient evidence of causality and are not considered pivotal for the assessment.
>
> Studies conducted in Bangladesh and Taiwan, China, indicated an extra risk of diabetes among high-exposure populations. In addition, recent findings suggest that in utero arsenic exposure impaired child thymic development and that enhanced morbidity and immunosuppression might occur. However, as a result of limitations in the studies, the relationship between arsenic exposure and these outcomes remains uncertain.

[1] For more information and primary references, the reader should refer to the monograph on arsenic contained in FAO/WHO (2011b).

The Committee concluded that the greatest strength of evidence for a causal association between inorganic arsenic and adverse effects in humans is for cancers of the skin, urinary bladder and lung and skin lesions (hyperkeratosis, hyperpigmentation and hypopigmentation) observed in studies in which levels of arsenic in drinking-water were relatively high (e.g. ≥100 μg/l). For this evaluation, studies were preferred that included documentation of exposure from drinking-water both at higher concentrations (e.g. ≥300 μg/l) and also at relatively lower concentrations (e.g. <100 μg/l). This was in order to assess effects across a broad gradient of exposure and to avoid extrapolation below the observed range in the dose–response modelling. For skin cancer, three of the four most recent studies of low-level exposure utilized toenail arsenic as a biomarker of exposure; however, the relationship between toenail arsenic and total dietary exposure to inorganic arsenic remains uncertain. Further, as arsenic-related skin lesions may be a possible precursor to skin cancer and have been reported at lower concentrations of arsenic in drinking-water compared with skin cancer, the Committee considered the data for skin lesions to be a more sensitive adverse effect than skin cancer. Thus, pivotal data were identified from epidemiological studies reporting a positive association with arsenic exposure and these effects (i.e. cancers of the lung and urinary tract and skin lesions).

## *6. PRACTICAL CONSIDERATIONS*

### *6.1 Analytical methods*

A silver diethyldithiocarbamate spectrophotometric method is available for the determination of arsenic; the detection limit is about 1 μg/l (ISO, 1982). Graphite furnace atomic absorption spectroscopy, hydride generation atomic absorption spectrophotometry and inductively coupled plasma mass spectrometry (ICP-MS) are more sensitive. High-pressure liquid chromatography in combination with ICP-MS can also be used to determine various arsenic species (Irgolic, 1982).

### *6.2 Prevention and control*

Sources such as mining and some pesticides and wood preservatives may contribute to human exposure and should be controlled in order to prevent environmental contamination. However, the great majority of exposure occurs through naturally contaminated groundwater, through drinking-water, water used in food preparation and water used to irrigate food crops, particularly rice.

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).

The ideal solution is to use alternative sources of water that are low in arsenic. However, it is important that this does not result in risk substitution—for example, if the alternative water source, although low in arsenic, increases exposure to waterborne pathogens and results in acute gastrointestinal infections, which are a major source of mortality and morbidity in many parts of the world (Howard, 2003). This is important for most alternative water sources other than water from tube wells.

Water safety frameworks should be used during planning, installation and management of all new water points, especially ones based on surface water and very shallow groundwater, to minimize risks from faecal and other non-arsenic contamination. Screening for arsenic and other possible chemical contaminants of concern that can cause problems with health or acceptability, including fluoride, nitrate, iron and manganese, is also important to ensure that new sources are acceptable. Occasional screening may also be required after a source is established to ensure that it remains safe.

Where there are large urban supplies, resources are often available to treat water to remove arsenic or to exploit alternative low-arsenic sources, such as surface water that can be treated to avoid microbiological and other hazards. These low-arsenic sources can be used to blend with higher-arsenic sources to lower the concentration to acceptable levels while still retaining the resource.

Many of the major problems lie in rural areas, where there are many small supplies, sometimes down to the household level. At this level, water availability and financial and technical resources are all limited. There are several available approaches, but there is a basic requirement for education. In particular, there is a need to understand the risks of high arsenic exposure and the sources of arsenic exposure, including the uptake of arsenic by crops from irrigation water and the uptake of arsenic into food from cooking water.

A number of approaches have been successfully used in rural areas, including source substitution and the use of both high- and low-arsenic sources blended together. These sources may be used to provide drinking-water and cooking water or to provide water for irrigation. High-arsenic water can still be used for bathing and clothes washing or other requirements that do not result in contamination of food. However, it is important to remember that there may be other contaminants present as well as arsenic, and so it is important to determine whether other contaminants of concern are present.

Low-cost approaches that have been developed to lower exposure to arsenic where contamination of groundwater is a problem include the following:

- alternative sources, including dug wells that are properly protected to prevent microbiological contamination and rainwater harvesting, which may be possible for at least some months of the year, with steps taken to minimize contamination;
- surface ponds, which require appropriate steps to minimize microbial and chemical contamination and also require treatment to ensure microbial safety before drinking;
- identifying high- and low-arsenic tube wells by painting them different colours and sharing wells (spatial variability in groundwater arsenic contamination in Argentina, Chile and the river deltas of South and South-east Asia is very high, so there are mixtures of arsenic-contaminated and arsenic-uncontaminated wells in most villages);

- sinking new wells into low-arsenic strata. This requires significant technical support to ensure that low arsenic levels are known and can be exploited without other problems arising. Deeper groundwater aquifers can be used to develop community water supplies, which generally succeed where there is community involvement in their establishment and operation;
- removal of arsenic by low-cost village or household treatment systems, usually using absorptive media, such as elemental iron, iron or aluminium oxides and carbon. Shallow groundwater that is anoxic (e.g. in South and South-east Asia) is generally high in dissolved iron, so a pretreatment step involving the formation and precipitation of iron hydroxide, which will then adsorb arsenic, is advantageous. Many household treatment systems in Bangladesh and West Bengal, India, may fail prematurely because of high levels of phosphate, which competes with inorganic arsenic species for adsorption, in the water. Safe disposal of arsenic-contaminated wastes should also be considered.

In areas where there is observable arsenicosis, there is usually no problem in persuading the local population to follow arsenic mitigation measures, even though they often require significant extra effort. Involvement of individuals and communities in the planning, implementation and management of the mitigation strategy is a key factor for successful intervention. Studies in Bangladesh have shown that most rural households prefer sharing of uncontaminated wells or filtration of low-arsenic surface water through sand to treatment of groundwater (Howard, 2003; Johnston, Hanchett & Khan, 2010).

Where arsenic levels are lower and the adverse effects of arsenic exposure are less obvious, there will be a much greater requirement for education in order for mitigation measures to be carried out effectively over an extended time period. More information can be found in sources such as Howard (2003) and JICA/AAN (2004).

## *7. PROVISIONAL GUIDELINE VALUE*

Inorganic arsenic compounds are classified by the International Agency for Research on Cancer (IARC, 1987) 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. USNRC (2001), in its updated evaluation, 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 USA exposed to 10 µg of arsenic per litre 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. 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 provisional tolerable weekly intake (PTWI) of 15 µg/kg of 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 (specifically for an increased risk of lung cancer) and was therefore no longer appropriate. The PTWI was therefore withdrawn (FAO/WHO, 2011a,b). JECFA concluded that for certain regions of the world where concentrations of inorganic arsenic in drinking-water exceed 50–100 µg/l, some epidemiological studies provide evidence of adverse effects.There are other areas where arsenic concentrations in water are elevated (e.g. above the WHO guideline value of 10 µg/l), but are less than 50 µg/l. In these circumstances, there is a possibility that adverse effects could occur as a result of exposure to inorganic arsenic from water and food, but these would be at a low incidence that would be difficult to detect in epidemiological studies.

Therefore, 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.

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