WHO/FWC/WSH/16.48

# Barium in Drinking-water

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

This document replaces document reference number WHO/SDE/WSH/03.04/76

## Preface

Access to safe drinking-water is essential to health, a basic human right and a component of effective policy for health protection. A major World Health Organization (WHO) function to support access to safe drinking-water is the responsibility "to propose ... regulations, and to make recommendations with respect to international health matters ...", including those related to drinking-water safety and management.

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 was published in 2011, and the first addendum to the fourth edition was published in 2017.

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 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 background document evaluating the risks for human health from exposure to the particular chemical in drinking-water was prepared. The draft health criteria document was submitted to a number of scientific institutions and selected experts for peer review. The draft document was also released to the public domain for comment. Comments were carefully considered and addressed as appropriate, taking into consideration the processes outlined in the *Policies and Procedures Used in Updating the WHO Guidelines for Drinking-water Quality* (http://apps.who.int/iris/bitstream/10665/70050/1/WHO_HSE_WSH_09.05_eng.pdf) and the *WHO Handbook for Guideline Development* (http://www.who.int/publications/guidelines/handbook_2nd_ed.pdf), and the revised draft was submitted for final evaluation at expert consultations.

During the preparation of background documents and at expert consultations, 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 Food and Agriculture Organization of the United Nations (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 website and in the current edition of the GDWQ.

**Acknowledgements**

The first draft of *Barium in drinking-water, Background document for development of WHO Guidelines for Drinking-water Quality* was prepared by Dr Santhini Ramasamy, United States Environmental Protection Agency, to whom special thanks are due.

The work of the following experts was crucial in the development of this document and others in the first addendum to the fourth edition:

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The draft text was discussed at the expert consultations for the first addendum to the fourth edition of the GDWQ, held on 2–5 December 2013 and 23–26 February 2015. The final version of the document takes into consideration comments from both peer reviewers and the public.

The coordinator was Ms J. De France, WHO Headquarters, with support from Mr P. Callan, Australia. Strategic direction was provided by Mr B. Gordon, WHO Headquarters. Dr A. Tritscher and Dr P. Verger, WHO Headquarters, provided liaisons with the Joint FAO/WHO Expert Committee on Food Additives and the Joint FAO/WHO Meeting on Pesticide Residues, whereas Dr R. Brown and Ms C. Vickers, WHO Headquarters, provided liaisons with the International Programme on Chemical Safety. Dr M. Perez contributed on behalf of the Radiation Programme, WHO Headquarters. Dr R. Yadav, WHO Headquarters, provided input on pesticides added to drinking-water for public health purposes.

Ms P. Ward and Ms L. Robinson provided invaluable administrative support at the expert consultations and throughout the review and publication process. Ms M. Sheffer of Canada and Dr H. Cadman of Australia were 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.

## Abbreviations

| | |
|---|---|
| $BMDL_{05}$ | lower 95% confidence limit on the benchmark dose for a 5% response |
| bw | body weight |
| FAO | Food and Agriculture Organization of the United Nations |
| $LD_{50}$ | median lethal dose |
| LOAEL | lowest-observed-adverse-effect level |
| mmHg | millimetres of mercury |
| NOAEL | no-observed-adverse-effect level |
| NTP | National Toxicology Program (USA) |
| TDI | tolerable daily intake |
| USA | United States of America |
| USEPA | United States Environmental Protection Agency |
| USGS | United States Geological Survey |
| WHO | World Health Organization |

**Contents**

## *1. GENERAL DESCRIPTION*

### *1.1 Identity*

Barium is a soft alkaline earth metal belonging to Group IIA of the periodic table. Its silver-white colour changes to silver-yellow when it is exposed to air. It does not exist in nature in the elemental form but occurs as compounds with other elements (see Table 1). The principal forms found in ore deposits are barite (barium sulfate) and witherite (barium carbonate). Barium compounds are also present in igneous and sedimentary rocks. Barium makes up 0.05% of Earth's crust (USEPA, 2005; ATSDR, 2007).

**Table 1. Identity of barium compounds**

| Compound | Chemical Abstracts Service No. | Molecular formula |
|---|---|---|
| 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 sulfate | 7727-43-7 | $BaSO_4$ |
| Barium acetate | 543-80-6 | $Ba(C_2H_3O_2)_2$ |
| Barium carbonate | 513-77-9 | $BaCO_3$ |

### *1.2 Physicochemical properties*

Physicochemical properties of select barium compounds are provided in Table 2.

**Table 2. Physicochemical properties of barium compounds**

| Compound | Melting point (°C) | Boiling point (°C) | Density ($g/cm^3$) | Water solubility (g/L) |
|---|---|---|---|---|
| BaS | 2 229 | No data | 4.3 | 89.4 at 25 °C |
| $BaCl_2$ | 962 | 1 560 | 3.9 | 370 at 25 °C |
| BaO | 1 972 | No data | 5.72 | 15 at 20 °C |
| $Ba(OH)_2$ | 408 | No data | 3.7 | 49.1 at 25 °C |
| $BaSO_4$ | 1 580 | No data | 4.5 | 0.003 at 20 °C |
| $Ba(C_2H_3O_2)_2$ | Decomposes at 110 | No data | 2.47 | 792 at 25 °C |
| $BaCO_3$ | 1 555 | No data | 4.3 | 0.001 4 at 20 °C |

Source: ATSDR (2007)

### *1.3 Organoleptic properties*

Data on the organoleptic properties of barium compounds are limited. However, available evidence indicates that barium carbonate and barium chloride are odourless compounds (ATSDR, 2007).

### *1.4 Major uses and sources in drinking-water*

Barium compounds (mainly as barium sulfate and barium carbonate) are present in nature as ore deposits. Leaching and erosion of natural deposits can contaminate groundwater sources. Barium sulfate ore is mined and used in several industries. It is used mostly by the oil and gas industry to make drilling muds, which make it easier to drill through rock by keeping the drill

bit lubricated. Barium sulfate is also used to make paints, bricks, tiles, glass, rubber and other barium compounds. Some barium compounds, such as barium carbonate, barium chloride and barium hydroxide, are used to make ceramics, insect and rat poisons, and additives for oils and fuels; in the treatment of boiler water; in the production of barium greases; as a component in sealants, paper manufacturing and sugar refining; in animal and vegetable oil refining; and to protect objects made of limestone from deterioration. Barium sulfate is sometimes used by doctors to perform medical tests and take X-ray photographs of the stomach and intestines (Miner, 1969; Brooks, 1986; USEPA, 2005).

### *1.5 Environmental fate*

Barium in water comes primarily from natural sources, although barium also enters the environment from industrial emissions and anthropogenic uses. Soluble barium compounds, such as barium nitrate and barium chloride, are expected to be mobile in the environment, depending upon soil characteristics. Volatilization from water surfaces and from moist and dry soil surfaces is not expected to be an important fate process. If released to water, barium may adsorb to suspended solids and sediment. The solubility of barium compounds increases with decreasing pH. In waters with a high sulfate or carbonate content, soluble barium can react with sulfates and carbonates in water, forming insoluble barium sulfate and barium carbonate salts. Hydrolysis is not expected to be an important environmental fate process, as barium compounds do not hydrolyse appreciably, except in highly alkaline environments (pH ≥10) (HSDB, 2014).

## *2. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE*

### *2.1 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. Also, fugitive dust emissions during the processing of barium ores contribute to barium's presence in the air. The concentration of barium in ambient air in the United States of America (USA) is estimated to be less than 0.05 µg/m$^3$ (IPCS, 1990). Similar air concentrations have been reported in Norway and the United Kingdom (ATSDR, 2007). If it is assumed that adults inhale daily 22 m$^3$ of air (IPCS, 1994) containing barium at 0.05 µg/m$^3$, intake of barium by adults would be approximately 1 µg/day.

### *2.2 Water*

The concentration of barium in groundwater in the Netherlands was measured at 60 locations, with mean and maximum concentrations of 0.23 and 2.5 mg/L, respectively (Van Duijvenbooden, 1989). In 83% of 262 locations surveyed in the Netherlands in 1983, barium concentrations in drinking-water were below 50 µg/L; the maximum concentration found was close to 200 µg/L (Fonds, Van Den Eshof & Smit, 1987). Barium concentrations in drinking-water in distribution systems in Canada were found to range from the limit of detection (5 µg/L) to 600 µg/L, with a median value of 18 µg/L; in 86% of the 122 locations surveyed, the concentrations were below 100 µg/L (Subramanian & Meranger, 1984). Levels of barium in municipal water supplies in Sweden ranged from 1 to 20 µg/L (HSDB, 2014). The median barium concentration in drinking-water in Norway was reported to be 9 µg/L (Flaten, 1991).

Barium was detected at concentrations of 13–140 µg/L in 39 treated drinking-water supplies and at concentrations of 7–660 µg/L in 60 different brands of bottled water in Italy (ATSDR, 2007). In the Tuscany region of Italy, concentrations of barium in municipal drinking-water derived from groundwater were reported to be between 700 and 1160 µg/L (Lanciotti et al., 1992). The detection limit for barium in water samples appears to range from 0.2 to 132 µg/L (ATSDR, 2007). The mean or median concentrations reported for various countries vary depending on how the samples with barium concentrations below the detection limit have been dealt with.

Barium has been detected in almost all drinking-water supplies sampled (approximately 99%) in the USA; concentrations ranged from <5 to 15 000 µg/L, with mean concentrations of 10–60 µg/L. In a study of water supplies of cities in the USA, a median concentration of 43 µg/L was reported; in 94% of all determinations, the concentrations found were below 100 µg/L (IPCS, 1990). In a report by the United States Geological Survey, barium was found in 625 of 630 samples collected from public supply wells; the median and 90th percentile concentrations were 46.7 µg/L and 164.1 µg/L, respectively, and the maximum concentration was 11 mg/L (USGS, 2010). Barium was detected at concentrations of 17–180 µg/L in residential drinking-water wells near the Gallaway Ponds Superfund Site in Gallaway, Tennessee, USA. Barium was detected in groundwater at various locations in Denver, Colorado, USA, at concentrations of 18–594 µg/L. The Illinois Environmental Protection Agency identified 16 cities and three subdivisions in northern Illinois, USA, that have drinking-water sources containing barium at 1.1–10.0 mg/L; these affected water supplies are from deep rock and drift wells (ATSDR, 2007).

If it is assumed that the average adult consumes daily 2 L of drinking-water containing an average barium concentration of 30 µg/L (taken from data from the USA), the intake of barium from drinking-water would be 60 µg/day (ATSDR, 2007).

### *2.3 Food*

Most foods contain barium at concentrations less than 0.002 mg/g (Gormican, 1970). Some cereal products and nuts may contain higher levels – for example, bran flakes, 0.0039 mg/g; pecans, 0.0067 mg/g; and Brazil nuts, up to 4 mg/g (Mertz, 1986). In a French Total Diet Study, the highest mean levels of barium were found in breakfast cereals (2.85 mg/kg), followed by chocolate (2.00 mg/kg), dried fruits, nuts and seeds (1.73 mg/kg) and pulses (1.20 mg/kg). All the other food groups had concentrations lower than 1 mg/kg (ANSES, 2011).

The barium intake in adults from the consumption of non-drinking-water dietary sources has been reported to range from 0.59 to 1.71 mg/day (ATSDR, 2007). The long-term mean dietary barium intake for adults has been estimated in several studies: 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, Tipton & Nason, 1972). In the Canadian Total Diet Study of 1993–1999, the average barium intake in young children aged 0–4 years ranged from 20 to 25 µg/kg body weight (bw) per day; in adults, the intake was close to 10 µg/kg bw per day (ATSDR, 2007). In a recent study in the Canary Islands, Spain, barium intake was reported as 0.685 mg/day, with cereals contributing the most to the dietary intake, compared with other food groups (Gonzalez-Weller et al., 2013). In a French Total Diet Study, the mean exposure to barium was estimated at 6.4 µg/kg bw per

day in adults (range 5.86–6.99 µg/kg bw per day) and 10.2 µg/kg bw per day in children (range 9.18–11.3 µg/kg bw per day). At the 95th percentile, exposure was estimated to be 10.5 µg/kg bw per day in adults (range 9.32–12.0 µg/kg bw per day) and 18.9 µg/kg bw per day in children (range 16.8–21.5 µg/kg bw per day). The major contributors to barium exposure were breads and dried bread products, compared with other food groups (ANSES, 2011).

Based on the above evidence, food appears to be the primary source of barium exposure for the general population.

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

On the basis of barium intakes reported by ATSDR (2007), the combined mean daily intake of barium from food, water and air is estimated to range from about 0.7 to 1.9 mg/day, with food being the primary source of intake for the non-occupationally exposed population. However, where barium levels in water are high (in the milligram per litre range), drinking-water may contribute significantly to barium intake.

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

Soluble barium salts are more readily absorbed than insoluble compounds, 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, Bligh & Duggan, 1962; McCauley & Washington, 1983; Clavel et al., 1987). Reported absorption of barium in experimental animal studies ranges from 1% to >80%, depending on the species tested and age of the animals (USEPA, 2005). 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. Barium is rapidly transported in blood plasma, principally to bone (USNRC, 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, Tipton & Nason, 1972). Barium is excreted in both urine and faeces, although the latter is the major route of excretion (Ohanian & Lappenbusch, 1983; USEPA, 2005).

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

### *4.1 Acute exposure*

Acute oral median lethal dose ($LD_{50}$) values in rats for barium chloride, barium carbonate and barium sulfide range from 118 to 800 mg/kg bw (NIOSH, 1989; IPCS, 1990).

### *4.2 Short-term exposure*

Groups of 10 male and 10 female B6C3F1 mice were administered barium chloride dihydrate in drinking-water for 13 weeks at a concentration of 0, 125, 500, 1000, 2000 or 4000 mg/L, corresponding to average barium doses of 0, 15, 55, 100, 205 and 450 mg/kg bw per day for

males and 0, 15, 60, 110, 200 and 495 mg/kg bw per day for females. Complete histopathological examinations were performed on all mice in the 0, 2000 and 4000 mg/L groups, and histopathological examinations of the kidneys were performed on the male mice in the 1000 mg/L group. Cardiovascular studies and haematological and serum electrolyte analyses were not performed on the mice. A no-observed-adverse-effect level (NOAEL) of 2000 mg/L was derived based on significant mortality and the incidence of chemical-related nephropathy at the lowest-observed-adverse-effect level (LOAEL) of 4000 mg/L. Although decreased absolute and relative liver weights were observed at the 1000, 2000 and 4000 mg/L doses in females, no histopathological effects on the liver were observed at the dose levels tested, and so the effect was deemed to be non-adverse (USNTP, 1994).

In an associated 13-week 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, corresponding to barium doses of 0, 10, 30, 65, 110 and 200 mg/kg bw per day for males and 0, 10, 35, 65, 115 and 180 mg/kg bw per day for females. Although water consumption and body weight were reduced in the top dose groups, there were no 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/L. A NOAEL of 1000 mg/L (equivalent to 65 mg/kg bw per day) and a LOAEL of 2000 mg/L (equivalent to 110 mg/kg bw per day) were identified in this study (USNTP, 1994).

No effects on blood pressure were seen in Sprague-Dawley rats exposed to 100 mg of barium per litre as barium chloride (equivalent to 1.5 mg/kg bw per day) in drinking-water 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/L, 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).

Ohgami et al. (2012) reported ototoxicity in ICR mice treated with two low dose levels of barium in drinking-water (0.7 and 7.0 mg/L, corresponding to 0.14 and 1.4 mg/kg bw per day) for 2 weeks. Severe hearing loss along with morphological changes of hair cells and spiral ganglion neurons and accumulation of barium in inner ears provided convincing evidence of barium-induced ototoxicity. However, interpretation of these findings for human health is limited by methodological issues; for example, the relevance of the strain tested for humans is not known, barium levels were measured in the inner ears long after the hearing levels were analysed and there were no changes in the barium levels in bones, as one would expect based on the available evidence (USNTP, 1994).

### *4.3 Long-term exposure*

A chronic study (USNTP, 1994) was carried out in which groups of 60 male and 60 female B6C3F1 mice received barium chloride dihydrate in drinking-water at a concentration of 0, 500, 1250 or 2500 mg/L for 103 weeks (males) or 104 weeks (females). The average barium doses for the treated groups using measured water consumption and body weights corresponded to 0, 30, 75 and 160 mg/kg bw per day for males and 0, 40, 90 and 200 mg/kg bw per day for females. 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 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/L were significantly lower than those of the controls, and the absolute and relative thymus weights of the male mice that received 2500 mg/L were marginally lower than those of the controls. Determination of haematological 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/L, 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/L (19/60 males; 37/60 females). The nephropathy at the highest dose was chemical related and morphologically distinct from the spontaneous degenerative lesions commonly observed in ageing B6C3F1 mice. Nephropathy was observed in 2/58 male mice and 1/60 female mice treated with 1250 mg/L. Two female mice in the 500 mg/L treatment group and one untreated male also exhibited signs of nephropathy. Based on the pathology data obtained for individual animals sacrificed or moribund at the interim evaluation and at the end of the study, the nephropathy found in animals from the intermediate dose group was qualified as mild and chemical related. 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. The incidences of neoplasms in the barium-exposed mice were not significantly higher than in control mice. In the 2500 mg/L 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.

USNTP (1994) considered 2500 mg/L (barium doses of 160 mg/kg bw per day for males and 200 mg/kg bw per day for females) to be the chronic LOAEL in this study, and the chronic NOAEL was identified as the next lower dose level, 1250 mg/L (barium doses of 75 mg/kg bw per day for males and 90 mg/kg bw per day for females). IPCS (2001) reported the same NOAEL and LOAEL. However, a low-level chemical-related nephropathy observed at the low dose levels might argue against these being the appropriate LOAEL and NOAEL (USEPA, 2005). The expert panel evaluating the barium database for the United States Environmental Protection Agency (USEPA) Toxicological Review identified the National Toxicology Program (NTP) chronic mouse study as the critical study for its reference dose derivation. The USEPA conducted benchmark dose modelling of the nephropathy findings in mice, and a lower 95% confidence limit on the benchmark dose for a 5% response ($BMDL_{05}$)

of 63 mg/kg bw per day for males was determined as the point of departure with which to derive the reference dose (USEPA, 2005).

In the same chronic study (USNTP, 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 barium doses for the treated groups using measured water consumption and body weights as 0, 15, 30 and 60 mg/kg bw per day for males and 0, 15, 45 and 75 mg/kg bw per day 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 study until they were moribund, died naturally or were 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 (per cent probability of survival: 62%, 58% and 67% for the 500, 1250 and 2500 mg/L 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. The final mean body weights for male rats in the 2500 mg/L group were 5% lower than in the control group. The final mean body weights of females receiving 1250 and 2500 mg/L were 6% and 11% lower, respectively, than that 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. Determination of haematology and clinical chemistry values at the 15-month interim evaluation showed no significant differences between control and exposed rats. 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/L. Although nephropathy was observed in the majority of the animals in all groups, these were not found to be chemical related; the only potential indication of renal toxicity was the increased relative kidney weight seen in the females at 2500 mg/L. In addition, there were no chemical-related histological changes in any other organs or tissues.

IPCS (2001) considered that the highest barium exposure level tested in this study, 2500 mg/L in drinking-water (barium doses of 60 mg/kg bw per day for males and 75 mg/kg bw 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 from the 13-week USNTP (1994) study in rats, in which increased relative and absolute kidney weights were seen in female rats receiving 2000 mg of barium per litre (115 mg/kg bw per day) in drinking-water and kidney lesions and greater increases in relative and absolute kidney weights were seen in female rats at 4000 mg/L (180 mg/kg bw per day), the increased relative kidney weights in females in the 2-year study were considered to be suggestive of potential renal effects. Therefore, the barium dose of 75 mg/kg bw per day was designated a chronic LOAEL and the dose of 45 mg/kg bw per day a chronic NOAEL for female rats for renal effects in the USNTP (1994) study (IPCS, 2001).

In a study on the lifetime exposure of Long-Evans rats to 5 mg of barium per litre as barium acetate in drinking-water (barium doses of 0.61 mg/kg bw per day for males and 0.67 mg/kg bw per day for females), 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 lifespan (barium doses of 1.18 mg/kg bw per day for males and 1.20 mg/kg bw per day for females), 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., 1989), equivalent to average barium doses of 0.06, 0.6 and 6.0 mg/kg bw per day (USEPA, 2005). 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 for barium can be considered to be 0.6 mg/kg bw per day, and the LOAEL is 6.0 mg/kg bw per day.

### *4.4 Reproductive and developmental toxicity*

There are only limited data on the reproductive and developmental toxicity of barium compounds. 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 bw per day (Dietz et al., 1992). There appear to be no suitable studies with which to make a meaningful assessment of developmental toxicity.

### *4.5 Immunological effects*

No pertinent studies relating barium exposure to immunological effects were identified.

### *4.6 Genotoxicity and related end-points*

Available information on the genotoxicity of barium compounds is relatively limited, with no in vivo studies. 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 *Salmonella* strains in the Ames test, 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). Barium chloride did induce gene mutations in L5178Y mouse lymphoma cells with, but not without, metabolic

activation (USNTP, 1994). The weight of evidence supports the conclusion that barium does not possess any significant genotoxic potential.

### *4.7 Carcinogenicity*

In well-conducted drinking-water studies on both mice and rats, described above (see Section 4.3), there was no indication of an increase in neoplasms (USNTP, 1994). In extremely limited lifetime bioassays of rats and mice exposed to 5 mg of barium (as barium acetate) per litre in drinking-water, no carcinogenic evidence was found on gross examination of tissues at necropsy (Schroeder & Mitchener, 1975a,b).

## *5. EFFECTS ON HUMANS*

Barium is not considered to be an essential element for human nutrition (Schroeder, Tipton & Nason, 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 contaminated 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). Many case reports indicate gastroenteritis, hypokalaemia, acute hypertension, cardiac arrhythmia, skeletal muscle paralysis and death following oral exposure to soluble barium salts (USEPA, 2005).

Associations between the barium content of drinking-water and mortality from cardiovascular disease have been evaluated 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, Abernethy & Morton, 1974) have been reported. Conversely, significantly higher sex- and age-adjusted death rates for "all cardiovascular diseases" and "heart disease" were reported in a number of communities in Illinois, USA, with high concentrations of barium in drinking-water (2–10 mg/L) compared with those with low concentrations (<0.2 mg/L) 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 in the drinking-water. Moreover, it was not possible to control for the use of water softeners in the home (USNRC, 1982). In addition, two of the four high-barium communities had about a 75% change in population between 1960 and 1970 but were retained in the study (USEPA, 2005).

A retrospective morbidity study was conducted by Brenniman & Levy (1985) on two communities in Illinois, USA: McHenry ($n$ = 1197) and West Dundee ($n$ = 1203), 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/L, whereas the mean concentration in West Dundee's drinking-water was 7.3 mg/L, measured over the period from 1971 to 1975. 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 aged 18 years or older in a random sample of blocks within each community. Blood pressures of all participants were measured (three measurements over a period of 20 minutes), 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.

In a clinical study, 11 "healthy" men were administered 1.5 L 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, barium was added at a concentration of 5 mg/L (equivalent to 0.11 mg/kg bw per day, using a reference body weight of 70 kg and drinking-water consumption of 1.5 L/day, as estimated by the USEPA), and for the final 4 weeks of the study, barium was added at a concentration of 10 mg/L (equivalent to 0.21 mg/kg bw per day). 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/L, which persisted at 10 mg/L; for total calcium, normalized for differences in albumin level, this increase was statistically significant, but was not considered to be clinically significant. 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 for barium of 0.21 mg/kg bw per day; in common with other studies in humans, the study did not identify a level at which any adverse effects were observed (Wones, Stadler & Frohman, 1990).

No studies linking barium exposure to nephropathy in humans were identified.

## *6. MODE OF ACTION FOR CRITICAL EFFECT*

The mechanism by which barium mediates its toxicity has not been fully elucidated. High-dose acute exposure to barium consistently results in a number of effects, including ventricular tachycardia, hypertension and/or hypotension, and muscle weakness and paralysis. There is strong evidence that many of these effects result from increases in intracellular potassium levels. Barium is reported to be a competitive potassium channel antagonist that blocks the passive efflux of intracellular potassium, resulting in a shift of potassium from extracellular to intracellular compartments (ATSDR, 2007). It is unclear whether hypokalaemia plays any role in the barium-mediated nephropathy observed in mice chronically exposed to barium in drinking-water. There is no evidence of nephropathy reported in the literature for humans.

## *7. PRACTICAL CONSIDERATIONS*

### *7.1 Analytical methods and achievability*

The USEPA has two approved methods for measuring barium in drinking-water that are publicly available: Method 200.7, which uses inductively coupled plasma–atomic emission spectroscopy; and Method 200.8, which uses inductively coupled plasma–mass spectrometry. The detection limits are 1.0 µg/L for Method 200.7 and 0.004–0.8 µg/L for Method 200.8 (USEPA, 2009).

### *7.2 Treatment methods and performance*

Krause & Stover (1982) reported that ion exchange, lime softening or direct filtration (with chemical precipitation) reduced the barium levels in water to below 1 mg/L. The average barium concentration in raw water in this study was 5.32 mg/L (range 0.4–8.5 mg/L). Ion exchange, reverse osmosis, lime softening and electrodialysis have proven to be effective for removing barium to below 2 mg/L in water (USEPA, 2014). Point of use reverse osmosis and point of entry cation exchange technologies are available to remove barium (and other contaminants) for home use (USEPA, 2006a,b), but these methods can be costly and are not readily available in many locations.

### *7.3 Prevention and control*

Barium is a naturally occurring constituent of the diet and drinking-water. Because of its diverse food sources, there is always a baseline level of exposure that cannot be avoided. Groundwaters in certain geological regions are more likely to contain barium, some with barium concentrations approaching 10 mg/L. Some of these groundwaters may be hard waters from the concurrent presence of calcium and/or magnesium due to the similar chemistry of the alkaline earth elements. The presence of calcium or magnesium might have a suppressive effect on barium uptake from water.

## *8. 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 tolerable daily intake (TDI) approach. For the previous guideline value derivation, the epidemiological study by Brenniman & Levy (1985) was selected as the critical study; however, this study has been identified as having several limitations (e.g. no effect observed at the single dose evaluated, limitations in the exposure methodology and design, no control for important risk factors for hypertension). For the current evaluation, the NTP chronic study in mice (USNTP, 1994) was selected as the best available study in the absence of appropriate studies evaluating chronic exposure of humans to barium. The kidney appears to be the target tissue for barium-mediated toxicity, and mice were found to be more sensitive for the nephrotoxic effects. Although nephropathy was observed in treated rats, it was also observed in control animals and was found not to be chemical related. In rats, the only indication of potential adverse renal effects was significantly increased relative kidney weights in high-dose females. The NTP study was considered more appropriate than the Perry et al. (1989) study because of the study quality (both sexes studied, more study parameters evaluated, longer duration of exposure) and because the changes in systolic blood pressure in the Perry et al. (1989) study were considered small.

The chronic study conducted by the NTP (USNTP, 1994) observed nephropathy in mice exposed to barium in drinking-water for 2 years. Benchmark modelling of the data on kidney lesions identified the point of departure ($BMDL_{05}$) as 63 mg/kg bw per day (USEPA, 2005). Using this point of departure, a TDI of 0.21 mg/kg bw per day was derived by applying an uncertainty factor of 300 to account for intraspecies variation (10×), interspecies variation (10×) and database deficiencies (3×). The uncertainty factor for database deficiency of 3 was considered appropriate to account for the lack of a developmental toxicity study.

As noted in Section 2, food is considered the primary source of intake for the non-occupationally exposed population, although drinking-water may contribute significantly to barium intake where barium levels in water are high (in the milligram per litre range). Based on minimal exposure via drinking-water compared with food, the default allocation of 20% of the TDI to drinking-water is considered reasonable. With the use of a 20% allocation factor and assuming a body weight of 60 kg and drinking-water consumption of 2 L/day, a guideline value of 1.3 mg/L (rounded figure) can be derived for barium in drinking-water. Rounding the guideline value to one significant figure was not considered appropriate in this case, as it would have significant practical implications for many water supplies. The guideline value derived based on the long-term mouse study is not inconsistent with health-based values that could be derived from limited human studies (Brenniman & Levy, 1985; Wones, Stadler & Frohman, 1990).

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. Ion exchange, lime softening and direct filtration have been found to be effective in removing barium from drinking-water to levels below the guideline value.

## *9. REFERENCES*

ANSES (2011). Second French Total Diet Study (TDS 2) Report 1. Inorganic contaminants, minerals, persistent organic pollutants, mycotoxins, and phytoestrogens. Maisons-Alfort: French Agency for Food, Environmental and Occupational Health & Safety (https://www.anses.fr/en/system/files/PASER2006sa0361Ra1EN.pdf, accessed 24 March 2016).

ATSDR (2007). Toxicological profile for barium and barium compounds. Atlanta (GA): United States Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry (http://www.atsdr.cdc.gov/toxprofiles/tp24.pdf, accessed 24 March 2016).

Brenniman GR, Levy PS (1985). Epidemiological study of barium in Illinois drinking water supplies. In: Calabrese EJ, Tuthill RW, Condie L, editors. Inorganics in water and cardiovascular disease. Princeton (NJ): Princeton Scientific Publishing Co.; 231–40 (Advances in Modern Environmental Toxicology, Vol. 9).

Brenniman GR, Namekata T, Kojola WH, Carnow BW, Levy PS (1979). Cardiovascular disease death rates in communities with elevated levels of barium in drinking water. Environ Res. 20(2):318–24.

Brooks SM (1986). Pulmonary reactions to miscellaneous mineral dusts, man-made mineral fibers, and miscellaneous pneumoconioses. In: Merchant JA, editor. Occupational respiratory diseases. Cincinnati (OH): United States Department of Health and Human Services, Appalachian Laboratory for Occupational Safety and Health; 401–58 (DHHS (NIOSH) Publication No. 86–102).

Clavel JP, Lorillot ML, Buthiau D, Gerbet D, Heitz F, Galli A (1987). Intestinal absorption of barium during radiological studies. Therapie. 42(2):239–43.

Dietz DD, Elwell MR, Davis WE Jr, Meirhenry EF (1992). Subchronic toxicity of barium chloride dihydrate administered to rats and mice in the drinking water. Fundam Appl Toxicol. 19(4):527–37.

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

Flaten TP (1991). A nationwide survey of the chemical composition of drinking water in Norway. Sci Total Environ. 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).

Gonzalez-Weller D, Rubio C, Gutierrez AJ, Gonzalez GL, Mesa JMC, Girones CR et al. (2013). Dietary intake of barium, bismuth, chromium, lithium, and strontium in a Spanish population (Canary Islands, Spain). Chem Toxicol. 62:856–68.

Gormican A (1970). Inorganic elements in foods used in hospital menus. J Am Diet Assoc. 56:397–403.

HSDB (2014). Barium compounds. Bethesda (MD): United States National Library of Medicine, Hazardous Substances Data Bank (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB, accessed 29 July 2014).

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; http://www.inchem.org/documents/ehc/ehc/ehc107.htm, accessed 14 September 2014).

IPCS (1994). Assessing human health risks of chemicals: derivation of guidance values for health-based exposure limits. Geneva: World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 170; http://www.inchem.org/documents/ehc/ehc/ehc170.htm, accessed 3 October 2014).

IPCS (2001). Barium and barium compounds. Geneva: World Health Organization, International Programme on Chemical Safety (Concise International Chemical Assessment Document 33; http://www.who.int/ipcs/publications/cicad/en/cicad33.pdf?ua=1, accessed 14 September 2014).

Krause TL, Stover EL (1982). Evaluating water treatment techniques for barium removal. J Am Water Works Assoc. 74(9):478–85.

Lanciotti E, Burrini D, Vallone G, Riva S, Capei R, Sacco C (1992). A survey on barium contamination in municipal drinking water of Tuscany. Ig Mod. 98(6):793–800.

Lisk DJ, Bache CA, Essick LA, Reid CM, Rutzke M, Crown K (1988). Absorption and excretion of selenium and barium in humans from consumption of Brazil nuts. Nutr Rep Int. 38:183–91.

McCauley PT, Washington IS (1983). Barium bioavailability as the chloride, sulfate, or carbonate salt in the rat. Drug Chem Toxicol. 6:209–17.

McCauley PT, Douglas BH, Laurie RD, Bull RJ (1985). Investigations into the effect of drinking water barium on rats. In: Calabrese EJ, Tuthill RW, Condie L, editors. Inorganics in drinking water and cardiovascular disease. Princeton (NJ): Princeton Scientific Publishing Co.; 197–210 (Advances in Modern Environmental Toxicology, Vol. 9).

Mertz W, editor (1986). Trace elements in human and animal nutrition, fifth edition. New York (NY): Academic Press; 418–20.

Miller RG, Featherstone JDB, Curzon MEJ, Mills TS, Shields CP (1985). Barium in teeth as indicator of body burden. In: Calabrese EJ, Tuthill RW, Condie L, editors. Inorganics in drinking water and cardiovascular disease. Princeton (NJ): Princeton Scientific Publishing Co.; 211–19 (Advances in Modern Environmental Toxicology, Vol. 9).

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

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

Nishioka H (1975). Mutagenic activities of metal compounds in bacteria. Mutat Res. 31:186–9.

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

Ohgami N, Hori S, Ohgami K, Tamura H, Tsuzuki T, Ohnuma S et al. (2012). Exposure to low dose barium by drinking water causes hearing loss in mice. Neurotoxicology. 33:1276–83.

Perry HM Jr, Kopp SJ, Perry EF, Erlander MW (1989). Hypertension and associated cardiovascular abnormalities induced by chronic barium feeding. J Toxicol Environ Health. 28(3):373–88.

Reeves AL (1986). Barium. In: Friberg L, Nordberg GF, Vouk VB, editors. Handbook on the toxicology of metals, second edition. Amsterdam: Elsevier/North Holland Biomedical Press; 84–94.

Schroeder HA, Kramer LA (1974). Cardiovascular mortality, municipal water, and corrosion. Arch Environ Health. 28:303–11.

Schroeder HA, Mitchener M (1975a). Life-term studies in rats: effects of aluminum, barium, beryllium and tungsten. J Nutr. 105:421–7.

Schroeder HA, Mitchener M (1975b). Life-term effects of mercury, methyl mercury and nine other trace elements on mice. J Nutr. 105:452–8.

Schroeder HA, Tipton IH, Nason P (1972). Trace metals in man: strontium and barium. J Chronic Dis. 25:491–517.

Shankle R, Keane JR (1988). Acute paralysis from barium carbonate. Arch Neurol. 45(5):579–80.

Stockinger HE (1981). The metals. In: Clayton GD, Clayton FE, editors. Patty's industrial hygiene and toxicology, third edition. Vol. 2A. New York (NY): John Wiley; 1493–2060.

Subramanian KS, Meranger JC (1984). A survey for sodium, potassium, barium, arsenic, and selenium in Canadian drinking water supplies. Atom Spectrosc. 5:34–7.

Taylor DM, Bligh PH, Duggan MH (1962). The absorption of calcium, strontium, barium and radium from the gastrointestinal tract of the rat. Biochem J. 83:25–9.

USEPA (2005). Toxicological review of barium and compounds. In support of summary information on the Integrated Risk Information System (IRIS). Washington (DC): United States Environmental Protection Agency.

USEPA (2006a). Point-of-use or point-of-entry treatment options for small drinking water systems. United States Environmental Protection Agency, Office of Ground Water and Drinking Water (EPA 815-R-06-010; https://www.epa.gov/sites/production/files/2015-09/documents/guide_smallsystems_pou-poe_june6-2006.pdf, accessed 24 March 2016).

USEPA (2006b). Research report on investigation of the capability of point-of-use/point-of-entry treatment devices as a means of providing water security. Cincinnati (OH): United States Environmental Protection Agency (EPA/600/R-06/012).

USEPA (2009). Analytical feasibility support document for the second six-year review of existing National Primary Drinking Water Regulations. Washington (DC): United States Environmental Protection Agency (EPA 815-B-09-003).

USEPA (2014). Basic information about barium in drinking water. United States Environmental Protection Agency (http://water.epa.gov/drink/contaminants/basicinformation/barium.cfm, accessed 29 July 2014).

USGS (2010). Quality of source water from public-supply wells in the United States, 1993–2007. United States Geological Survey, National Water-Quality Assessment Program (Scientific Investigations Report 3010-5024).

USNRC (1977). Drinking water and health. Vol. 1. Washington (DC): United States National Research Council, National Academy of Sciences.

USNRC (1982). Drinking water and health. Vol. 4. Washington (DC): United States National Research Council, National Academy Press; 167–70.

USNTP (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): United States 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).

Wones RG, Stadler BL, Frohman LA (1990). Lack of effect of drinking water barium on cardiovascular risk factors. Environ Health Perspect. 85:355–9.