

Barium in Drinking-water

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

© World Health Organization 2004

Requests for permission to reproduce or translate WHO publications - whether for sale or for non-commercial distribution - should be addressed to Publications (Fax: +41 22 791 4806; e-mail: permissions@who.int).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

The World Health Organization does not warrant that the information contained in this publication is complete and correct and shall not be liable for any damage incurred as a result of its use.

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 in 1998, addressing selected chemicals. An addendum on microbiological aspects reviewing selected microorganisms was published in 2002.

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/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 examined in drinking-water.

For each chemical contaminant or substance considered, a lead institution prepared a health criteria 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 requested health criteria documents.

Under the responsibility of the coordinators for a group of chemicals considered in the guidelines, 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 before the documents were submitted for final evaluation by the experts meetings. A “final task force” meeting reviewed the health risk assessments and public and peer review comments and, where appropriate, decided upon guideline values. During preparation of the third edition of the GDWQ, it was decided to include a public review via the world wide web in the process of development of the health criteria documents.

During the preparation of health criteria documents and at experts 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.

Acknowledgements

Barium in Drinking-water, Background document for development of WHO *Guidelines for Drinking-water Quality*, is an update of the background document published in the second edition of the Guidelines. The update was prepared by Mr J.K. Fawell and Mr R. Mascarenhas, United Kingdom, to whom special thanks are due.

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

Mr J.K. Fawell, United Kingdom (*Organic and inorganic constituents*)
Dr E. Ohanian, Environmental Protection Agency, USA (*Disinfectants and disinfection by-products*)
Ms M. Giddings, Health Canada (*Disinfectants and disinfection by-products*)
Dr P. Toft, Canada (*Pesticides*)
Prof. Y. Magara, Hokkaido University, Japan (*Analytical achievability*)
Mr P. Jackson, WRc-NSF, United Kingdom (*Treatment achievability*)

The contribution of peer reviewers is greatly appreciated. The draft text was posted on the world wide web for comments from the public. The revised text and the comments were discussed at the Final Task Force Meeting for the third edition of the GDWQ, held on 31 March to 4 April 2003, at which time the present version was finalized. The input of those who provided comments and of participants in the meeting is gratefully reflected in the final text.

The WHO coordinators were as follows:

Dr J. Bartram, Coordinator, Water Sanitation and Health Programme, WHO Headquarters, and formerly WHO European Centre for Environmental Health
Mr P. Callan, Water Sanitation and Health Programme, WHO Headquarters
Mr H. Hashizume, Water Sanitation and Health Programme, WHO Headquarters

Ms C. Vickers provided a liaison with the International Chemical Safety Programme, WHO Headquarters.

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

CAS	Chemical Abstracts Service
DNA	deoxyribonucleic acid
EPA	Environmental Protection Agency (USA)
LD ₅₀	median lethal dose
LOAEL	lowest-observed-adverse-effect level
NOAEL	no-observed-adverse-effect level
TDI	tolerable daily intake
USA	United States of America

Table of contents

1. GENERAL DESCRIPTION	1
1.1 Identity	1
1.2 Physicochemical properties	1
1.3 Major uses	1
1.4 Environmental fate	1
2. ANALYTICAL METHODS	2
3. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE	2
3.1 Air	2
3.2 Water	2
3.3 Food	3
3.4 Estimated total exposure and relative contribution of drinking-water	3
4. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS	3
5. EFFECTS ON LABORATORY ANIMALS AND <i>IN VITRO</i> TEST SYSTEMS	4
5.1 Acute exposure	4
5.2 Short-term exposure	4
5.3 Long-term exposure	5
5.4 Reproductive and developmental toxicity	7
5.5 Mutagenicity and related end-points	8
5.6 Carcinogenicity	8
6. EFFECTS ON HUMANS	8
7. GUIDELINE VALUE	10
8. REFERENCES	11

1. GENERAL DESCRIPTION

1.1 Identity

Barium is present as a trace element in both igneous and sedimentary rocks. Although it is not found free in nature (US EPA, 1985a), it occurs in a number of compounds, most commonly barium sulfate (barite) and, to a lesser extent, barium carbonate (witherite).

<i>Compound</i>	<i>CAS No.</i>	<i>Molecular formula</i>
Barium sulfide	21109-95-5	BaS
Barium chloride	10361-37-2	BaCl ₂
Barium oxide	1304-28-5	BaO
Barium hydroxide	17194-00-2	Ba(OH) ₂
Barium bromide	10553-31-8	BaBr ₂
Barium nitrate	10022-31-8	Ba(NO ₃) ₂
Barium nitrite	13465-94-6	Ba(NO ₂) ₂
Barium sulfate	7727-43-7	BaSO ₄
Barium acetate	543-80-6	Ba(C ₂ H ₃ O ₂) ₂

1.2 Physicochemical properties (US EPA, 1985b; Lide, 1992–1993)

<i>Compound</i>	<i>Melting point (°C)</i>	<i>Boiling point (°C)</i>	<i>Density (g/cm³)</i>	<i>Water solubility (g/litre)</i>
BaS	1200	–	4.25	readily soluble
BaCl ₂	960	1560	3.856 at 24 °C	310 at 0 °C
BaO	1923	2000	5.32–5.72	15 at 0 °C
Ba(OH) ₂	77.9	800	2.18 at 16 °C	38.9 at 20 °C
BaBr ₂	847	decomposes	4.781 at 24 °C	980 at 0 °C
Ba(NO ₃) ₂	592	decomposes	3.24 at 23 °C	92 at 20 °C
Ba(NO ₂) ₂	217	decomposes	3.23	675 at 20 °C
BaSO ₄	1580	–	4.50 at 15 °C	0.000 285 at 30 °C
Ba(C ₂ H ₃ O ₂) ₂	–	–	2.47	770 at 26 °C

1.3 Major uses

Barium compounds, including barium sulfate and barium carbonate, are used in the plastics, rubber, electronics and textile industries, in ceramic glazes and enamels, in glass-making, brick-making and paper-making, as a lubricant additive, in pharmaceuticals and cosmetics, in case-hardening of steel and in the oil and gas industry as a wetting agent for drilling mud (Miner, 1969; Brooks, 1986).

1.4 Environmental fate

Barium in water comes primarily from natural sources. The acetate, nitrate and halides are soluble in water, but the carbonate, chromate, fluoride, oxalate, phosphate

BARIUM IN DRINKING-WATER

and sulfate are quite insoluble. The solubility of barium compounds increases as the pH level decreases (US EPA, 1985a). The highest levels to be found in drinking-water are likely to be associated with groundwater of low pH from granite-like igneous rocks, alkaline igneous and volcanic rocks and manganese-rich sedimentary rocks. Concentrations are, therefore, expected to be relatively stable.

Organic barium compounds are ionic and are hydrolysed in water (Cotton & Wilkinson, 1980). The concentration of barium ions in natural aquatic systems is limited by the presence of naturally occurring anions and possibly also by the adsorption of these ions onto metal oxides and hydroxides (Hem, 1959).

2. ANALYTICAL METHODS

Barium concentrations in water may be determined by atomic absorption spectroscopy using either direct aspiration into an air-acetylene flame (detection limit 2 µg/litre) or atomization in a furnace (detection limit 100 µg/litre) (US EPA, 1985a). Barium in water may also be determined by inductively coupled plasma atomic emission spectrometry, the detection limits being equivalent or superior to those of flame atomic absorption spectroscopy (OME, 1988).

3. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

3.1 Air

Barium is generally present in air in particulate form as a result of industrial emissions, particularly from combustion of coal and diesel oil and waste incineration. Concentrations ranging from 0.000 15 to 0.95 µg/m³ have been reported. The estimated respiratory intake for an adult male is in the range of 0.03–22 µg/day (US EPA, unpublished data, 1984).

3.2 Water

The concentration of barium in groundwater in the Netherlands was measured at 60 locations; the mean and maximum concentrations were 0.23 and 2.5 mg/litre, respectively (Van Duijvenbooden, 1989).

Barium concentrations in distribution drinking-water in Canada were found to range from detectable (detection limit 5 µg/litre) to 600 µg/litre, with a median value of 18 µg/litre; in 86% of the 122 locations surveyed, the concentrations were below 100 µg/litre (Subramanian & Meranger, 1984). In 83% of 262 locations surveyed in the Netherlands in 1983, barium concentrations in drinking-water were below 50 µg/litre; the maximum concentration found was below 200 µg/litre (Fonds et al., 1987). In a study of water supplies of cities in the USA, a median value of 43 µg/litre was reported; in 94% of all determinations, the concentrations found were below 100 µg/litre (IPCS, 1990). Levels of barium in municipal water supplies in Sweden ranged from 1 to 20 µg/litre (IPCS, 1990). The median value for barium in drinking-water in Norway was reported to be 9 µg/litre (Flaten, 1991); in the Tuscany region of Italy,

concentrations in municipal drinking-water derived from groundwater were reported to be between 700 and 1160 µg/litre (Lanciotti et al., 1992). In the Cambrian-Vendian aquifer in Estonia, which is low in sulfate, barium concentrations ranged from 0.07 to 6.37 mg/litre, with a median value of 0.8 mg/litre. However, there was a significant variation in concentration over the aquifer; in one anomalous area, the median concentration was 2.41 mg/litre (A. Marandi, personal communication, 2003).

If an average daily water consumption of 2 litres is assumed, intake from drinking-water will range from about 2 to 1200 µg. The great majority of intakes will be below 200 µg, and most will be below 100 µg.

3.3 Food

Most foods contain less than 0.002 mg of barium per g (Gormican, 1970). Some cereal products and nuts may contain high levels: e.g., bran flakes, 0.0039 mg/g; pecans, 0.0067 mg/g; and Brazil nuts, up to 4 mg/g (Mertz, 1986).

The long-term mean dietary barium intake for adults has been found to be 0.75 mg/day (range 0.44–1.8 mg/day), including food and fluids (ICRP, 1975); 0.6 mg/day from total diet (IPCS, 1990); and 1.24 mg/day (range 0.65–1.8 mg/day) for food only (Schroeder et al., 1972).

Barium sulfate is the major barium compound used medicinally. Often called a barium “meal,” this very poorly soluble compound is employed as an opaque contrast medium for X-ray studies of the gastrointestinal tract.

3.4 Estimated total exposure and relative contribution of drinking-water

On the basis of the above considerations, the mean daily intake of barium from food, water and air is estimated to be slightly more than 1 mg/day, food being the primary source for the non-occupationally exposed population. However, where barium levels in water are high, drinking-water may contribute significantly to barium intake.

4. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

Soluble barium salts are most readily absorbed, although insoluble compounds may also be absorbed to a significant extent (McCauley & Washington, 1983; Clavel et al., 1987). The degree of absorption of barium from the gastrointestinal tract also depends on the animal species, the contents of the gastrointestinal tract, diet and age (Taylor et al., 1962; McCauley & Washington, 1983; Clavel et al., 1987). Data on gastrointestinal absorption in humans are limited to a study conducted by Lisk et al. (1988); in this mass balance study of one man consuming a single dose of 179.2 mg of barium in 92 g of Brazil nuts, it was estimated that at least 91% of the dose was absorbed (List et al., 1988; US EPA, 1999).

BARIUM IN DRINKING-WATER

Barium is rapidly transported in blood plasma, principally to bone (US NRC, 1977). Approximately 91% of the total body burden of barium is in the bone (IPCS, 1990). Elevated barium/calcium ratios were found in the teeth of children exposed to drinking-water containing 10 mg of barium per litre (Miller et al., 1985). It has been reported that barium crosses the placental barrier in humans (Schroeder et al., 1972).

The faecal route of excretion of barium is the most important in humans and animals (Ohanian & Lappenbusch, 1983); in humans, 20% of an ingested dose is excreted in the faeces and 7% in the urine within 24 h (US NRC, 1977; IPCS, 1990).

5. EFFECTS ON LABORATORY ANIMALS AND IN VITRO TEST SYSTEMS

5.1 Acute exposure

Acute oral LD₅₀ values in rats for barium chloride, barium carbonate and barium sulfide range from 118 to 800 mg/kg of body weight (NIOSH, 1989; IPCS, 1990; ATSDR, 1992).

5.2 Short-term exposure

No effects on blood pressure were seen in Sprague-Dawley rats exposed to 100 mg of barium per litre as barium chloride in drinking-water (equivalent to 1.5 mg/kg of body weight per day) for up to 20 weeks (McCauley et al., 1985). In the same series of studies, no changes were seen in blood pressure in hypertension-susceptible Dahl and uninephrectomized rats exposed for 16 weeks to up to 1000 mg of barium per litre in distilled water or 0.9% saline. At 1000 mg/litre, however, ultrastructural changes in the glomeruli of the kidney were discernible by electron microscopy. In addition, no significant electrocardiographic changes during (-)-norepinephrine challenge were observed in Sprague-Dawley rats ingesting drinking-water containing 250 mg of barium per litre for 5 months (McCauley et al., 1985).

Groups of 10 male and 10 female mice were administered barium chloride dihydrate in drinking-water for 13 weeks at concentrations of 0, 125, 500, 1000, 2000 or 4000 mg/litre for 13 weeks, corresponding to average daily doses of 0, 15, 55, 100, 205 and 450 mg of barium per kg of body weight in males and 0, 15, 60, 110, 200 and 495 mg of barium per kg of body weight in females. Complete histopathological examinations were performed on all mice in the control, 2000 mg/litre and 4000 mg/litre groups, and histopathological examinations of the kidneys were performed on the male mice in the 1000 mg/litre group. Cardiovascular studies and haematological and serum electrolyte analyses were not performed on the mice. A NOAEL of 2000 mg/litre was derived based on significant mortality at the 4000 mg/litre dose and on the incidence of chemical-related nephropathy. Although decreased absolute and relative liver weights were observed at the 1000, 2000 and 4000 mg/litre doses in females, no histopathological effects on the liver were observed at any dose level, and so the effect was deemed to be non-adverse (US NTP, 1994).

In an associated subchronic study, groups of 10 male and 10 female F344/N rats received drinking-water containing 0, 125, 500, 1000, 2000 or 4000 mg of barium chloride dihydrate per litre for 13 weeks, corresponding to 0, 10, 30, 65, 110 and 200 mg of barium per kg of body weight per day in males and 0, 10, 35, 65, 115 and 180 mg of barium per kg of body weight per day in females. Although water consumption and body weight were reduced in the top dose groups, there were no clearly chemical-related differences in any parameters except for renal tubular dilatation at the top dose and elevated serum phosphorus levels at 2000 and 4000 mg/litre. A NOAEL of 1000 mg/litre (equivalent to 65 mg of barium per kg of body weight per day) was identified in this study (US NTP, 1994).

5.3 Long-term exposure

In a study on the lifetime exposure of Long-Evans rats to 5 mg of barium per litre as barium acetate in drinking-water, the only significant effect reported was an increase in proteinuria in males (Schroeder & Mitchener, 1975a). In a similar study in which 5 mg of barium per litre as barium acetate was administered in drinking-water to Charles River CD mice over their entire life span, there was a slight reduction in the survival of males, but no effects on body weight gain, oedema or blanching of incisor teeth (Schroeder & Mitchener, 1975b). No histopathological effects were found in 34 tissues of male and female Sprague-Dawley rats exposed to 1, 10, 100 or 250 mg of barium per litre as barium chloride in drinking-water for up to 68 weeks (McCauley et al., 1985).

Groups of female Long-Evans rats were exposed to 1, 10 or 100 mg of barium per litre as barium chloride in drinking-water for 1, 4 or 16 months (Perry et al., 1983), equivalent to average doses of 0.051, 0.51 and 5.1 mg of barium per kg of body weight per day (US EPA, 1985b). Mean systolic pressure remained unchanged in animals exposed to the lowest dose for 16 months. At the intermediate dose, there were mean increases in blood pressure of 0.533–0.933 kPa (4–7 mmHg) by 8 months, which persisted thereafter. In rats receiving the highest dose, significant and persistent increases in mean systolic pressure of 1.60 kPa (12 mmHg) were seen after only 1 month, gradually increasing to a mean of 2.13 kPa (16 mmHg) after 16 months of exposure. Rates of cardiac contraction, electrical excitability and high-energy phosphate and phosphorylation potential were decreased. As increases in systolic pressure of 0.533–0.933 kPa (4–7 mmHg) are deemed small enough not to constitute an adverse effect, the NOAEL can be considered to be 0.51 mg of barium per kg of body weight per day, and the LOAEL is 5.1 mg of barium per kg of body weight per day.

A chronic study (US NTP, 1994) was carried out in which groups of 60 male and 60 female B6C3F1 mice received barium chloride dihydrate in drinking-water at concentrations of 0, 500, 1250 or 2500 mg/litre for 103 weeks (males) and 104 weeks (females). The average daily doses for the treated groups using measured water consumption and body weights corresponded to 30, 75 and 160 mg of barium per kg of body weight for males and 40, 90 and 200 mg of barium per kg of body weight for females.

BARIUM IN DRINKING-WATER

At the 15-month interim evaluation, venous blood was collected from all mice for haematology and clinical chemistry examination. In addition, a limited number of mice from each of the four dose groups were sacrificed at 15 months. The remaining animals continued on the study until they were moribund, died naturally or were sacrificed at the end of the study. Necropsy and complete histopathological examinations were performed on all animals. At the 15-month interim evaluation, the absolute and relative spleen weights of the female mice that received 2500 mg/litre were significantly lower than those of the controls, and the absolute and relative thymus weights of the male mice that received 2500 mg/litre were marginally lower than those of the controls. Determination of haematology and clinical chemistry parameters (e.g., phosphorus, calcium and urea nitrogen) at the 15-month interim evaluation showed no significant differences between control and exposed mice. At 2500 mg/litre, survival rates for mice at the end of the study (65% for males and 26% for females) were significantly lower than those of the controls (89% for males and 76% for females). Survival was not significantly lower relative to controls at the lower dose levels. In high-dose male and female mice, the final mean body weights were 8% and 12% lower, respectively, than those of the corresponding control groups. Water consumption was not affected by the treatment.

The incidence of nephropathy at the end of the study was significantly increased in mice receiving 2500 mg/litre. The nephropathy at the highest dose was chemical related and morphologically distinct from the spontaneous degenerative lesions commonly observed in aging B6C3F1 mice. Lymphoid depletions in the spleen, thymus and lymph nodes were observed in high-dose male and female mice, particularly in animals that died early, and were thought to be the result of debilitation associated with nephropathy. There were no other chemical-related histological changes. Thus, it was considered that 1250 mg/litre (75 mg of barium per kg of body weight per day in males and 90 mg of barium per kg of body weight per day in females) was the NOAEL in this study.

The incidences of neoplasms in the barium-exposed mice were not significantly higher than in control mice. In the 2500 mg/litre female mice, the incidences of several neoplasms were significantly lower than in the controls; the authors attributed this finding to the marked reduction in survival in the barium-exposed animals.

In the same chronic study (US NTP, 1994), groups of 60 male and 60 female F344/N rats received drinking-water containing 0, 500, 1250 or 2500 mg of barium chloride dihydrate per litre for 104 weeks (males) or 105 weeks (females). The authors estimated daily doses for the treated groups using measured water consumption and body weights as 15, 30 and 60 mg of barium per kg of body weight for males and 15, 45 and 75 mg of barium per kg of body weight for females. As in the study on mice, a 15-month interim evaluation was performed with venous blood being collected from all rats for haematology and clinical chemistry examination. In addition, a limited number of rats were sacrificed. The remaining animals stayed on the study until they were moribund, died naturally or were terminally sacrificed. Necropsy and complete histopathological examinations were performed on all animals. Body weights were

monitored throughout the study, and organ weights were determined in the animals killed at 15 months. Neurobehavioural and cardiovascular studies were not performed.

A marginally increased survival of males in the exposed groups (percent probability of survival: 62%, 58% and 67% for the 500, 1250 and 2500 mg/litre groups, respectively) compared with that of the male controls (44%) was attributed to a decreased incidence of leukaemia. Survival of the females was not significantly affected. For male rats receiving 2500 mg/litre, the final mean body weights were 5% lower than for controls. The final mean body weights of females receiving 1250 and 2500 mg/litre were 6% and 11% lower, respectively, than those of controls.

Water consumption was decreased in a dose-related manner; at the highest exposure level, the decrease, relative to controls, was 22% in males and 25% in females.

Absolute and relative organ weights, determined only at the 15-month interim evaluation, were not affected in the males. In the females, a statistically significant increase in relative kidney weights occurred at 2500 mg/litre. Determination of haematology and clinical chemistry values at the 15-month interim evaluation showed no significant differences between control and exposed rats. Chemical-related kidney lesions were not observed in rats in these 2-year studies; the only potential indication of renal toxicity was the increased relative kidney weight seen in the females at 2500 mg/litre. In addition, there were no chemical-related histological changes in any other organs or tissues.

The IPCS working group (IPCS, 2001) considered that the highest exposure level tested in this study, 2500 mg of barium per litre in drinking-water (60 mg of barium per kg of body weight per day for males and 75 mg of barium per kg of body weight per day for females), could be a chronic NOAEL or LOAEL for rats, depending on interpretation of the increased relative kidney weight in females.

However, when taking into account the results in the 13-week US NTP (1994) study in rats, in which increased relative and absolute kidney weights were seen in female rats receiving 2000 mg of barium per litre in drinking-water (115 mg of barium per kg of body weight per day) and kidney lesions and greater increases in relative and absolute kidney weights were seen in female rats at 4000 mg/litre (180 mg of barium per kg of body weight per day), the increased relative kidney weights in females of the 2-year study were considered to be suggestive of potential renal effects. Therefore, 75 mg of barium per kg of body weight per day was designated a chronic LOAEL and 45 mg of barium per kg of body weight per day a chronic NOAEL for female rats for renal effects in the US NTP (1994) study (IPCS, 2001).

5.4 Reproductive and developmental toxicity

There are only limited data on the reproductive and developmental toxicity of barium compounds; however, in a one-generation reproductive study in mice and rats, there was no indication of reproductive or developmental toxicity at dose levels up to 200 mg/kg of body weight per day (Dietz et al., 1992).

BARIUM IN DRINKING-WATER

The inhalation of barium carbonate dust adversely affected spermatogenesis in male rats exposed to 22.6 mg/m³ and shortened the estrous cycle and disturbed the morphological structure of the ovaries in female rats exposed to 13.4 or 3.1 mg/m³ for 4 months (Tarasenko et al., 1977). There appear to be no suitable studies with which to make a meaningful assessment of developmental toxicity.

5.5 Mutagenicity and related end-points

The information available on the genotoxicity of barium compounds is relatively limited, with no *in vivo* studies available. The data available have been reviewed by IPCS (2001). The majority of the *in vitro* studies conducted indicate that barium chloride and barium nitrate do not induce gene mutations in bacterial assays, with or without metabolic activation (IPCS, 2001). In particular, barium has consistently given negative results in several Ames *Salmonella* strains, and it did not induce chromosome aberrations or sister chromatid exchanges in Chinese hamster ovary cells *in vitro*. Barium chloride did not increase the frequency of mutation in repair-deficient strains of *Bacillus subtilis* (Nishioka, 1975) or induce errors in viral DNA transcription *in vitro* (Loeb et al., 1978). Barium chloride did induce gene mutations in L5178Y mouse lymphoma cells with, but not without, metabolic activation (US NTP, 1994). The weight of evidence supports the conclusion that barium does not possess any significant genotoxic potential.

5.6 Carcinogenicity

In extremely limited lifetime bioassays of rats and mice exposed to 5 mg/litre of barium (as barium acetate) in drinking-water, no evidence was found on gross examination at autopsy to show that barium is carcinogenic (Schroeder & Mitchener, 1975a,b). In well conducted studies on both mice and rats, described above, there was no indication of an increase in neoplasms (US NTP, 1994).

6. EFFECTS ON HUMANS

Barium is not considered to be an essential element for human nutrition (Schroeder et al., 1972).

At high concentrations, barium causes vasoconstriction by its direct stimulation of arterial muscle, peristalsis as a result of the violent stimulation of smooth muscles and convulsions and paralysis following stimulation of the central nervous system (Stockinger, 1981). Depending on the dose and solubility of the barium salt, death may occur in a few hours or a few days. The acute toxic oral dose is between 3 and 4 g (Reeves, 1986). Repeated exposures to barium chloride in table salt are believed to have caused recurrent outbreaks of “pa-ping” disease (a transient paralysis resembling familial periodic paralysis) in China (Shankle & Keane, 1988), but recovery was usually rapid (IPCS, 1990).

BARIUM IN DRINKING-WATER

The prevalence of dental caries was reported to be significantly lower in 39 children from a community ingesting drinking-water containing 8–10 mg of barium per litre than in 36 children from another community ingesting drinking-water containing <0.03 mg/litre (Zdanowicz et al., 1987). However, the study population was small, and dental examinations were not conducted in a blind manner.

The impact of high doses of barium on blood pressure has resulted in interest in the possibility of low concentrations also having an adverse effect over time.

Associations between the barium content of drinking-water and mortality from cardiovascular disease have been observed in several ecological epidemiological studies. Significant negative correlations between barium concentrations in drinking-water and mortality from atherosclerotic heart disease (Schroeder & Kramer, 1974) and total cardiovascular disease (Elwood et al., 1974) have been reported. Conversely, significantly higher sex- and age-adjusted death rates for “all cardiovascular diseases” and “heart disease” have been reported in an unspecified number of Illinois communities with high concentrations of barium in drinking-water (2–10 mg/litre) compared with those with low concentrations (<0.2 mg/litre) in 1971–1975 (Brenniman et al., 1979). There were, however, several confounding factors; although the communities were matched for demographic characteristics and socioeconomic status, population mobility differed between the communities with high and low barium levels. Moreover, it was not possible to control for the use of water softeners in the home (US NRC, 1982).

A retrospective morbidity study was reported by Brenniman & Levy (1985) on two Illinois communities, McHenry and West Dundee, which had similar demographic and socioeconomic characteristics, but a 70-fold difference in barium concentrations in drinking-water. The mean barium concentration in McHenry’s drinking-water was 0.1 mg/litre, whereas the mean concentration in West Dundee’s drinking-water was 7.3 mg/litre. The levels of other minerals in the drinking-water of the two communities were stated to be similar. Subjects were selected randomly from a pool that included every person 18 years of age or older in a random sample of blocks within each community. Blood pressures of all participants were measured, and data on the occurrence of cardiovascular, cerebrovascular and renal disease and possible confounding factors were obtained by means of questionnaires administered by trained survey workers. No significant differences in mean systolic or diastolic blood pressures or in history of hypertension, heart disease, stroke or kidney disease were found for men or women of the two communities.

A more controlled study (Brenniman & Levy, 1985) was conducted on a subpopulation of the McHenry and West Dundee subjects who did not have home water softeners, were not taking medication for hypertension and had lived in the study community for more than 10 years. No significant differences were observed between the mean systolic or diastolic blood pressures for men or women of these subpopulations in the low-barium (0.1 mg/litre, 0.0029 mg of barium per kg of body weight per day, assuming water ingestion of 2 litres/day and 70-kg body weights) and elevated-barium (7.3 mg/litre, 0.21 mg of barium per kg of body weight per day)

BARIUM IN DRINKING-WATER

communities. The authors concluded that blood pressure in adults does not appear to be adversely affected, even following prolonged ingestion of drinking-water containing more than 7 mg of barium per litre.

In a clinical study, 11 “healthy” men were administered 1.5 litres of distilled drinking-water containing various levels of barium chloride per day. Barium concentrations in drinking-water that the subjects had been drinking prior to the study were known to be very low. The first 2 weeks of the trial served as a control period, and no barium was added to the water. For the ensuing 4 weeks, 5 mg of barium per litre (equivalent to 0.11 mg of barium per kg of body weight per day using a reference body weight of 70 kg) were added, and 10 mg of barium per litre (0.21 mg of barium per kg of body weight per day) were added for the final 4 weeks of the study (Wones et al., 1990). Attempts were made to control several of the risk factors for cardiovascular disease, including diet, exercise, smoking and alcohol consumption, throughout the study period (although subjects were not continuously monitored in this regard). No consistent indication of any adverse effects was found. There was, however, a trend towards an increase in serum calcium between 0 and 5 mg/litre, which persisted at 10 mg/litre; for total calcium, normalized for differences in albumin level, this increase was statistically significant, but this was not considered to be clinically significant (IPCS, 2001). The lack of adverse effects observed in this study may be attributable to the small number of subjects included or the short period of exposure. This study identified a NOAEL of 0.21 mg of barium per kg of body weight per day; in common with other studies in humans, the study did not identify a level at which any adverse effects were observed.

There appear to be no studies of nephropathy in humans.

7. GUIDELINE VALUE

As there is no evidence that barium is carcinogenic (IPCS, 1990), the guideline value for barium in drinking-water is derived using the TDI approach. Barium has been shown to cause nephropathy in laboratory animals, but the toxicological end-point of greatest concern to humans at the relatively low concentrations encountered in the environment appears to be the potential effect on blood pressure.

In the most sensitive epidemiological study conducted to date, there were no significant differences in blood pressure or in the prevalence of cardiovascular disease between a population drinking water containing a mean barium concentration of 7.3 mg/litre and one whose water contained a concentration of 0.1 mg/litre (Brenniman & Levy, 1985). Using the NOAEL of 7.3 mg/litre obtained from this study and an uncertainty factor of 10 to account for intraspecies variation, a guideline value of 0.7 mg/litre (rounded figure) was derived for barium in drinking-water.

Analytical methods for barium are adequate for measuring concentrations well below the guideline value. Barium is a naturally occurring constituent of drinking-water and can be controlled only by source selection or drinking-water treatment. Precipitation softening and ion exchange softening are the only treatment processes capable of

removing a substantial proportion (>90%) of barium from drinking-water (Willey, 1987).

8. REFERENCES

ATSDR (1992) *Toxicological profile for barium*. Atlanta, GA, US Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry.

Brenniman GR, Levy PS (1985) Epidemiological study of barium in Illinois drinking water supplies. In: Calabrese EJ, Tuthill RW, Condie L, eds. *Inorganics in water and cardiovascular disease*. Princeton, NJ, Princeton Scientific Publishing Co., pp. 231–240 (Advances in Modern Environmental Toxicology, Vol. 9).

Brenniman GR et al. (1979) Cardiovascular disease death rates in communities with elevated levels of barium in drinking water. *Environmental Research*, 20:318–324.

Brooks SM (1986) Pulmonary reactions to miscellaneous mineral dusts, man-made mineral fibers, and miscellaneous pneumoconioses. In: Merchant JA, ed. *Occupational respiratory diseases*. Cincinnati, OH, US Department of Health and Human Services, Appalachian Laboratory for Occupational Safety and Health, pp. 401–458 (DHHS (NIOSH) Publication No. 86-102).

Clavel JP et al. (1987) Intestinal absorption of barium during radiological studies. *Therapie*, 42(2):239–243.

Cotton FA, Wilkinson G (1980) *Advanced inorganic chemistry: comprehensive text*, 4th ed. New York, NY, John Wiley, p. 286.

Dietz DD et al. (1992) Subchronic toxicity of barium chloride dihydrate administered to rats and mice in the drinking water. *Fundamental and Applied Toxicology*, 19:527–537.

Elwood PC, Abernethy M, Morton M (1974) Mortality in adults and trace elements in water. *Lancet*, 2:1470–1472.

Flaten TP (1991) A nationwide survey of the chemical composition of drinking water in Norway. *The Science of the Total Environment*, 102:35–74.

Fonds AW, Van Den Eshof AJ, Smit E (1987) *Integrated criteria document barium*. Bilthoven, National Institute of Public Health and Environmental Protection (RIVM Report No. 218108004).

Gormican A (1970) Inorganic elements in foods used in hospital menus. *Journal of the American Dietetic Association*, 56:397–403.

Hem JD (1959) *Study and interpretation of the chemical characteristics of natural water. US Geologic Survey sampling data*. Washington, DC, US Government Printing Office (Water Supply Paper 1473).

ICRP (1975) *Report of the Task Group on Reference Man*. New York, NY, Pergamon Press (International Commission on Radiological Protection Publication 23).

IPCS (1990) *Barium*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 107).

IPCS (2001) *Barium and barium compounds*. Geneva, World Health Organization, International Programme on Chemical Safety (Concise International Chemical Assessment Document 33).

Lanciotti E et al. (1992) A survey on barium contamination in municipal drinking water of Tuscany. *Igiene Moderna*, 98(6):793–800.

BARIUM IN DRINKING-WATER

Lide DR, ed. (1992–1993) *CRC handbook of chemistry and physics*, 73rd ed. Boca Raton, FL, CRC Press.

Lisk DJ et al. (1988) Absorption and excretion of selenium and barium in humans from consumption of Brazil nuts. *Nutrition Reports International*, 38:183–191.

Loeb L, Sirover M, Agarwal S (1978) Infidelity of DNA synthesis as related to mutagenesis and carcinogenesis. In: *Advances in Experimental Medicine and Biology*, 91:103 [cited in US EPA, 1984].

McCaughey PT, Washington IS (1983) Barium bioavailability as the chloride, sulfate, or carbonate salt in the rat. *Drug and Chemical Toxicology*, 6:209–217.

McCaughey PT et al. (1985) Investigations into the effect of drinking water barium on rats. In: Calabrese EJ, Tuthill RW, Condie L, eds. *Inorganics in drinking water and cardiovascular disease*. Princeton, NJ, Princeton Scientific Publishing Co., pp. 197–210 (Advances in Modern Environmental Toxicology, Vol. 9).

Mertz W, ed. (1986) *Trace elements in human and animal nutrition*, 5th ed. New York, NY, Academic Press, pp. 418–420.

Miller RG et al. (1985) Barium in teeth as indicator of body burden. In: Calabrese EJ, Tuthill RW, Condie L, eds. *Inorganics in drinking water and cardiovascular disease*. Princeton, NJ, Princeton Scientific Publishing Co., pp. 211–219 (Advances in Modern Environmental Toxicology, Vol. 9).

Miner S (1969) *Preliminary air pollution survey of barium and its compounds. A literature review*. Raleigh, NC, US Department of Health, Education, and Welfare, National Air Pollution Control Administration.

NIOSH (1989) *Registry of Toxic Effects of Chemical Substances (RTECS) database*. Washington, DC, US Department of Health and Human Services, National Institute of Occupational Safety and Health.

Nishioka H (1975) Mutagenic activities of metal compounds in bacteria. *Mutation Research*, 31:186–189.

Ohanian EV, Lappenbusch WL (1983) *Problems associated with toxicological evaluations of barium and chromium in drinking water*. Washington, DC, US Environmental Protection Agency, Office of Drinking Water.

OME (1988) *The determination of trace metals in surface metals by ICP-AAS*. Toronto, Ontario, Ontario Ministry of the Environment, Laboratory Services Branch.

Perry HM et al. (1983) Cardiovascular effects of chronic barium ingestion. *Trace Substances and Environmental Health*, 16:155–164.

Reeves AL (1986) Barium. In: Friberg L, Nordberg GF, Vouk VB, eds. *Handbook on the toxicology of metals*, 2nd ed. Amsterdam, Elsevier/North Holland Biomedical Press, pp. 84–94.

Schroeder HA, Kramer LA (1974) Cardiovascular mortality, municipal water, and corrosion. *Archives of Environmental Health*, 28:303–311.

Schroeder HA, Mitchener M (1975a) Life-term studies in rats: effects of aluminum, barium, beryllium and tungsten. *Journal of Nutrition*, 105:421–427.

Schroeder HA, Mitchener M (1975b) Life-term effects of mercury, methyl mercury and nine other trace elements on mice. *Journal of Nutrition*, 105:452–458.

- Schroeder HA, Tipton IH, Nason P (1972) Trace metals in man: strontium and barium. *Journal of Chronic Diseases*, 25:491–517.
- Shankle R, Keane JR (1988) Acute paralysis from barium carbonate. *Archives of Neurology*, 45(5):579–580.
- Stockinger HE (1981) The metals. In: Clayton GD, Clayton FE, eds. *Patty's industrial hygiene and toxicology*, 3rd ed. Vol. 2A. New York, NY, John Wiley, pp. 1493–2060.
- Subramanian KS, Meranger JC (1984) A survey for sodium, potassium, barium, arsenic, and selenium in Canadian drinking water supplies. *Atomic Spectroscopy*, 5:34–37.
- Tarasenko NY, Pronin OA, Silayev AA (1977) Barium compounds as industrial poisons (an experimental study). *Journal of Hygiene, Epidemiology, Microbiology, and Immunology*, 21:361–373.
- Taylor DM, Bligh PH, Duggan MH (1962) The absorption of calcium, strontium, barium and radium from the gastrointestinal tract of the rat. *Biochemical Journal*, 83:25–29.
- US EPA (1984) *Health effects assessment for barium*. Washington, DC, US Environmental Protection Agency.
- US EPA (1985a) *Health advisory — barium*. Washington, DC, US Environmental Protection Agency, Office of Drinking Water.
- US EPA (1985b) *Drinking water criteria document for barium*. Washington, DC, US Environmental Protection Agency, Office of Drinking Water.
- US EPA (1999) *Toxicological review of barium and compounds. In support of summary information on the Integrated Risk Information System (IRIS)*. Washington, DC, US Environmental Protection Agency.
- US NRC (1977) *Drinking water and health*. Vol. 1. Washington, DC, US National Research Council, National Academy of Sciences.
- US NRC (1982) *Drinking water and health*. Vol. 4. Washington, DC, US National Research Council, National Academy Press, pp. 167–170.
- US NTP (1994) *NTP technical report on the toxicology and carcinogenesis studies of barium chloride dihydrate (CAS No. 10326-27-9) in F344/N rats and B6C3F1 mice (drinking water studies)*. Research Triangle Park, NC, US Department of Health and Human Services, Public Health Service, National Toxicology Program (NTP TR 432; NIH Publication No. 94-3163; NTIS PB94-214178).
- Van Duijvenbooden W (1989) *The quality of ground water in the Netherlands*. Bilthoven, National Institute of Public Health and Environmental Protection (RIVM Report No. 728820001).
- Willey BR (1987) Finding treatment options for inorganics. *Water/Engineering and Management*, 134(10):28–31.
- Wones RG, Stadler BL, Frohman LA (1990) Lack of effect of drinking water barium on cardiovascular risk factors. *Environmental Health Perspectives*, 85:355–359.
- Zdanowicz JA et al. (1987) Inhibitory effect of barium on human caries prevalence. *Community Dentistry and Oral Epidemiology*, 15:6–9.