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Mercury in Drinking-water

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

Preface

One of the primary goals of 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 on selected chemicals in 1998 and on microbial aspects in 2002. The third edition of the GDWQ was published in 2004, and the first addendum to the third edition was published in 2005.

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, Denmark, Finland, France, Germany, Italy, Japan, Netherlands, Norway, Poland, Sweden, United Kingdom and United States of America prepared the documents for the third edition and addenda.

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 Meetings 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.

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

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The draft text was discussed at the Working Group Meeting for the first addendum to the third edition of the GDWQ, held on 17–21 May 2004. 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 in the meeting is gratefully acknowledged.

The WHO coordinator was Dr J. Bartram, Coordinator, Water, Sanitation and Health Programme, WHO Headquarters. Ms C. Vickers provided a liaison with the International Programme on Chemical Safety, WHO Headquarters. Mr Robert Bos, Water, Sanitation and Health Programme, WHO Headquarters, provided input on pesticides added to drinking-water for public health purposes.

Ms Penny Ward provided invaluable administrative support at the Working Group Meeting and throughout the review and publication process. Ms Marla 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 comment are greatly appreciated.

Acronyms and abbreviations used in the text

AAS	atomic absorption spectrometry
DNA	deoxyribonucleic acid
FAO	Food and Agriculture Organization of the United Nations
GDWQ	*Guidelines for Drinking-water Quality*
ICP	inductively coupled plasma
Ig	immunoglobulin
IPCS	International Programme on Chemical Safety (WHO)
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LD_{50}	median lethal dose
LOAEL	lowest-observed-adverse-effect level
NOAEL	no-observed-adverse-effect level
NTP	National Toxicology Program (USA)
PTWI	provisional tolerable weekly intake
TDI	tolerable daily intake
USA	United States of America
WHO	World Health Organization

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1. GENERAL DESCRIPTION

1.1 Identity

Mercury is a metallic element that occurs naturally in the environment.

1.2 Physicochemical properties

Property	*Value*
Physical state	Dense, silver-white metal; liquid at normal temperatures and pressures
Vapour pressure	0.16 Pa at 20 °C
Stability	Carbon–mercury bond in organic mercury compounds is chemically stable

1.3 Major uses and sources in drinking-water

Naturally occurring mercury has been widely distributed by natural processes such as volcanic activity. The use of mercury in industrial processes significantly increased following the industrial revolution of the 19th century. Mercury is or has been used for the cathode in the electrolytic production of chlorine and caustic soda, in electrical appliances (lamps, arc rectifiers, mercury cells), in industrial and control instruments (switches, thermometers, barometers), in laboratory apparatus and as a raw material for various mercury compounds. The latter are used as fungicides, antiseptics, preservatives, pharmaceuticals, electrodes and reagents. However, mercury's industrial uses are decreasing because of environmental concerns and environmental legislation in many countries. Mercury has also been widely used in dental amalgams. A less well characterized use is in ethnic and folk remedies, some of which can give rise to significant exposure of individuals (IPCS, 2003).

1.4 Environmental fate

The solubility of mercury compounds in water varies: elemental mercury vapour is insoluble, mercury(II) chloride is readily soluble, mercury(I) chloride is much less soluble and mercury sulfide has a very low solubility.

Methylation of inorganic mercury is an important process in water and occurs in both fresh water and seawater (IPCS, 1989). Bacteria (*Pseudomonas* spp.) isolated from mucous material on the surface of fish and soil were able to methylate mercury under aerobic conditions. Some anaerobic bacteria that possess methane synthetase are also capable of mercury methylation (Wood & Wang, 1983). Once methylmercury[1] is released from microbes, it enters the food-chain as a consequence of rapid diffusion and tight binding to proteins in aquatic biota. The enzymology of CH_3Hg^+ hydrolysis and mercury(II) ion reduction is now understood in some detail. Environmental levels of methylmercury depend on the balance between bacterial methylation and demethylation (IPCS, 1990).

[1] The generic term "methylmercury" is used throughout this text to refer to monomethylmercury compounds.

2. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

2.1 Air

Mercury levels in air are in the range 2–10 ng/m^3.

2.2 Water

Levels of mercury in rainwater are in the range 5–100 ng/litre, but mean levels as low as 1 ng/litre have been reported (IPCS, 1990). Naturally occurring levels of mercury in groundwater and surface water are less than 0.5 µg/litre, although local mineral deposits may produce higher levels in groundwater. A small number of groundwaters and shallow wells surveyed in the USA were shown to have mercury levels that exceeded the maximum contaminant level of 2 µg/litre set by the US Environmental Protection Agency for drinking-water (Ware, 1989). An increase in the mercury concentration up to 5.5 µg/litre was reported for wells in Izu Oshima Island (Japan), where volcanic activity is frequent (Magara et al., 1989). The concentration range for mercury in drinking-water is the same as in rain, with an average of about 25 ng/litre (IPCS, 1990).

In a contaminated lake system in Canada, methylmercury was found to constitute a varying proportion of total mercury, depending on the lake (IPCS, 1990). There have been no reports of methylmercury being found in drinking-water.

2.3 Food

Food is the main source of mercury in non-occupationally exposed populations. Fish and fish products account for most of the organic mercury in food. The average daily intake of mercury from food is in the range 2–20 µg, but may be much higher in regions where ambient waters have become contaminated with mercury and where fish constitute a high proportion of the diet (Galal-Gorchev, 1991).

2.4 Dental amalgams

The use of dental amalgams for repair work has been widespread and is considered to be an important source of exposure for those with amalgam dental work (IPCS, 2003).

2.5 Estimated total exposure and relative contribution of drinking-water

On the assumption of an ambient air level of 10 ng/m^3, the average daily intake of inorganic mercury by inhalation would amount to about 0.2 µg. If a level in drinking-water of 0.5 µg/litre is assumed, the average daily intake of inorganic mercury from this source would amount to about 1 µg. The average daily intake of mercury from food is in the range 2–20 µg. Mercury in drinking-water is considered to be a minor source of exposure to mercury except in circumstances of significant pollution.

3. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

About 7–8% of ingested mercury in food is absorbed; absorption from water may be 15% or less, depending on the compound. About 80% of inhaled metallic mercury

vapour is retained by the body, whereas liquid metallic mercury is poorly absorbed via the gastrointestinal tract. Inhaled aerosols of inorganic mercury are deposited in the respiratory tract and absorbed to an extent depending on particle size (IPCS, 1991). The extent of transport of inorganic mercury across the intestinal tract is probably dependent on its solubility, ease of dissociation in the gastrointestinal tract and intestinal pH (Friberg & Nordberg, 1973; Endo et al., 1990). Nutritional status with regard to essential divalent cations such as Cu^{2+} and Zn^{2+} may also influence gastrointestinal absorption (IPCS, 2003).

Inorganic mercury compounds are rapidly accumulated in the kidney, the main target organ for these compounds. The biological half-time is very long, probably years, in both animals and humans. Mercury salts are excreted via the kidney, liver, intestinal mucosa, sweat glands, salivary glands and milk; the most important routes are via the urine and faeces (IPCS, 1991, 2003).

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

4.1 Short-term exposure

The toxic effects of inorganic mercury compounds are mainly in the kidney. Lesions in the proximal tubular cells were detected after a single intraperitoneal injection of 1 µmol of mercury(II) chloride per kg of body weight (0.2 mg/kg of body weight as mercury) in male rats. Accumulation of mercury in the kidneys, however, indicated that the absorption efficiency was much greater than that expected from the gastrointestinal tract (Miura et al., 1981).

When rats were given mercury(II) chloride (3 mg/kg of body weight) by gavage twice a week for 60 days, examination by immunofluorescence showed that deposits for IgG were present in the renal glomeruli. Morphological lesions of the ileum and colon were also observed, with abnormal deposits of IgA in the basement membranes of the intestinal glands and of IgG in the basement membranes of the lamina propria (Andres, 1984).

When rats were exposed to mercury(II) chloride (1 mg/kg of body weight per day) by gavage or subcutaneous injection for up to 11 weeks, the rate of body weight gain decreased after 20 days, and actual weight loss occurred after 65–70 days. There were also neuropathological effects, first detected after 2 weeks, namely peripheral vacuolization of cells in the dorsal root ganglia, followed by the development of multiple small lesions in the ganglia (Chang & Hartmann, 1972).

In a 2-week study, groups of five male and five female rats were given mercury(II) chloride by gavage at doses of 0, 1.25, 2.5, 5.0, 10 or 20 mg of mercury per kg of body weight per day, 5 days per week. This treatment resulted in a significant increase in absolute and relative kidney weights at doses of 2.5 mg/kg of body weight per day and above in males and 5.0 mg/kg of body weight per day and above in females, while a dose-related increase in the severity of tubular necrosis was observed at 5.0 mg/kg of body weight per day and above. These findings were confirmed in a study in which rats were administered mercury(II) chloride in deionized water by gavage at mercury doses equivalent to 0, 0.23, 0.46, 0.93, 1.9 or 3.7 mg/kg of body weight per day, 5 days per week, for 26 weeks. The NOAEL for increased absolute and relative kidney weights was identified as 0.23 mg/kg of body weight per day (NTP, 1993).

In a similar 26-week study in mice given mercury(II) chloride at doses of 0, 5, 10, 20, 40 or 80 mg/kg of body weight per day, most animals receiving the highest dose of 80 mg/kg of body weight per day died. Absolute kidney weights were increased in males at all dose levels and in females at 40 mg/kg of body weight per day, whereas relative kidney weights were greater than in controls in all dosed animals. Acute renal tubular necrosis was observed to be treatment related (NTP, 1993).

Increased absolute and relative kidney weights were also observed in female Wistar rats given mercury(II) chloride at 1.1 mg/kg of body weight per day and above in the diet for 4 weeks (Jonker et al., 1993). In a drinking-water study in which male mice received mercury(II) chloride for 7 weeks, slight degeneration of the kidney tubular epithelial cells was observed at 2.9 mg of mercury per kg of body weight per day, and low-grade renal nephropathy was seen at 14.3 mg/kg of body weight per day (Dieter et al., 1992).

A number of studies have reported effects on the liver and adrenal following oral exposure to mercury(II) salts (IPCS, 2003).

4.2 Long-term exposure

Rats injected subcutaneously 3 times weekly for up to 8 months with doses of inorganic mercury ranging from 0.05 to 2.5 mg/kg of body weight per injection (0.02–1.07 mg/kg of body weight per day) developed renal damage. This was characterized by an initial production of antiglomerular basement membrane antibodies, followed by the appearance of immune complex deposits in the glomerular tufts and small renal arteries accompanied by proteinuria and hypoalbuminaemia (Makker & Aikawa, 1979).

In a 2-year study in which groups of 60 rats of each sex received 0, 2.5 or 5 mg of mercury(II) chloride per kg of body weight per day by gavage for 5 days per week (doses equivalent to 0, 1.9 and 3.7 mg/kg of body weight per day; IPCS, 2003), survival of treated males was lower than in controls. After 15 months, relative kidney weights were significantly increased in dosed animals, and males, but not females, showed increased severity of nephropathy. Both males and females showed minimal or mild hyperplasia of the basal cell layer in the forestomach. After 2 years, chronic nephropathy was observed to have developed more quickly, and this was associated with a range of secondary effects. Forestomach hyperplasia was significantly increased in incidence with increasing dose in males and increased in high-dose females with an associated increase in the incidence of squamous cell papillomas in males. The incidence of inflammation of the nasal mucosa was also increased in high-dose animals. The LOAEL for renal effects was 1.9 mg/kg of body weight per day (NTP, 1993).

In a parallel study in mice, doses were 0, 5 or 10 mg/kg of body weight per day given by gavage for 5 days per week (doses equivalent to 0, 3.7 and 7.4 mg/kg of body weight per day; IPCS, 2003). At 15 months, males, but not females, showed an increased severity of vacuolation of the renal tubular epithelium associated with treatment. Both males and females showed an increased incidence of olfactory epithelial inflammation. After 2 years, survival of high-dose males and dosed females was lower than that of controls. The incidence and severity of nephropathy were

increased in dosed animals, but secondary effects were not observed. The incidence of olfactory epithelial metaplasia showed a dose–response relationship in both males and females (NTP, 1993).

Similar findings were reported in Sprague-Dawley rats given 7 mg of mercury per kg of body weight per day as mercury(II) chloride in drinking-water for 350 days (Carmignani et al., 1989).

4.3 Reproductive and developmental toxicity

Controlled mating tests in which male mice were injected with single doses of mercury(II) chloride (1 mg of mercury per kg of body weight) showed a significant decrease in fertility compared with controls (Lee & Dixon, 1975). Normal fertility was restored after about 2 months.

Gradual changes in testicular tissues were noted in rats treated with mercury(II) chloride at doses of 0.05 or 0.1 mg/kg of body weight intraperitoneally over 90 days (Chowdhury et al., 1986). There was a decrease in seminiferous tubule diameter, spermatogenic cell counts and Leydig's cell nuclear diameter compared with controls.

Of female hamsters given a total of 3–4 mg of mercury(II) chloride during the first estrous cycle, 60% did not ovulate by day 1 of the third cycle (Lamperti & Printz, 1974). Ovulation was inhibited in female hamsters injected with mercury(II) chloride at high doses (6.4 or 12.8 mg of mercury per kg of body weight) during day 1 of the estrous cycle (Watanabe et al., 1982). Female hamsters injected with 1 mg of mercury(II) chloride per day during one estrous cycle exhibited significantly higher levels of follicle-stimulating hormone in their pituitaries compared with controls (Lamperti & Niewenhuis, 1976).

Pregnant Wistar rats were exposed intravenously to mercury(II) chloride on different days of gestation. At mid-gestation, the minimum effective teratogenic dose of mercury (0.79 mg/kg of body weight) was high in relation to the maternal LD_{50}, and the incidence of fetal malformations, mainly brain defects, was 23% in all live fetuses. In rats of different gestational ages, uptake of Hg^{2+} by the fetuses at this dose level decreased sharply between days 12 and 13 (Holt & Webb, 1986).

4.4 Mutagenicity and related end-points

There appear to be no data available from bacterial assays for point mutations. A number of studies have shown that mercury(II) chloride binds to DNA and can cause strand breaks *in vitro* (IPCS, 2003). Mercury(II) chloride has also been shown to increase chromosome aberrations in Chinese hamster ovary cells *in vitro* (Howard et al., 1991). The overall weight of evidence is that mercury(II) chloride possesses weak genotoxic activity but does not cause point mutations.

4.5 Carcinogenicity

The conclusions of the NTP (1993) studies on mercury(II) chloride were that there was some evidence of carcinogenic activity in rats based on an increased incidence of squamous cell papillomas in the forestomach. An equivocal increase in renal tubular tumours was observed in male mice, but no increase in tumours was observed in

female mice. The overall weight of evidence is that mercury(II) chloride has the potential to increase the incidence of some benign tumours at sites where tissue damage is apparent.

5. EFFECTS ON HUMANS

5.1 Acute exposure

Mercury will cause severe disruption of any tissue with which it comes into contact in sufficient concentration, but the two main effects of mercury poisoning are neurological and renal disturbances. The former is characteristic of poisoning by methyl- and ethylmercury(II) salts, in which liver and renal damage are of relatively little significance, the latter of poisoning by inorganic mercury.

In general, however, the ingestion of acute toxic doses of any form of mercury will result in the same terminal signs and symptoms, namely shock, cardiovascular collapse, acute renal failure and severe gastrointestinal damage. Acute oral poisoning results primarily in haemorrhagic gastritis and colitis; the ultimate damage is to the kidney. Clinical symptoms of acute intoxication include pharyngitis, dysphagia, abdominal pain, nausea and vomiting, bloody diarrhoea and shock. Later, swelling of the salivary glands, stomatitis, loosening of the teeth, nephritis, anuria and hepatitis occur (Stockinger, 1981).

Ingestion of 500 mg of mercury(II) chloride causes severe poisoning and sometimes death in humans (Bidstrup, 1964). Acute effects result from the inhalation of air containing mercury vapour at concentrations in the range of 0.05–0.35 mg/m^3 (Teisinger & Fiserova-Bergerova, 1965; Neilsen-Kudsk, 1972). Exposure for a few hours to 1–3 mg/m^3 may give rise to pulmonary irritation and destruction of lung tissue and occasionally to central nervous system disorders (Skerfving & Vostal, 1972).

Dermal exposure to alkylmercurials may give rise to acute toxic dermatitis and eczematous changes.

5.2 Long-term exposure

Many studies involving the observation of more than 1000 individuals indicate that the classical signs and symptoms of elemental mercury vapour poisoning (objective tremors, mental disturbances and gingivitis) may be expected to appear after chronic exposure to air mercury concentrations above 0.1 mg/m^3 (IPCS, 1991). Non-specific neurological and physiological symptoms were also associated with lower exposure levels.

Considerable mercury exposure of children of workers at a thermometer plant has been reported (Hudson et al., 1987). The median urine mercury level of 23 such children was 25 µg/litre, compared with 5 µg/litre in 39 controls. No signs of mercury intoxication were seen on clinical examination or reported by parents (IPCS, 1990).

A number of studies of dentists and dental assistants preparing mercury amalgam dental preparations have failed to demonstrate any clear adverse effects, although exposure characterization was often limited (IPCS, 2003).

6. PRACTICAL ASPECTS

6.1 Analytical methods and analytical achievability

Limits of detection for inorganic mercury are 0.6 µg/litre by ICP and 5 µg/litre by flame AAS (Japan Water Works Association, 2001). The dithizone method can be used to detect mercury in a sample with more than 1 µg of mercury per 10-ml final volume. Alternatively, cold vapour AAS can also be used for the detection of mercury, with a detection limit of 0.05 µg/litre (APHA et al., 1995). Multi-component simultaneity analysis is possible with metals by AAS and ICP (Japan Water Works Association, 2001).

6.2 Treatment and control methods and technical achievability

The concentration of mercury in drinking-water sources is usually less than 0.5 µg/litre, but on some occasions mercury can be found in groundwater at concentrations higher than this.

Conventional chemical coagulation, sedimentation and filtration can achieve removals of up to 80% for inorganic mercury, but only 20–40% for organic mercury. Ferric sulfate is more effective than aluminium sulfate, and removal is more effective in the presence of high concentrations of suspended solids. Powdered activated carbon is effective for the removal of inorganic and organic mercury and can be used to enhance removal during coagulation. Granular activated carbon treatment is also effective (Sorg, 1979). Ion exchange could be an alternative method (Chiarle et al., 2000). It should, therefore, be possible to achieve a concentration below 1 µg/litre by treatment of raw waters that are not grossly contaminated with mercury.

7. GUIDELINE VALUE

Almost all mercury in uncontaminated drinking-water is thought to be in the form of Hg^{2+}. Thus, it is unlikely that there is any direct risk of the intake of organic mercury compounds, and especially of alkylmercurials, as a result of the ingestion of drinking-water. However, there is a real possibility that methylmercury will be converted into inorganic mercury.

In 1972, JECFA established a PTWI of 5 µg of total mercury per kg of body weight, of which no more than 3.3 µg/kg of body weight should be present as methylmercury (JECFA, 1972). This PTWI was reaffirmed in 1978 (JECFA, 1978). In 1988, JECFA reassessed methylmercury, as new data had become available; it confirmed the previously recommended PTWI for the general population, but noted that pregnant women and nursing mothers were likely to be at greater risk from the adverse effects of methylmercury. The available data were considered insufficient, however, to allow a specific methylmercury intake to be recommended for this population group (JECFA, 1989a,b). In 2003, JECFA further considered methylmercury and, in the light of new data from exposed populations, recommended a PTWI of 1.6 µg/kg of body weight (JECFA, 2004).

An IPCS Working Group (IPCS, 2003) recommended a TDI of 2 µg/kg of body weight for inorganic mercury based on the NOAEL of 0.23 mg/kg of body weight per

day for kidney effects in the NTP 26-week study in rats and applying an uncertainty factor of 100 (for inter- and intraspecies variation) after adjusting for 5 days per week dosing. A similar TDI was obtained by applying an uncertainty factor of 1000 (an additional uncertainty factor of 10 for adjustment from a LOAEL to a NOAEL) to the LOAEL for renal effects of 1.9 mg/kg of body weight per day in the 2-year NTP study in rats.

Assuming a 60-kg adult drinking 2 litres of water per day and allocating 10% of the TDI to drinking-water, since the major sources of exposure are through food, the guideline value for inorganic mercury is 6 µg/litre. Methods are available to adequately measure inorganic mercury at this concentration.

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