Concise International Chemical Assessment Document 33

BARIUM AND BARIUM COMPOUNDS

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FOREWORD

Concise International Chemical Assessment Documents (CICADs) are the latest in a family of publications from the International Programme on Chemical Safety (IPCS) — a cooperative programme of the World Health Organization (WHO), the International Labour Organization (ILO), and the United Nations Environment Programme (UNEP). CICADs join the Environmental Health Criteria documents (EHCs) as authoritative documents on the risk assessment of chemicals.

International Chemical Safety Cards on the relevant chemical(s) are attached at the end of the CICAD, to provide the reader with concise information on the protection of human health and on emergency action. They are produced in a separate peer-reviewed procedure at IPCS. They may be complemented by information from IPCS Poison Information Monographs (PIM), similarly produced separately from the CICAD process.

CICADs are concise documents that provide summaries of the relevant scientific information concerning the potential effects of chemicals upon human health and/or the environment. They are based on selected national or regional evaluation documents or on existing EHCs. Before acceptance for publication as CICADs by IPCS, these documents undergo extensive peer review by internationally selected experts to ensure their completeness, accuracy in the way in which the original data are represented, and the validity of the conclusions drawn.

The primary objective of CICADs is characterization of hazard and dose–response from exposure to a chemical. CICADs are not a summary of all available data on a particular chemical; rather, they include only that information considered critical for characterization of the risk posed by the chemical. The critical studies are, however, presented in sufficient detail to support the conclusions drawn. For additional information, the reader should consult the identified source documents upon which the CICAD has been based.

Risks to human health and the environment will vary considerably depending upon the type and extent of exposure. Responsible authorities are strongly encouraged to characterize risk on the basis of locally measured or predicted exposure scenarios. To assist the reader, examples of exposure estimation and risk characterization are provided in CICADs, whenever possible. These examples cannot be considered as representing all possible exposure situations, but are provided as guidance only. The reader is referred to EHC 170[1] for advice on the derivation of health-based guidance values.

While every effort is made to ensure that CICADs represent the current status of knowledge, new information is being developed constantly. Unless otherwise stated, CICADs are based on a search of the scientific literature to the date shown in the executive summary. In the event

that a reader becomes aware of new information that would change the conclusions drawn in a CICAD, the reader is requested to contact IPCS to inform it of the new information.

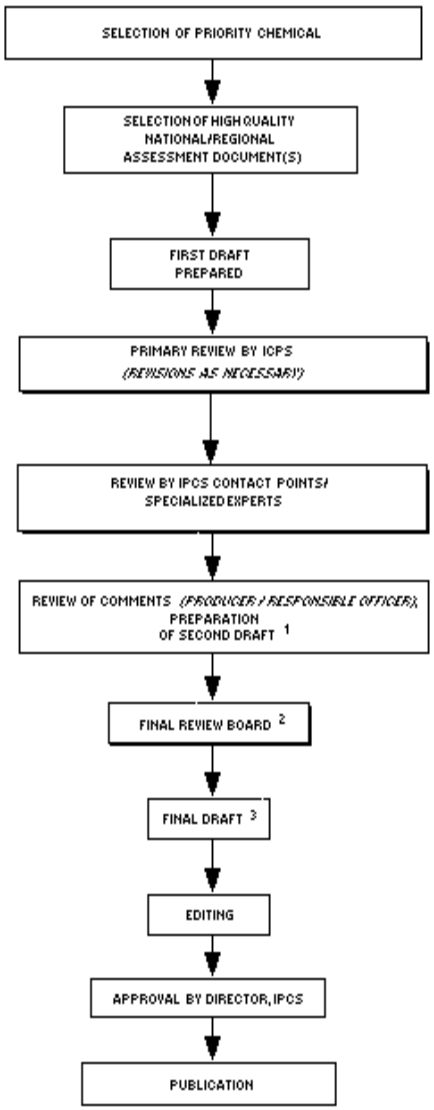
Procedures

The flow chart on page 2 shows the procedures followed to produce a CICAD. These procedures are designed to take advantage of the expertise that exists around the world — expertise that is required to produce the high-quality evaluations of toxicological, exposure, and other data that are necessary for assessing risks to human health and/or the environment. The IPCS Risk Assessment Steering Group advises the Co-ordinator, IPCS, on the selection of chemicals for an IPCS risk assessment, the appropriate form of the document (i.e., EHC or CICAD), and which institution bears the responsibility of the document production, as well as on the type and extent of the international peer review.

The first draft is based on an existing national, regional, or international review. Authors of the first draft are usually, but not necessarily, from the institution that developed the original review. A standard outline has been developed to encourage consistency in form. The first draft undergoes primary review by IPCS and one or more experienced authors of criteria documents to ensure that it meets the specified criteria for CICADs.

The draft is then sent to an international peer review by scientists known for their particular expertise and by scientists selected from an international roster compiled by IPCS through recommendations from IPCS national Contact Points and from IPCS Participating Institutions. Adequate time is allowed for the selected experts to undertake a thorough review. Authors are required to take reviewers' comments into account and revise their draft, if necessary. The resulting second draft is submitted to a Final Review Board together with the reviewers' comments.

CICAD PREPARATION FLOW CHART



1 Taking into account the comments from reviewers.
2 The second draft of documents is submitted to the Final Review Board together with the reviewers' comments.
3 Includes any revisions requested by the Final Review Board.

A consultative group may be necessary to advise on specific issues in the risk assessment document.

The CICAD Final Review Board has several important functions:

- to ensure that each CICAD has been subjected to an appropriate and thorough peer review;
- to verify that the peer reviewers' comments have been addressed appropriately;
- to provide guidance to those responsible for the preparation of CICADs on how to resolve any remaining issues if, in the opinion of the Board, the author has not adequately addressed all comments of the reviewers; and
- to approve CICADs as international assessments.

Board members serve in their personal capacity, not as representatives of any organization, government, or industry. They are selected because of their expertise in human and environmental toxicology or because of their experience in the regulation of chemicals. Boards are chosen according to the range of expertise required for a meeting and the need for balanced geographic representation.

Board members, authors, reviewers, consultants, and advisers who participate in the preparation of a CICAD are required to declare any real or potential conflict of interest in relation to the subjects under discussion at any stage of the process. Representatives of nongovernmental organizations may be invited to observe the proceedings of the Final Review Board. Observers may participate in Board discussions only at the invitation of the Chairperson, and they may not participate in the final decision-making process.

1. EXECUTIVE SUMMARY

This CICAD on barium and barium compounds was prepared by the US Environmental Protection Agency (EPA) and the United Kingdom's Health and Safety Executive (HSE) to update the WHO Environmental Health Criteria monograph on barium (IPCS, 1990). The source documents were the US EPA's *Toxicological review of barium and compounds* (US EPA, 1998), the Agency for Toxic Substances and Disease Registry's *Toxicological profile for barium* (ATSDR, 1992), and the HSE's *Barium sulphate risk assessment document*, which concentrates on occupational exposure (Ball et al., 1997). Current (1998) literature searches for toxicological data were used in the preparation of the US EPA (1998) review. Updated literature searches of on-line databases were conducted in January 1999 to identify any references containing toxicological or ecological information on barium that were published subsequent to those incorporated in the above-listed source documents. Data on barium sulfate identified as of September 1997 were covered in the HSE document. A further literature search was performed up to April 1999 to identify any extra information published since this review was completed. Information on the nature of the peer review and the availability of the source documents is presented in Appendix 1. Information on the peer review of this CICAD is presented in Appendix 2. This CICAD was approved as an international assessment at a meeting of the Final Review Board, held in Helsinki, Finland, on 26–29 June 2000. Participants at the Final Review Board meeting are listed in Appendix 3. The International Chemical Safety Cards for barium (ICSC 1052), barium chlorate (ICSC 0613), barium chloride (ICSC 0614), barium chloride dihydrate (ICSC 0615), barium oxide (ICSC 0778), barium peroxide (ICSC 0381), and barium sulfate (ICSC 0827), produced by the International Programme on Chemical Safety (IPCS, 1993, 1999a–f), have been reproduced in this document.

Barium is a dense alkaline earth metal that occurs in nature as a divalent cation in combination with other elements. In addition to its natural presence in the Earth's crust, and therefore its natural occurrence in most surface waters, barium is also released to the environment via industrial emissions. The residence time of barium in the atmosphere may be up to several days.

Barium sulfate exists as a white orthorhombic powder or crystals. Barite, the mineral from which barium sulfate is produced, is a moderately soft crystalline white opaque to transparent mineral. The most important impurities are iron(III) oxide, aluminium oxide, silica, and strontium sulfate.

Barite is used primarily as a constituent in drilling muds in the oil industry. It is also used as a filler in a range of industrial coatings, as a dense filler in some plastics and rubber products, in brake linings, and in some sealants and adhesives. The use dictates the particle size to which barite is milled. For example, drilling muds are ground to an average particle diameter of 44 μm, with a maximum of 30% of particles less than 6 μm in diameter.

There is no evidence that barium undergoes biotransformation other than as a divalent cation. The toxicokinetics of barium ions would be expected to be the same as the toxicokinetics of soluble barium salts. Studies in rats using a soluble salt (barium chloride) have indicated that the absorbed barium ions are distributed via the blood and deposited primarily in the skeleton. The principal route of elimination for barium following oral, inhalation, or intratracheal administration is in the faeces. Following introduction into the respira tory tract, the appearance of barium sulfate in the faeces represents mucociliary clearance from the lungs and subsequent ingestion.

In humans, ingestion of high levels of soluble barium compounds may cause gastroenteritis (vomiting, diarrhoea, abdominal pain), hypopotassaemia, hypertension, cardiac arrhythmias, and skeletal muscle paralysis. Insoluble barium sulfate has been extensively used at large doses (450 g) as an oral radiocontrast medium, and no adverse systemic effects have been reported. No experimental data are available on barium sulfate; however, due to the limited absorption of barium sulfate from the gastrointestinal tract or skin, it is unlikely that any significant systemic effects would occur.

The acute oral toxicity of barium compounds in experimental animals is slight to moderate. Intravenous infusion of barium chloride results in increased blood pressure and cardiac arrhythmias.

Barium hydroxide is strongly alkaline and therefore corrosive. Barium nitrate caused mild skin irritation and severe eye irritation in rabbits. The lack of reports of skin or eye irritation in humans, despite its widespread use, suggests that barium sulfate, often used as a contrast medium, is not a strong irritant. Useful information on the sensitization potential of barium compounds was not identified.

The kidney appears to be the most sensitive target organ in rats and mice exposed repeatedly to barium chloride in drinking-water. Long-term studies of barium exposure in laboratory animals have not confirmed the blood pressure, cardiac, and skeletal muscle effects seen in humans and laboratory animals orally exposed to acutely high levels.

Inhalation exposure of humans to insoluble forms of barium results in radiological findings of baritosis, without evidence of altered lung function and pathology. Information on the toxicity of inhaled barium in animals is limited. Repeated exposure to barium oxide via inhalation may cause bronchitis to develop, with cough, phlegm, and/or shortness of breath. In a limited study, minor histopathological changes were seen in the lungs of rats exposed to barium sulfate at 40 mg/m^3 for 5 h/day, 5 days/week, but there was no evidence of fibrogenic potential.

Animal studies involving respiratory tract instillation of barium sulfate have shown inflammatory responses and granuloma formation in the lungs; this would be expected with exposure to substantial amounts of any low-solubility dust, leading to a change in lung clearance and subsequently to lung effects.

Currently available data indicate that barium does not appear to be a reproductive or developmental hazard, although animal studies are limited. Barium was not carcinogenic in standard National Toxicology Program rodent bioassays. Although no *in vivo* data are available, *in vitro* data indicate that barium compounds have no mutagenic potential.

Oral intake from drinking-water and food is the most prevalent route of exposure to barium compounds for the general population. For the occupational environment, data from industry in the United Kingdom and predictions made using the Estimation and Assessment of Substance Exposure (EASE) model suggest that exposures can be controlled to less than 10 mg/m^3 8-h time-weighted average (total inhalable dust). In some situations, control will be to levels significantly below this value. Short-term exposures may be higher than 10 mg/m^3 for some tasks.

The critical end-points in humans for toxicity resulting from exposure to barium and barium compounds appear to be hypertension and renal function. Using a no-observed-adverse-effect level (NOAEL) in humans of 0.21 mg barium/kg body weight per day, a tolerable intake value of 0.02 mg/kg body weight per day for barium and barium compounds has been developed in this document.

Dissolved barium in aquatic environments may represent a risk to aquatic organisms such as daphnids, but it is apparently of lesser risk to fish and aquatic plants, although data are limited. No adverse effects have been reported in ecological assessments of terrestrial plants or wildlife, although some plants are known to bioaccumulate barium from the soil.

2. IDENTITY AND PHYSICAL/CHEMICAL PROPERTIES

Barium (Ba; CAS No. 7440-39-3) is a dense alkaline earth metal in Group IIA of the periodic table (atomic number 56; atomic mass 137.34). The free element is a silver-white soft metal that oxidizes readily in moist air and reacts with water. Barium does not exist in nature in the elemental form but occurs as the divalent cation in combination with other elements (ATSDR, 1992).

Two commonly found forms of barium are barium sulfate (CAS No. 7727-43-7) and barium carbonate (CAS No. 513-77-9), often found as underground ore deposits. These forms of barium are not very soluble in water: 0.020 g/litre (at 20 °C) for barium carbonate and 0.001 15 g/litre (at 0 °C) for barium sulfate.

Barium sulfate exists as a white orthorhombic powder or crystals. Barite, the mineral from which barium sulfate is produced, is a moderately soft crystalline white opaque to transparent mineral. The most important impurities are iron(III) oxide, aluminium oxide, silica, and strontium sulfate. Some of the more commonly used synonyms of barium sulfate include barite, barytes, heavy spar, and blanc fixe.

The barium compound most commonly used in toxicity studies is barium chloride (water solubility 375 g/litre at 20 °C).

Additional physical/chemical properties of barium and barium compounds are presented in the International Chemical Safety Cards

reproduced in this document.

3. ANALYTICAL METHODS

Information on analytical methods for determining barium levels in environmental samples is available in Table 1. There are no published methods for the quantitative measurement of barium particles (e.g., barium sulfate) in air. NIOSH (1987) suggested a flame atomic absorption method to determine soluble barium particles in air following collection on a cellulose ester membrane filter and re-extraction with hot hydrochloric acid solu tion. Insoluble barium compounds require an ashing procedure prior to measurement. The estimated limit of detection by this method is 2 µg per sample, and its precision is 2.5% at 43–180 µg per sample. Another approach is to collect respirable dust samples and assess them gravimetrically (US OSHA, 1990). Atomic absorption spectroscopy is the most commonly used analytical method for measuring low levels of barium and its compounds in air, water, wastewater, geological materials, and various other materials. Sample preparation typically involves digestion with nitric acid, although dilution with other agents may also be employed to solubilize barium. Flame atomic absorption spectroscopy and graphite furnace atomic absorption spectroscopy are analytical methods used to determine levels of barium in water and wastewater in the ranges of parts per billion and parts per trillion. Other analytical techniques include the less sensitive methods of X-ray fluorescence spectroscopy and neutron activation analysis and the less commonly used methods of scintillation spectroscopy and spectrography (ATSDR, 1992). In general, analytical procedures measure total barium ion present and do not allow for speciation of barium compounds.

Table 1: Analytical methods for determining barium in environmental samples.[a,b]

Sample matrix	Preparation method	Analytical method	Detection limit	Percent recovery
Air	Collect sample on cellulose and extract with hot acid; evaporate extract to dryness and dissolve residue in acid	FAAS	No data	No data
Air (occupational exposure)		XFS	15 µg	
Water	Acidify sample and pass through ion-exchange resin	FAAS	3 mg/litre	11.6% RSD
	Pass sample through ion-exchange resin	FAES	mg/litre levels	No data
	Extract sample with buffered HFA solution	FAAS	5 mg/litre	No data

	No data	GFAAS	7 mg/litre	No data
	Inject sample directly into graphite furnace	GFAAS	0.6 mg/litre (seawater) 0.2 mg/litre (fresh water)	13% RSD
Water and wastewater	Digest sample and evaporate to dryness; dissolve residue in acid	FAAS, GFAAS, ICP-AES	100 mg/litre (FAAS) 2 mg/litre (GFAAS)	94–113% (FAAS) 96–102% (GFAAS)
Industrial wastewater	Digest sample; mix with cation-exchange resin, dry, and analyse	XFS	290 mg/litre (on a 500-ml sample)	5.1% RSD
Unused lubricating oil	Dissolve sample in 2-methylpropan-2-ol: toluene (3:2); add potassium naphthenate solution	FAAS	No data	No data

[a] From ATSDR (1992); Ball et al. (1997).

[b] FAAS = flame atomic absorption spectroscopy; FAES = flame atomic emission spectroscopy; GFAAS = graphite furnace atomic absorption spectroscopy; HFA = hexafluoroacetylacetone; ICP-AES = inductively coupled plasma–atomic emission spectrometry; RSD = relative standard deviation; XFS = X-ray fluorescence spectroscopy.

Inductively coupled plasma–atomic emission spectrometry is a relatively effective and sensitive method for measuring low levels of barium in water, blood, urine, and bones. Detection limits of 0.25 mg barium/litre of urine, 0.6 mg barium/litre of blood, and 0.0005 mg barium/g of bone have been achieved. However, in a given sample containing barium, there is potential for interference from spectral bands of other compounds (e.g., boric acid or sodium borate) that may be present. Detection limits of 7 µg barium/litre of erythrocytes and 66 µg barium/litre of plasma have been obtained using neutron activation analysis (ATSDR, 1992).

4. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE

Barium is the 16th most abundant non-gaseous element of the Earth's crust, constituting approximately 0.04% of it. The two most prevalent naturally occurring barium ores are barite (barium sulfate) and witherite (barium carbonate). Barite occurs largely in sedimentary formations, as residual nodules resulting from weathering of barite-containing sediments, and in beds along with fluorspar, metallic sulfides, and other minerals. Witherite is found in veins and is often associated with lead sulfide. Barium is found in coal at concentrations up to 3000 mg/kg, as well as in fuel oils (IPCS, 1990; ATSDR, 1992). Estimates of terrestrial and marine concentrations of barium are 250 and 0.006 g/tonne, respectively (Considine, 1976).

Barite ore is the raw material from which nearly all other barium compounds are derived. Barite is mined in Morocco, China, India, and the United Kingdom. Crude barite ore is washed free of clay and other impurities, dried, and then ground before use. Barite is usually imported as crude ore or crushed ore for milling or as ready-milled ore. Barite can be 90–98% barium sulfate. World production of barite in 1985 was esti mated to be 5.7 million tonnes.

Because of its high specific gravity, low abrasiveness, chemical stability, and lack of magnetic effects, barite is used as a weighting agent for oil and gas well drilling muds, which counteracts high pressures encountered in the substrata (IPCS, 1990). It is also used as a filler in a range of industrial coatings, as a dense filler in some plastics and rubber products, in brake linings, and in some sealants and adhesives. The use dictates the source of barite used. Some sources produce very pure white barite, which is used in coatings, while barite from other sources is off-white and is used in applications where the colour is unimportant. The use will also dictate the particle size to which barite is milled. For example, drilling muds are ground to an average particle diameter of 44 μm, with a maximum of 30% of particles less than 6 μm in diameter. Barium and its compounds are used in diverse industrial products ranging from ceramics to lubricants. Barium is used in the manufacture of alloys, soap, rubber, and linoleum; in the manufacture of valves; as a loader for paper; and as an extinguisher for radium, uranium, and plutonium fires. Barium compounds are used in cement, specialty arc welding, glass industries, electronics, roentgenography, cosmetics, pharmaceuticals, inks, and paints. They have also been used as insecticides and rodenticides (e.g., barium metaborate, barium polysulfide, and barium fluorosilicate).

Anthropogenic sources of barium are primarily industrial. Emissions may result from mining, refining, or processing of barium minerals and manufacture of barium products. Barium is released to the atmosphere during the burning of coal, fossil fuels, and waste. Barium is also discharged in wastewater from metallurgical and industrial processes. Deposition on soil may result from human activities, including the disposal of fly ash and primary and secondary sludge in landfills (IPCS, 1990). Estimated releases of barium and barium compounds to the air, water, and soil from manufacturing and processing facilities in the USA during 1998 were 900, 45, and 9300 tonnes, respectively.[2]

5. ENVIRONMENTAL TRANSPORT, DISTRIBUTION, AND TRANSFORMATION

Both specific and non-specific adsorption of barium onto oxides and soils have been observed. Specific sorption occurs onto metal oxides and hydroxides. Adsorption onto metal oxides probably acts as a control over the concentration of barium in natural waters. Electrostatic forces account for a large fraction of the non-specific sorption of barium on soil and subsoil. The retention of barium, like that of other alkaline earth cations, is largely controlled by the cation-exchange capacity of the sorbent. Complexation by soil organic material occurs to a limited extent. The K_d (soil sorption) value, the dissociation constant between sediment and barium in sediments, is 5.3×10^5 ml/g (McComish & Ong, 1988).

Examination of dust falls and suspended particulates indicates that most contain barium. The presence of barium is mainly attributable to industrial emissions, especially the combustion of coal and diesel oil and waste incineration, and may also result from dusts blown from soils and mining processes. Barium sulfate and carbonate are the forms of barium most likely to occur in particulate matter in the air, although the presence of other insoluble compounds cannot be excluded. The residence time of barium in the atmosphere may be several days, depending on the particle size. Most of these particles, however, are much larger than 10 μm in size and rapidly settle back to earth. Particles can be removed from the atmosphere by rainout or washout wet deposition.

Soluble barium and suspended particulates can be transported great distances in rivers, depending on the rates of flow and sedimentation. Cartwright et al. (1978) studied the chemical control of barium solubility and showed that, for most water samples, barium ion concentration is controlled by the amount of sulfate ion in the water.

While some barium in water is removed by precipitation, exchange with soil, or other processes, most barium in surface waters ultimately reaches the ocean. Once freshwater sources discharge into seawater, barium and the sulfate ions present in salt water form barium sulfate. Due to the relatively higher concentration of sulfate present in the oceans, only an estimated 0.006% of the total barium brought by freshwater sources remains in solution (Chow et al., 1978). This estimate is supported by evidence that outer-shelf sediments have lower barium concentrations than those closer to the mainland.

Marine concentrations of barium generally increase with depth, suggesting that barium may be incorporated into organisms in the euphotic zone and subsequently sedimented and released in deeper waters (IPCS, 1990). In laboratory testing, the uptake of barium by algae in culture media was 30–60% after 15 days of exposure to barium concentrations of 0.04, 0.46, and 4.0 mg/litre of medium, the relative accumulation being inversely related to the barium concentration in the medium and directly related to the exposure duration (Havlik et al., 1980). Barium was not incorporated into organic components but was bound primarily to the cell membrane or other non-extractable components. Accumulation of barium ions (^{133}Ba) in the cells of the alga *Scenedesmus obliquus* has been shown to increase with increasing pH between pH 4 and 7, then remain constant over the pH range 7–9 at a barium concentration of 10^{-6} mol/litre, with a calculated affinity constant (K_m) of 4.8 (Stary et al., 1984). In a marine environment contaminated with heavy metals (including barium), Guthrie et al. (1979) measured barium concentrations of 7.7 mg/litre in water and 131.0 mg/kg wet weight in sediment. Among barnacles, crabs, oysters, clams, and polychaete worms tested for barium content in this marine environment, only barnacles showed higher concentrations of barium (40.5 mg/kg wet weight) than that of the water.

Barium sulfate is present in soil through the natural process of soil formation; barium concentrations are high in soils formed from limestone, feldspar, and biotite micas of the schists and shales (Clark & Washing ton, 1924). When soluble barium-containing minerals weather and come into contact with solutions containing sulfates, barium sulfate is deposited in available geological faults. If there is insufficient sulfate to combine with barium, the soil material formed is partially saturated with barium. In soil, barium replaces other sorbed alkaline earth metals from manganese dioxide, silicon dioxide, and titanium dioxide under typical environmental conditions, by ion exchange (Bradfield, 1932; McComish & Ong, 1988). However, other alkaline earth metals displace barium from aluminium oxide (McComish & Ong, 1988).

Barium sulfate in soils is not expected to be very mobile because of the formation of water-insoluble salts and its inability to form soluble complexes with humic and fulvic materials. Under acid conditions, however, some of the water-insoluble barium compounds (e.g., barium sulfate) may become soluble and move into groundwater (US EPA, 1984).

Despite relatively high concentrations in soils, only a limited amount of barium accumulates in plants. Barium is actively taken up by legumes, grain stalks, forage plants, red ash (*Fraxinus pennsylvanica*) leaves, and black walnut (*Juglans nigra*), hickory (*Carya* sp.), and brazil nut (*Bertholletia excelsa*) trees; Douglas-fir (*Pseudotsuga menziesii*) trees and plants of the genus *Astragallu* also accumulate barium (IPCS, 1990). Barium has also been shown to accumulate in mushrooms (Aruguete et al., 1998). No studies of barium particle uptake from the air have been reported, although vegetation is capable of removing significant amounts of contaminants from the atmosphere. Plant leaves act only as deposition sites for particulate matter. Although levels of barium in wildlife have not been documented, barium has been found in dairy products and eggs (Gormican, 1970; IPCS, 1990), indicating that barium uptake occurs in animals.

A bioconcentration factor (BCF) for soil to plants was estimated as 0.4 (0.02 standard error of the mean [SEM]), based on samples of a variety of plant species (mean barium concentration of 29.8 mg/kg [13.7 SEM]) that were taken from a site in which the mean concentration of barium in the soil was 104.2 mg/kg (9.5 SEM) (Hope et al., 1996). Based on the ratio of barium concentration in the soil to whole-body barium concentra tion, the same authors computed bioaccumulation factors of 0.2 (0.002 SEM) for terrestrial insects, 0.02 (0.0004 SEM) for white-footed mice (*Peromyscus leucopus*), and 0.02 (0.0005 SEM) for hispid cotton rats (*Sigmodon hispidus*). Based on dissolved barium concentrations in surface water of 0.07 mg/litre (0.02 SEM) and whole-body barium concentrations of 2.1 mg/kg (0.5 SEM) in fish, measured at the same study site, a BCF of 129.0 litres/kg (13.5 SEM) was estimated. The authors also estimated mean depuration rates in white-footed mice and hispid cotton rats to be 0.4/day (0.01 SEM) and 0.2/day (0.01 SEM), respectively, indicating that barium is "lost from these receptors at a fairly rapid rate." Field data were collected during a single summer sampling event, and the authors advise caution in extrapolating the results to terrestrial systems in general.

There is no evidence that barium undergoes environmental biotransformation other than as a divalent cation (IPCS, 1990).

6. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

6.1 Environmental levels

The levels of barium in air are not well docu mented, and in some cases the results are contradictory. Tabor & Warren (1958) detected barium concentrations ranging from <0.005 to 1.5 mg/m^3 in the air in 18 cities and 4 suburban areas in the USA. No distinct pattern between ambient levels of barium in the air and the extent of industrialization was observed. In general, however, higher concentrations were observed in areas where metal smelting occurred (Tabor & Warren, 1958; Schroeder, 1970). In a more recent survey in the USA, ambient barium concentrations ranged from 0.0015 to 0.95 mg/m^3 (US EPA, 1984). In three communities in New York City, USA, barium was measured in dust fall and household dust (Creason et al., 1975). With standard methods (US EPA, 1974), the dust fall was found to contain an average of 137 mg barium/g, while the house dust contained 20 mg barium/g.

Barium is found in almost all surface waters that have been examined (NAS, 1977). The concentrations are extremely variable and depend on local geology, water treatment, and water hardness (NAS, 1977). Barium concentrations of 7–15 mg/litre and 6 mg/litre have been measured in fresh water and seawater, respectively (Schroeder et al., 1972). The mean barium content of various US surface waters ranges from 43 to 57 mg/litre (Durum, 1960; Kopp, 1969; Kopp & Kroner, 1970; Schroeder, 1970; Bradford, 1971). The concentrations of barium in sediments of the Iowa River, USA, were measured to be 450–3000 mg/kg (Tsai et al., 1978), suggesting that barium in the water is removed by precipitation and silting.

Studies of drinking-water quality in cities in the USA have revealed levels of barium ranging from trace to 10 mg/litre (Durfor & Becker, 1964; Barnett et al., 1969; McCabe et al., 1970; McCabe, 1974; Calabrese, 1977; AWWA, 1985). Drinking-water levels of at least 1000 mg barium/litre have been reported when the barium is present mainly in the form of insoluble salts (Kojola et al., 1978). Levels of barium in Canadian water supplies have been reported to range from 5 to 600 mg/litre (Subramanian & Meranger, 1984), and barium concentrations ranging from 1 to 20 mg/litre have been measured in municipal water in Sweden (Reeves, 1986).

The concentration of barium in seawater varies greatly among different oceans and varies with factors such as latitude and depth within a

given ocean. Several studies have shown that the barium content in the open ocean increases with the depth of water (Chow & Gold berg, 1960; Bolter et al., 1964; Turekian, 1965; Chow & Patterson, 1966; Anderson & Hume, 1968). A Geosecs III study of the south-west Pacific by Bacon & Edmond (1972) found a barium profile of 4.9 mg/litre in surface waters to 19.5 mg/litre in deep waters. Later studies by Chow (1976) and Chow et al. (1978) corroborated these values. Measured barium concentrations in the north-east Pacific ranged from 8.5 to 32 mg/litre (Wolgemuth & Broecker, 1970). Bernat et al. (1972) found that barium concentration profiles for the eastern Pacific Ocean and the Mediterranean Sea ranged from 5.2 to 25.2 mg/litre and from 10.6 to 12.7 mg/litre, respec tively. Anderson & Hume (1968) reported concentrations in the Atlantic Ocean ranging from 0.8 to 37.0 mg/litre in the equatorial region and from 0.04 to 22.8 mg/litre in the North Atlantic, with mean values of 6.5 and 7.6 mg/litre, respectively. In Atlantic Ocean waters off Bermuda, barium concentrations of 15.9– 19.1 mg/litre have been measured (Chow & Patterson, 1966).

The background level of barium in soils is considered to range from 100 to 3000 mg/kg, with an average of 500 mg/kg (Brooks, 1978).

Various studies document concentrations of barium in Brazil nuts ranging from 1500 to 3000 mg/kg (Robinson et al., 1950; Smith, 1971a). Barium is also present in wheat, although most is concentrated in the stalks and leaves rather than in the grain (Smith, 1971b). Tomatoes and soybeans also concentrate soil barium; the BCF ranges from 2 to 20 (Robinson et al., 1950). Levels of barium found in other food items range from <0.2 mg/kg in meats to 27 mg/kg in dry tea bags (Gormican, 1970). McHargue (1913) reported that the barium content of dry tobacco leaves was in the range of 88–293 mg/kg. Later measurements yielded 24–170 mg/ kg, with an average value of 105 mg/kg (Voss & Nicol, 1960). Most of this barium is likely to remain in the ash during burning. The concentrations of barium in tobacco smoke have not been reported.

6.2 Human exposure

The most important route of exposure to barium appears to be ingestion of barium through drinking-water and food. Particles containing barium may be inhaled into the lung, but little is known regarding the absorption of barium by this route.

Schroeder et al. (1972) estimated that the mean daily intake of barium is 1.24 mg in food. Hamilton & Minski (1972) estimated the total intake of barium from the diet to be 603 µg/day. The ICRP (1974) estimated barium intake from dietary sources to be approximately 0.67 mg/day. WHO (1996) reported daily dietary intake of barium for adults for the period 1970–1991 as 0.18 (minimum), 0.30 (median), and 0.72 (maximum) mg/ person. In a number of dietary studies, the average intake of barium ranged from 0.3 to 1.77 mg/day (Tipton et al., 1966, 1969; Gormican, 1970; ICRP, 1974). This is equivalent to 0.004–0.025 mg barium/kg body weight per day, assuming a 70-kg adult body weight. The barium content in school lunches from 300 schools in 19 states in the USA ranged from 0.09 to 0.43 mg/ lunch, with a mean of 0.17 mg/lunch (Murphy et al., 1971).

The barium content in drinking-water seems to depend on regional geochemical conditions. In a study of the water supplies of the 100 largest cities in the USA, a median value of 0.43 mg/litre was reported; 94% of all determinations were <0.100 mg/litre (Durfor & Becker, 1964). Assuming daily water consumption of 2 litres/person, this represents an average intake of <0.200 mg barium/day. More recent studies by Letkiewicz et al. (1984) indicated that approximately 214 million people in the USA using public water supplies are exposed to barium levels ranging from 0.001 to 0.020 mg/litre. In certain regions of the USA, however, barium levels may reach 10 mg/litre, and the average intake could be as high as 20 mg/day (Calabrese, 1977). Levels of barium in municipal water in Sweden as high as 20 mg/litre have been reported (Reeves, 1986).

Due to the paucity of information on the levels of barium in ambient air, it is difficult to estimate the intake from this source. The levels of barium in air rarely exceed 0.05 mg/m^3 (Tabor & Warren, 1958). This value can be used to estimate daily barium intake via the lungs. Assuming that the average lung ventilation rates for newborn babies, male adults undergoing light activity, and male adults undergoing heavy activity are 0.5, 20, and 43 litres/min, respectively (ICRP, 1974; IPCS, 1994), the intake via inhalation would range from 0.04 to 3.1 mg/day. Other age groups and females are included in this range. Earlier, the ICRP (1974) reported that intake of barium through inhalation ranges from 0.09 to 26 mg/day. Using 0.95 mg/m^3 (the upper-end estimate of ambient barium concentrations from US EPA, 1984) and the ventilation rates of ICRP (1974) for babies and adult males, a range of intakes via inhalation of 0.68–59 mg/day can be estimated.

The ICRP (1974) reported the total dietary intake of barium to be 0.75 mg/day, including both food and fluids. Schroeder et al. (1972) estimated a total of 1.33 mg/day, including food, water, and air (0.001 mg) intake.

Available data from industry in the United King dom indicate that airborne exposure to barium sulfate can range from 3.5 to 9.1 mg/m^3 (8-h time-weighted average [TWA], total inhalable dust) during the manual addition of barite to mixing hoppers in the oil drilling industry, with short-term (10-min TWA, total inhalable dust) exposures as high as 34.1 mg/m^3. During the processing of barite ore, in industries that typically use enclosed processes and local exhaust ventilation (LEV), exposures usually ranged between 1.3 and 3.7 mg/m^3 (total inhalable dust), with highest values in one factory reaching 55.4 mg/m^3. Exposure levels in the formulation of plastics and coatings, where the process is usually enclosed and LEV is used, are in the region of 1– 3.5 mg/m^3 (Ball et al., 1997).

The wiring used in some speciality arc welding processes has been shown to contain 20–40% soluble barium compounds, and fumes produced during these processes contain 25% barium (Dare et al., 1984). Welders using such wire are exposed to estimated airborne concentrations of 2.2–6.2 mg soluble barium/m^3 (NIOSH, 1978).

Personal air sampling in the vicinity of oven-charger and batch-mixer workers in art glass manufacturing plants revealed median ambient air concentrations of 0.041 and 0.0365 mg barium/m^3, respectively (Apostoli et al., 1998). Mean concentrations of barium measured by personal sampling methods in various locations within ceramic factories in Spain ranged from 0.0012 to 0.0758 mg/m^3 (Roig-Navarro et al., 1997).

Data from industry in the United Kingdom and predictions made using the Estimation and Assessment of Substance Exposure (EASE)[3] model suggest that exposures to barium sulfate can be controlled to less than 10 mg/m^3 8-h TWA (total inhalable dust). In some situations, control will be to levels significantly below this value. Short-term exposures may be higher than this for some tasks.

EASE Version 2 predicts that during manual addition of barite to mixing hoppers, exposure to barium would be 2–5 mg/m^3 with LEV and 5–50 mg/m^3 without LEV; during dry crushing and grinding, 2–10 mg/m^3 with LEV and 50–200 mg/m^3 without LEV; and during dry manipulation in plastics formulation, in the range 2–5 mg/m^3 with LEV and 5–50 mg/m^3 without LEV. These predictions are consistent with the data from industry.

Barium sulfate is the major barium compound used in medicinal diagnostics; it is employed as an opaque contrast medium for roentgenographic studies of the gastrointestinal tract, providing another possible source of human exposure to barium (IPCS, 1990).

7. COMPARATIVE KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

Information on the gastrointestinal absorption of barium in humans is limited. Lisk et al. (1988) reported the results of a mass balance study of one man who consumed a single dose of 179.2 mg barium (species not reported) in 92 g of Brazil nuts; it was estimated that at least 91% of the dose was absorbed. Barium excreted in the urine was 1.8 and 5.7% of the total dietary barium in two subjects studied by Tipton et al. (1969). Thirty-seven people were each administered a single dose (between 88 and 195 µg of barium) of one of five barium sulfate X-ray contrast media (Clavel et al., 1987). In 24 h, the total amount of barium collected in the urine ranged from 18 to 35 µg and showed a positive correlation with the amount of barium ingested. The eliminated barium was stated to be in the range 0.16– 0.26 µg/g of barium administered. Another study also indicated that a very small proportion of barium sulfate was absorbed after ingestion of barium sulfate as a radiopaque (Mauras et al., 1983).

A wide range of absorption efficiencies has been reported in animal studies. The range of reported oral absorption for all animal studies was 0.7–85.0%. This large variation may be explained in part by differences in study duration (length of time that gastrointestinal absorption was monitored), species, age, and fasting status of the animals; however, these experimental parameters did not affect gastrointestinal absorption of barium consistently among the different studies. The presence of food in the gastrointestinal tract appears to decrease barium absorption, and barium absorption appears to be higher in young animals than in older ones (US EPA, 1998).

Richmond et al. (1960, 1962a,b) studied the gastrointestinal absorption of barium chloride in several animal species. Gastrointestinal absorption was approximately 50% (barium chloride) in beagle dogs compared with 30% (barium sulfate) in rats and mice. Using the 30-day retention data from a study by Della Rosa et al. (1967), Cuddihy & Griffith (1972) estimated gastro intestinal absorption efficiencies of 0.7–1.5% in adult beagle dogs and 7% in younger beagle dogs (43– 250 days of age).

McCauley & Washington (1983) and Stoewsand et al. (1988) compared absorption efficiencies of several barium compounds. Barium sulfate and barium chloride were absorbed at "nearly equivalent rates" (based on blood and tissue levels) in rats following a single gavage dose of similar barium concentrations (McCauley & Washington, 1983). Similar concentrations of barium were found in the bones of rats fed diets with equivalent doses of barium chloride or barium from Brazil nuts. McCauley & Washington (1983) suggested that the similarity in absorption efficiency between barium sulfate and barium chloride may have been due to the ability of hydrochloric acid in the stomach to solubilize small quantities of barium sulfate (barium chloride, barium sulfate, or barium carbonate had been adminis tered to the rats at a concentration of 10 mg ^{133}Ba/litre in the drinking-water at pH 7.0). This is supported by the finding that barium carbonate in a vehicle containing sodium bicarbonate was poorly absorbed. The buffering capacity of sodium bicarbonate may have impaired the hydrochloric acid-mediated conversion of barium carbonate to barium chloride. The results of these studies suggest that soluble barium compounds and/or barium compounds that yield a dissociated barium ion in the acid environment of the upper gastrointestinal tract have similar absorption efficiencies.

There is no direct evidence in humans that barium is absorbed by the respiratory tract. However, Zschiesche et al. (1992) reported increased plasma and urine levels of barium compounds in workers exposed to barium during welding, thus indicating that airborne barium is absorbed either by the respiratory system or by the gastrointestinal tract following mucociliary clearance. Following termination of barite exposure, Doig (1976) showed a clearing of lung opacities in workers.

A suspension of 23, 233, or 2330 mg ^{133}Ba in isotonic saline was instilled into the trachea and then blown into the "deep respiratory tract" of rats (Cember et al., 1961). Four rats from each group were sacrificed at intervals up to 20 days after administration, and lungs, kidneys, spleen, and tracheobronchial lymph nodes were extracted and examined radiologically for the presence of the ^{133}Ba. The clearance half-time of the ^{133}Ba from the deep respiratory tract for all dose levels was determined to be between 8 and 10 days and was not influenced by the dose administered. Less than 0.1% of the instilled dose of ^{133}Ba was detected in the tissues analysed (excluding lungs).

Animal studies provide evidence that barium compounds, including poorly water soluble barium sulfate, are cleared from the respiratory tract. Collectively, these studies suggest that barium is absorbed following inhalation exposure. Morrow et al. (1964) estimated that the biological half-time of $^{131}BaSO_4$ in the lower respiratory tract was 8 days in dogs inhaling 1.1 mg barium sulfate/ litre for 30–90 min. Twenty-four hours after an intratracheal injection of $^{133}BaSO_4$, 15.3% of the radioactivity was cleared from the lungs. The barium sulfate was cleared via mucociliary clearance mechanisms (7.9% of initial radioactive burden) and via lung-to-blood transfer (7.4% of radioactivity) (Spritzer & Watson, 1964). Clearance half-times of 66 and 88 days were calculated for the cranial and caudal regions of the trachea in rats intratracheally administered 2 mg $^{133}BaSO_4$ (Takahashi & Patrick, 1987). Cuddihy et al. (1974) showed uptake of barium in the bone following inhalation exposure in rats.

Differences in water solubility appear to account for observed differences in respiratory tract clearance rates for barium compounds. The clearance half-times were proportional to solubility in dogs exposed to aerosols of barium chloride, barium sulfate, heat-treated barium sulfate (likely oxidized), or barium incorporated in fused montmorillonite clay particles (Cuddihy et al., 1974).

No data are available on dermal absorption of barium compounds.

The highest concentrations of barium (approximately 91% of the total body burden) are found in the bone (IPCS, 1990). Reeves (1986) noted that osseous uptake of barium was 1.5–5 times higher than that of calcium or strontium. In the bone, barium is primarily deposited in areas of active bone growth (IPCS, 1990). The uptake of barium into the bone appears to be rapid. One day after rats were exposed to barium chloride aerosols, 78% of the total barium body burden was found in the skeleton; by 11 days post-exposure, more than 95% of the total body burden was found in the skeleton (Cuddihy et al., 1974).

The remainder of the barium in the body is found in soft tissues, particularly aorta, brain, heart, kidney, spleen, pancreas, and lung (IPCS, 1990). High concentrations of barium are sometimes found in the eye, primarily in the pigmented structures (Reeves, 1986). McCauley & Washington (1983) found that 24 h after administration of an oral dose of $^{133}BaCl_2$ to dogs, ^{133}Ba levels in the heart were 3 times higher than in the eye, skeletal muscle, and kidneys, which had similar concentrations. Levels in these tissues were higher than the whole-blood concentration, suggesting that they con centrated barium.

Barium is excreted primarily in the faeces following oral, inhalation, and parenteral exposure, but it is also excreted in the urine. At a normal intake level of 1.33 mg barium/day (1.24, 0.086, and 0.001 mg/day from food, water, and air, respectively), humans eliminated approximately 90% of the barium in the faeces and 2% in the urine (Schroeder et al., 1972). Tipton et al. (1969) found similar results; in two men studied, 95–98% and 2–5% of the daily barium intake were excreted in the faeces and urine, respectively. In the tracheal instillation study of Cember

et al. (1961), urine and faeces were collected for 21 days in two high-dose animals. Faecal elimination accounted for around two-thirds of the radioactivity administered, and the urine for around 10%. Overall, this study indicated that very little of the administered barium is absorbed, with the majority of the compound being eliminated in the faeces.

The biological half-times of barium of 3.6, 34.2, and 1033 days were estimated in humans using a three-component exponential function (Rundo, 1967). Following inhalation exposure to $^{140}BaCl_2$–$^{140}LaCl_2$, a half-time of 12.8 days was estimated in beagle dogs (Cuddihy & Griffith, 1972).

8. EFFECTS ON LABORATORY MAMMALS AND *IN VITRO* TEST SYSTEMS

8.1 Single exposure

Acute oral LD_{50} values in rats for barium chloride, barium carbonate, and barium sulfide range from 118 to 800 mg/kg body weight (IPCS, 1990; ATSDR, 1992). Acute effects include fluid accumulation in the trachea, intestinal inflammation, decreased liver/brain weight ratio, darkened liver, increased kidney/body weight ratio, and decreased body weight (Borzelleca et al., 1988). No data were available regarding the lethality of barium sulfate in laboratory animals.

In rabbits administered single intratracheal doses of ^{147}Ba (85% barium sulfate) in the range of 0.015– 0.6 ml/kg body weight, soft X-rays of the lungs revealed dose-related shadows, and transient bronchopneumonia, bronchitis, or bronchiolitis was observed (Uchiyama et al., 1995).

Barium sulfate instilled in the trachea or bronchus of laboratory animals was present in the lungs for up to 126 days after administration and induced local increases in the number of polymorphonuclear leukocytes 1 day post-instillation, followed by an increase in macrophages. Small foci of atelectasis or emphysema were seen post-instillation, whereas hyperplasia and/or granulomas in bronchial tissue (without evidence of pulmonary fibrosis) appeared between days 7 and 42 post-instillation (Huston & Cunningham, 1952; Willson et al., 1959; Nelson et al., 1964; Stirling & Patrick, 1980; Ginai et al., 1984; Slocombe et al., 1989). None of the investigators reported systemic effects.

Intravenous infusion of barium chloride into anaesthetized dogs (0.5–2 µmol/kg body weight per minute) or guinea-pigs (1.7 mg/kg body weight per minute) resulted in increased blood pressure and cardiac arrhythmias (Roza & Berman, 1971; Hicks et al., 1986). The study in dogs also reported skeletal muscle flaccidity and paralysis (Roza & Berman, 1971). Determination of plasma potassium concentrations in the dogs revealed severe hypopotassaemia, which was attributed to an extracellular-to-intracellular shift of potassium. Simultaneous infusion of potassium into the dogs abolished the cardiac effects and the skeletal muscle flaccidity but did not affect hypertension. The hypertension did not appear to be mediated through the renin–angiotensin system, because it was not prevented by bilateral nephrectomy of the dogs. Dose-dependent cardiac arrhythmias were also noted in conscious rabbits following infusion of barium chloride (Mattila et al., 1986).

8.2 Irritation and sensitization

Barium hydroxide is strongly alkaline and therefore corrosive. Topical and ocular applications (24-h exposure) of barium nitrate and barium

oxide in rabbits caused mild skin irritation and severe eye irritation (RTECS, 1985). No data are available on skin or eye irritation caused by barium sulfate. However, the physicochemical properties of barium sulfate and the lack of reports of skin or eye irritation in humans despite its widespread use, particularly for X-ray purposes, suggest that barium sulfate is not irritating or corrosive to either skin or eyes.

Useful information on the sensitization potential of barium compounds was not identified.

8.3 Short-term exposure

Increased blood pressure was reported in rats exposed to barium chloride in drinking-water for 1 month at an estimated daily dose of 7.1 mg barium/kg body weight (Perry et al., 1983, 1985, 1989). No chemically related adverse effects were seen in rats exposed to up to 2000 mg barium chloride dihydrate/litre in drinking-water (average daily doses of up to 110 mg barium/kg body weight) for 15 days. In mice similarly exposed to up to 692 mg/litre (average daily doses of up to 70 and 85 mg barium/kg body weight in males and females, respectively), the only significant adverse effect was an increased relative liver weight in high-dose males (NTP, 1994).

Muller (1973) exposed rats to barium sulfate dust at an exposure level of 40 mg/m^3 (particle size 1–2 µm), 5 h/day, 5 days/week, for up to 8 weeks. Following a single exposure period, thickening of the alveolar septa, loss of ciliated epithelial cells, and formation of multi cellular epithelium were noted. At 14 days of treatment, rats exhibited normal alveolar septa. However, the investigator reported unspecified changes in bronchiolar epithelium that were still present following a 28-day recovery period.

8.4 Medium-term exposure

NTP (1994) treated groups of rats (10 per sex per group) with barium chloride dihydrate in drinking-water at concentrations of 0, 125, 500, 1000, 2000, or 4000 mg/litre for 13 weeks (average daily doses of 0, 10, 30–35, 65, 110–115, or 180–200 mg barium/kg body weight). Effects observed in the 4000 mg/litre rats included reduced water consumption, significantly reduced final mean body weights, and death of three males and one female during the last week of the study. It may be noted that the 4000 mg/litre (180–200 mg barium/kg body weight) dose is comparable to the LD_{50} of 180 mg barium/kg body weight in rats. There were no clearly chemical-related clinical findings of toxicity or cardiovascular (heart rate, systolic blood pressure, electrocardiogram) effects. Toxicologically significant (*P* æ 0.01) organ weight changes consisted of increased absolute and relative kidney weights in 2000 and 4000 mg/litre female rats, increased relative kidney weights in 4000 mg/litre male rats, and decreased absolute and/or relative liver weights in 4000 mg/litre rats of both sexes. Organ weight changes in the kidney were considered to be associated with chemical-induced renal lesions consisting of minimal to mild, focal to multifocal areas of dilatation of the proximal convoluted tubules seen in three rats of each sex at the 4000 mg/litre exposure level. Crystals were not present in the kidney tubules. Decreased liver weights and lymphoid depletions in spleen, thymus, and/or lymph nodes of 4000 mg/litre rats were attributed to reduced body weight and stress. There were no biologically significant changes in serum electrolytes or haematology values that were considered to be chemical related. Significant decreases in the magnitude of undifferentiated motor activity were observed at day 90 in 4000 mg/litre rats of both sexes. Marginal decreases in undifferentiated motor activity were seen in all other barium-exposed groups except the 1000 mg/litre female rats. No significant or dose-related changes were observed in other neuro behavioural end-points. Although NTP (1994) con sidered the no-observed-adverse-effect level (NOAEL) to be 115 mg/kg body weight per day (the 2000 mg/litre exposure level), US EPA (1998) suggested that this level might be considered a lowest-observed-adverse-effect level (LOAEL), based on significant (*P* æ 0.01) increased kidney weight in female rats and an observed LD_{50} of 118 mg/kg body weight in rats (RTECS, 1985). The NOAEL would

then be 65 mg/kg body weight per day (the 1000 mg/litre exposure level).

NTP (1994) also treated groups of mice (10 per sex per group) with barium chloride dihydrate in drinking-water at concentrations of 0, 125, 500, 1000, 2000, or 4000 mg/litre for 13 weeks (average daily doses of 0, 15, 55–60, 100–110, 200–205, or 450– 495 mg barium/kg body weight). Adverse effects in the 4000 mg/litre groups included death of 6 males and 7 females, chemical-related nephropathy in 10 males and 9 females, significantly reduced body weights in both sexes, reduced absolute kidney weight in males, and increased relative kidney weight in females, relative to controls. Kidney lesions were characterized by tubule dilatation, renal tubule atrophy, tubule cell regeneration, and the presence of crystals, primarily in the lumen of the renal tubules. Relative and absolute thymus weights were decreased in both sexes. Lymphoid depletions in spleen, thymus, and/or lymph nodes of 4000 mg/litre mice were attributed to reduced body weight and stress. A significant decrease in forelimb grip strength of 4000 mg/litre female mice, observed at 90 days, was attributed to debilitation; no significant dose-related changes were observed in other neurobehavioural end-points. Cardiovascular tests were not performed in mice. The LOAEL is 495 mg/kg body weight per day, based on nephropathy and mortality at the 4000 mg/litre exposure level; the NOAEL is 205 mg/kg body weight per day.

Tardiff et al. (1980) exposed male and female Charles River rats continuously to barium chloride in drinking-water for up to 13 weeks. The authors estimated doses as 0, 1.7, 8.1, or 38.1 mg barium/kg body weight per day for males and 0, 2.1, 9.7, or 45.7 mg barium/kg body weight per day for females. Rats were fed a diet of Tekland mouse/rat diet pellets, which contributed a baseline dose of 0.5 µg barium/kg body weight per day. The only reported adverse effects were depressed water consumption in the high-dose groups of both sexes and slight decreases in relative adrenal weights in mid-dose males at 8 weeks and in all exposed groups of females at 13 weeks; these changes were not dose related. Blood pressure and end-points sensitive for glomerular damage (electron microscopic examination or urinary excretion of protein) were not investigated.

In a series of longer-term histological, electron microscopic, electrocardiographic, and blood pressure studies (McCauley et al., 1985), CD Sprague-Dawley rats were given barium in drinking-water for various durations and fed Purina rat chow (containing 12 mg barium/kg) or Tekland rat chow (insignificant barium intake). In the histology studies, three exposure regimens were used with the Purina rat chow diet, and the estimated total barium intakes were 1, 1.15, 2.5, 16, or 38.5 mg/kg body weight per day for 36–68 weeks. Histological evaluations of an extensive number of tissues did not reveal barium-related lesions. No alterations in haematocrit levels were observed. A retinal lesion ("focal absence of the outer layers of the retina") was observed but did not appear to be dose or duration related; its relationship to barium exposure is uncertain. No significant increases in incidences of neoplasms were observed in the barium-exposed rats, but the study duration is less than a lifetime and may not have been of sufficient duration for the detection of late-developing tumours.

In a 16-week blood pressure study (McCauley et al., 1985), normotensive rats were fed Tekland rat chow (0.5 mg barium/kg body weight per day) and administered barium in drinking-water or in 0.9% sodium chloride solution as drinking-water (estimated daily barium doses of 0, 0.45, 1.5, 4.5, or 15 mg/kg body weight). Unilaterally nephrectomized rats were similarly treated (estimated daily doses of 0.15, 1.5, 15, or 150 mg barium/kg body weight), while groups of Dahl salt-sensitive and Dahl salt-resistant rats received esti mated daily doses of 0.15, 1.5, 15, or 150 mg barium/kg body weight in 0.9% sodium chloride as drinking-water. The authors stated that all groups showed fluctuations of blood pressure. No indications of hypertension were observed, but there were no 0 mg barium/litre / 0.9% sodium chloride controls in the study. Electron microscopic examination of kidneys in all the rats in the blood pressure studies demonstrated no changes in arteriolar vessel walls or in tubules of the nephrons. However, structural changes in glomeruli were observed in the high-dose (150 mg barium/kg body weight per day) nephrectomized, Dahl salt-sensitive, and Dahl salt-resistant groups. No glomerular effects were seen at the next lower exposure level

in any group of rats.

Data on the toxicity of barium compounds in animals following inhalation exposure are limited to a study in which male albino rats were exposed to barium carbonate at 0, 1.15, or 5.20 mg/m^3 (0, 0.80, or 3.6 mg barium/m^3) for 4 h/day, 6 days/week, for 4 months (Tarasenko et al., 1977). At 5.20 mg/m^3 (but not 1.15 mg/m^3), reported alterations included a 21% decrease in body weight gain, a 32% increase in arterial pressure, altered haematological parameters, altered serum chemistry parameters, increased calcium levels in the urine, impaired liver function, and histological alterations in the heart, liver, kidneys, and lungs. The authors noted that the heart, liver, and kidneys "had a character of mild protein (‘granular’) dystrophy."

8.5 Long-term exposure and carcinogenicity

NTP (1994) treated male and female F344/N rats (60 animals per dose group per sex) with deionized drinking-water containing 0, 500, 1250, or 2500 mg barium chloride dihydrate/litre for 2 years. Daily doses of barium were estimated to be 0, 15, 30, or 60 mg/kg body weight for males and 0, 15, 45, or 75 mg/kg body weight for females. The animals were fed an NIH-07 mash diet; the barium content of the diet was not reported. In this study, neurobehavioural and cardiovascular tests were not performed. Reported exposure-related effects included reduced body weights in some mid-and high-dose rats, dose-related decreased water consumption, and significantly increased relative kidney weights in high-dose females (the only indication of potential adverse renal effects). Thus, the 2500 mg/litre exposure level (60 mg barium/kg body weight per day for males and 75 mg barium/kg body weight per day for females) may be a chronic NOAEL or LOAEL for rats, depending on interpretation of the increased relative kidney weight in females. When considered together with the results in the 13-week NTP (1994) study in rats, in which increased relative and absolute kidney weights were seen in female rats receiving 2000 mg barium/litre in drinking-water (115 mg barium/kg body weight per day) and kidney lesions accompanied by increases in relative and absolute kidney weights were seen in female rats at 4000 mg/litre (180 mg barium/kg body weight per day), the increased relative kidney weight in females of the 2-year study is suggestive of potential renal effects. Therefore, 75 mg barium/kg body weight per day is designated a chronic LOAEL and 45 mg barium/kg body weight per day a chronic NOAEL for female rats for renal effects in the NTP (1994) study. There were no significant increases in incidences of neoplasms in the barium-exposed rats. Significant negative trends were observed in the incidences of mononuclear cell leukaemia in male rats, benign and malignant adrenal pheochromocytoma in male rats, and mammary gland neoplasms (fibroadenoma, adenoma, or carcinoma) in female rats.

NTP (1994) also treated $B6C3F_1$ mice (60 animals per dose group per sex) with drinking-water containing 0, 500, 1250, or 2500 mg barium chloride dihydrate/litre for 2 years. Estimated daily doses were 0, 30, 75, or 160 mg barium/kg body weight for males and 0, 40, 90, or 200 mg barium/kg body weight for females. The animals were fed an NIH-07 mash diet; the barium con tent of the diet was not reported. Neurobehavioural and cardiovascular tests were not performed. At the 15-month interim evaluation, the absolute and relative spleen weights of the 2500 mg/litre female mice were significantly ($P \leq 0.01$) lower than those of the controls, and the absolute and relative thymus weights of the 2500 mg/litre male mice were marginally lower than those of the controls. Additionally, survival rates for the 2500 mg/litre mice at the end of study were significantly ($P \leq 0.01$) lower than those of the controls, which was attributed to chemical-related renal lesions. These renal lesions were characterized by tubule dilatation, renal tubule atrophy, tubule cell regeneration, hyaline cast formation, multifocal interstitial fibrosis, and the presence of crystals, primarily in the lumen of the renal tubules. Lymphoid depletions in the spleen, thymus, and lymph nodes were observed in 2500 mg/litre male and female mice, particularly in animals that died early, and were thought to be the result of debilitation associated with nephropathy. Thus, the chronic LOAEL in mice is 2500 mg/litre (160 mg barium/kg body weight per day for males and 200 mg barium/kg body weight per day for females). The next lower exposure level, 1250 mg/litre (75 mg barium/kg body weight

per day in males and 90 mg barium/kg body weight per day in females), is a chronic NOAEL. 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.

Schroeder & Mitchener (1975a) exposed Long-Evans rats (52 per sex per group) to 0 or 5 mg barium/ litre (as barium acetate) in drinking-water from weaning to natural death (approximately 2 years). Dosages from drinking-water were 0.61 mg barium/kg body weight per day for males and 0.67 mg barium/kg body weight per day for females based on reference body weights and water intakes from US EPA (1988). The diet was characterized as a "low metal" diet, and it included 60% rye flour, 30% dried skim milk, 9% corn oil, 1% iodized chloride, and assorted vitamins; the barium content was not reported. Barium had no significant effect on the growth of males, but increased the growth of older females. The incidence of proteinuria in males exposed to barium for approximately 152 days (at 173 days of age) was significantly higher than in controls. Female rats at 532 and 773 days of age had higher serum choles terol concentrations, and males at these ages had serum glucose levels different from controls; the authors attached no biological or toxicological significance to these serum chemistry results. Histopathology of heart, lung, kidney, liver, and spleen did not reveal alterations. No significant increases in the number of gross tumours were observed in the barium-exposed male or female rats.

Kopp et al. (1985) treated weanling female Long-Evans rats with barium chloride in their drinking-water (100 mg/litre) for 16 months and compared them with a control group supplied with water containing no barium. All animals received a standard rye-based diet, low in heavy metal content. Random batches of this feed were assayed for metal content and contained 1.5 µg barium/g feed. Average final body weights for both groups were found to be the same (control, 421 g; 100 mg barium/litre, 431 g). Furthermore, the measured haematological characteristics as well as feed and water consumption were not affected during the 16-month experiment. However, a significant increase in the average systemic blood pressure was detected in the barium-exposed rats after 1 month exposure and thereafter.

In similarly exposed Charles River CD white-mice (36–54 per sex) (Schroeder & Mitchener, 1975b), dosages from drinking-water were 1.18 mg barium/kg body weight per day for males and 1.20 mg barium/kg body weight per day for females (US EPA, 1988). Growth and body weights were not affected by the barium treatment. Histology of the heart, lung, liver, kidney, and spleen was normal. In males, longevity (defined as the mean life span of the last surviving five animals of each sex in each treatment group) was significantly reduced. The mean life span, however, was not affected. The incidences of lymphoma leukaemia and lung tumours in the male and female mice exposed to barium were not significantly different from the inci dences in the control mice.

Perry et al. (1983, 1985, 1989) exposed female weanling Long-Evans rats to 0, 1, 10, or 100 mg barium/ litre (as barium chloride) in drinking-water for 1, 4, and 16 months. Drinking-water was fortified with five essential metals (1 mg molybdenum/litre, 1 mg cobalt/ litre, 5 mg copper/litre, 10 mg manganese/litre, and 50 mg zinc/litre). All animals received a rye-based diet with low trace metal content based on that used by Schroeder & Mitchener (1975a,b). After 8 months of exposure to 10 mg/litre, mean systolic blood pressure had increased by 6 mmHg (800 Pa) and continued to be significantly elevated through 16 months (+4 mmHg [530 Pa]). Significant increases in mean systolic blood pressure were evident at 100 mg/litre starting at 1 month (+12 mmHg [1600 Pa]) and continuing through 16 months (+16 mmHg [2130 Pa]). An additional 12 rats, exposed for 16 months to 100 mg/litre, exhibited a reduction of ATP and phosphocreatinine content of the myocardium, depressed rates of cardiac contraction, and depressed electrical excitability (compared with 18 control rats). Since this study used a diet low in essential metals, specifically calcium, the observation of barium chloride-related effects on hypertension in rats is of questionable significance to humans.

8.6 Genotoxicity and related end-points

There is a limited amount of information available on the genotoxicity of barium compounds. No *in vivo* studies have been conducted. Most *in vitro* studies have found that barium chloride and barium nitrate did not induce gene mutations in bacterial assays with or with out metabolic activation. Ames assays with *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA97, TA98, and TA100 with or without metabolic activation (Monaco et al., 1990, 1991; NTP, 1994), rec assays with *Bacillus subtilis* strains H17 and H45 (Nishioka, 1975; Kanematsu et al., 1980), and a microscreen assay with *Escherichia coli* with metabolic activation (Rossman et al., 1991) have produced negative results with barium chloride. Negative results have also been observed for barium nitrate in the rec assay using *B. subtilis* strains H17 and H45 (Kanematsu et al., 1980). Barium chloride induced gene mutations in L5178Y mouse lymphoma cells with, but not without, metabolic activation (NTP, 1994). Neither barium acetate nor barium chloride decreased the fidelity of DNA synthesis in avian myeloblastosis virus DNA polymerase (Sirover & Loeb, 1976). In mammalian cells, barium chloride did not induce sister chromatid exchanges or chromosomal aberrations in cultured Chinese hamster ovary cells, with or without activation (NTP, 1994). In summary, except for the mouse lymphoma assay, results of *in vitro* tests have been generally negative.

8.7 Reproductive toxicity

Data on the reproductive and developmental toxicity of barium compounds are limited. Decreased ovary weight and ovary/brain weight ratio were seen in female rats administered oral gavage doses of 198 mg barium/kg body weight per day, once a day for 10 days (Borzelleca et al., 1988). In single-generation reproductive toxicity studies in rats and mice (Dietz et al., 1992), groups of 20 male and 20 female F344/N rats and $B6C3F_1$ mice were exposed to barium chloride dihydrate in drinking-water for up to 60 days. The barium chloride dihydrate concentrations were 0, 1000, 2000, or 4000 mg/litre (estimated by the authors to be 0, 50, 100, and 200 mg/kg body weight per day) for the rats and 0, 500, 1000, or 2000 mg/litre (estimated by the authors to be 0, 50, 100, and 200 mg/kg body weight per day) for the mice. The authors measured weekly body weight changes and water consumption, which were used to estimate daily barium exposure in both mice and rats. After the completion of the exposure period (60 days), males and females from the same dosage groups were housed together until there was evidence of mating or until the end of the mating period (8 days). This rodent study reported fertility index, fetal and maternal toxicity, and developmental toxicity end-points in fetus and neonates. There were no indications of reproductive or developmental toxicity in any of the exposure groups. However, the results should be interpreted cautiously because of below-normal pregnancy rates in all groups of exposed, as well as control, rats and mice.

Ridgeway & Kanofsky (1952) examined the developmental toxicity of barium by injecting 20 mg barium chloride into the yolk sac of developing chick embryos. When injection was made on day 8 of development, developmental defects were observed in toes. In contrast, no effects were seen when injection was made on day 4 of development.

Tarasenko et al. (1977) also reported that a shortening of the mean duration of the estrous cycle and an alteration in the proportion of mature and dying ovarian follicles were observed in rats exposed to 13.4 mg bar ium carbonate/m^3 (9.3 mg barium/m^3) for 4 months, compared with a control group. These effects were not observed in rats exposed to 3.1 mg/m^3 (2.2 mg barium/ m^3). The authors also reported that rats in the 13.4 mg/ m^3 group gave birth to underdeveloped offspring that showed considerable mortality and slow body weight gain during the first 2 postnatal months.

8.8 Immunological and neurological effects

Only limited information is available on the immunotoxicity and neurotoxicity of barium compounds (IPCS, 1990). Intravenous infusion of barium chloride into anaesthetized dogs resulted in muscle flaccidity and paralysis, which appeared to result from severe hypo potassaemia (Roza & Berman, 1971).

9. EFFECTS ON HUMANS

9.1 Case reports

Intentional or accidental ingestion of barium compounds (i.e., barium carbonate, barium chloride) causes gastroenteritis (vomiting, diarrhoea, abdominal pain), hypopotassaemia, hypertension, cardiac arrhythmias, and skeletal muscle paralysis. Potassium infusion is used clinically to reverse the toxic effects of barium (Diengott et al., 1964; Gould et al., 1973; IPCS, 1990; US EPA, 1990, 1998).

According to RTECS (1985), the lowest lethal acute oral doses for barium chloride and barium carbonate are 11.4 and 57 mg/kg body weight, respectively; for barium carbonate, a dose as low as 29 mg/kg body weight causes flaccid paralysis, paraesthesia, and muscle weakness.

Opacities were detected on lung X-rays of three patients for up to 2 years following accidental aspiration of barium sulfate orally administered for observation of the gastrointestinal tract (Buschman, 1991).

In a case report involving the grinding of barite ore, a worker was exposed over a period of 10 years to extremely high total dust concentrations (approximately 212 000 particles/cm^3 for 1.5 h and 60 000 particles/cm^3 for 1 h), although it was not stated how these measurements were made (Pendergrass & Greening, 1953). Analysis indicated that 49% of the workplace airborne dust was barium sulfate, although particle size was not stated. After 2 years of exposure to the barite ore dust, fine nodulation was observed on lung X-rays, apparently due to the presence of barium sulfate. The presence of barium sulfate in the lung tissue was confirmed by chemical analysis and light microscopy at autopsy 11 years after cessation of exposure. Several histo pathological findings were observed, including fibrosis (although mostly characteristic of silicosis). The histo pathological findings were considered to be due to the silica and anthracite exposure; the X-ray opacities seen were attributed to the presence of the barium sulfate.

In an extensive study, temperature and pulse rate measurements were taken as an indication of an acute inflammatory response for 291 humans administered a single unstated dose of a 50% w/v barium sulfate suspension for bronchographic purposes (Nelson et al., 1964). The method of administration was unstated, but the suspension was presumed to have been instilled into the trachea and then blown into the lungs. In 154 patients, there was radiological evidence of the presence of barium sulfate in the bronchial tree at the time of the last available X-ray (various time points ranging from <1 week to >1 year after administration); in 135 patients, on the other hand, there was no radiological evidence of residual barium sulfate in the lungs 1 year after bronchography. Forty-one of these patients exhibited complete elimination of the barium sulfate from the lungs within 1 week; it was stated that in some of these patients, this clearance occurred within 24 h.

Wones et al. (1990) administered 1.5 litres/day of distilled drinking-water containing various levels of barium chloride to 11 healthy male volunteers aged 27–61 years (mean 39.5 years, median 41 years). None of the subjects was taking any medications, and none had

hypertension, diabetes, or cardiovascular disease. Barium concentrations in the drinking-water consumed by the subjects prior to the study were known to be very low. No barium was added for the first 2 weeks, which served as a control period; drinking-water containing 5 mg barium/litre (0.14 mg barium/kg body weight per day using reference values of 2 litres/day for water consumption and 70 kg for body weight) was administered for the next 4 weeks, and drinking-water containing 10 mg barium/litre (0.21 mg barium/kg body weight per day) was administered for the last 4 weeks of the study. Diets were controlled to mimic US dietary practices (barium content of the diet was not determined, but the authors mentioned that a typical hospital diet provides 0.75 mg barium/day, or 0.011 mg barium/kg body weight per day using a 70-kg reference weight). All beverages and food were provided, and subjects were instructed to consume only what was provided. The sub jects were also instructed to keep their level of exercise constant and to abstain from alcohol, and smokers were told to smoke consistently throughout the study. Systolic and diastolic blood pressures were measured in the morning and evening. Blood was collected at the beginning and periodically, particularly as four consecutive daily samples at the end of each of the three study periods. Twenty-four-hour urine collections were per formed at the end of each study period. Twenty-four-hour continuous electrocardiographic monitoring was performed on 2 consecutive days at the end of each study period.

Blood pressures were not significantly affected by barium exposure (Wones et al., 1990). A trend towards increased total serum calcium with barium exposure was noted but was not considered to be clinically significant. No significant changes were observed in plasma total cholesterol, triglycerides, low-density lipoprotein (LDL) or high-density lipoprotein (HDL) cholesterol, LDL:HDL ratio, and apolipoproteins A1, A2, and B. Serum glucose, albumin, and potassium levels and urinary levels of sodium, potassium, or metanephrines (catecholamine breakdown products) were unchanged. Electrocardiograms revealed no changes in cardiac cycle intervals, including the QT interval; the study authors noted that the lack of shortening of the QT interval provided evidence that the slight increase in serum calcium was not clinically significant. In addition, no significant arrhythmias, no increase in ventricular irritability, and no apparent conduction problems were seen with barium exposure. This study did not identify a LOAEL; the NOAEL is 0.21 mg barium/kg body weight per day.

Transient cell transformations resembling severe premalignant dysplasia were noted following single topical applications (four times at intervals of 4– 6 weeks) of 1.25 mmol barium chloride/litre to the cervix of a woman with no known history of abnormal cervical cytology (Ayre, 1966). In another case (Ayre & LeGuerrier, 1967), cell transformations similar to extreme dysplasia and resembling cell findings of cancer *in situ* were observed following a single topical appli cation of 1.25 mmol barium chloride/litre (mixed with equal amounts of 70% dimethylsulfoxide) to the cervix.

9.2 Epidemiological studies

Brenniman & Levy (1984) reported an ecological epidemiological study of mortality and morbidity in populations living in communities in Illinois, USA, with elevated levels of barium in municipal drinking-water (2–10 mg/litre, 0.06–0.3 mg barium/kg body weight per day assuming water consumption of 2 litres/day and weight of 70 kg) or low levels of barium in drinking-water (0.2 mg/litre, 0.006 mg barium/kg body weight per day). Barium was the only drinking-water contaminant that exceeded drinking-water regulations of the time in any of the public drinking-water supplies. The communities were matched for demographic character istics and socioeconomic status. Communities that were industrialized or geographically different were excluded. Although the study attempted to exclude communities with high rates of population change, two of the four high-barium communities had about 75% change in population between 1960 and 1970; these were kept in the study for lack of satisfactory replacements.

In the mortality study (Brenniman & Levy, 1984), age-adjusted mortality rates for cardiovascular diseases (combined), heart diseases

(arteriosclerosis), and all causes for both sexes together were significantly higher in the elevated-barium communities compared with the low-barium communities for the years 1971–1975. These differences were largely confined to the population 65 years of age or older. This study did not measure the barium exposure of individual subjects and did not control for several important variables, such as population mobility (approximately 75% turnover in two of the four high-barium communities from 1960 to 1970), use of water softeners that would remove barium from and add sodium to the water supply, use of medication by study subjects, and other risk factors, such as smoking, diet, and exercise. As a result, it is not possible to assign a causal relationship between mortality and exposure to barium.

The morbidity study (Brenniman & Levy, 1984) was conducted on two Illinois, USA, 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 concentration in McHenry's drinking-water was 0.1 mg barium/litre, whereas the mean concentration in West Dundee's drinking-water was 7.3 mg barium/litre. The levels of other minerals in the drinking-water of the two communities were stated to be similar. Subjects (2000) 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. All subjects underwent three blood pressure measurements (taken over a 20-min period with a calibrated electronic blood pressure apparatus) and responded to a health questionnaire that included such variables as sex, age, weight, height, smoking habits, family history, occupation, medication, and physician-diagnosed heart disease, stroke, and renal disease. Data were analysed using the signed rank test for age-specific rates, the weighted Z test for prevalence rates, and analysis of variance for blood pressures. No significant differences in mean systolic or diastolic blood pressures or in history of hypertension, heart disease, stroke, or kidney disease (which included serum and urinary protein and creatinine levels) were found for men or women of the two communities. A more controlled study was con ducted 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 barium/litre, 0.0029 mg barium/kg body weight per day assuming water ingestion of 2 litres/day and 70-kg body weight) and elevated-barium communities (7.3 mg barium/litre, 0.21 mg barium/kg body weight per day).

The database on the toxicity of inhaled barium compounds in humans consists primarily of studies of occupational exposure to barium sulfate or barite ore or to unspecified soluble barium compounds. Several case reports (e.g., Pendergrass & Greening, 1953; Seaton et al., 1986) and a prospective study conducted by Doig (1976) have reported baritosis in barium-exposed workers. Baritosis is considered to be a benign pneumoconiosis resulting from the inhalation of barite ore or barium sulfate. The most outstanding feature of baritosis is the intense radiopacity of the discrete opacities that are usually profusely disseminated throughout the lung fields; in some cases, the opacities may be so numerous that they appear confluent. The Third Conference of Experts on Pneumoconiosis (ACGIH, 1992) noted that barium sulfate produced a non-collagenous type of pneumoconiosis in which there is a minimal stromal reaction that consists mainly of reticulin fibres, intact alveolar architecture, and potentially reversible lesions. The available human data on baritosis suggest that the accumulation of barium in the lungs does not result in medical disability or symptomatology. A decline in the profusion and opacity density, suggesting a decrease in the amount of accumulated barium in the lung, has been observed several years after termination of exposure.

Doig (1976) reported on a series of cross-sectional examinations of workers at a barite grinding facility. During the initial investigation in 1947, five workers employed for more than 3.5 years were examined. No evidence of baritosis was observed in any of the workers. In 1961, eight workers (26–45 years of age, mean 32 years) employed for 3.5–18 years (mean 9 years) were examined (one of these workers was also examined in 1947). Seven of the workers reported no respiratory symptoms; one worker reported a slight occasional cough. No abnormal symptoms were noted during the physical examination of seven of the workers; crepitations dispelled by cough were observed in one worker

(not the same worker reporting an occasional cough). Pneumoconiosis was detected in the radiographs of seven workers. Three other workers employed for 1 month to 1 year were also examined in 1961. Two of these workers reported having slight coughs, but no abnormal findings were observed during the physical examination, and the chest radiographs were normal. The concentration of barium in the dust was not measured. Barite samples were analysed for quartz, silica, and iron content. No quartz was detected, and the total silica and total iron (as iron oxide) concentrations were 0.07–1.96% and 0.03–0.89%, respectively.

Ten of the 11 workers examined in 1961 were re-examined in 1963 (18 months later) (Doig, 1976). Two new cases of pneumoconiosis were diagnosed. Thus, 9 of 10 workers exposed to barium sulfate for 1.5– 19.5 years (mean 8.2 years) had well-marked baritosis. Three of these workers reported a slight or occasional cough, and none had dyspnoea. Among the nine workers with baritosis, three did not smoke, four smoked 1 pack/day, and two smoked >1 pack/day. In six of the seven workers with previously diagnosed baritosis, no significant changes in the degree of pneumoconiosis were observed; an increase in the number of opacities was observed in the seventh worker. Spirometric lung function tests (vital capacity, flow rate, and forced expiratory volume) were performed in five workers. For three of these workers, the results of the lung function tests were similar to predicted normal values (89–119% of predicted values). Lung function was below normal in the other two workers (70–85% of predicted values). It is questionable whether the impaired lung function was related to barium exposure. One of the two workers was an alcoholic and heavy smoker, and the other had a fibrotic right middle lung lobe that probably resulted from a childhood illness.

The barite grinding facility closed in 1964, and follow-up examinations were performed in 1966, 1969, and 1973 on five of the workers (Doig, 1976). Termination of barium exposure resulted in a decline in the profusion and density of opacities. In 1966, there was a slight clearing of opacities; by 1973, there was a marked decrease in profusion and density. No significant changes in lung function were observed during this 10-year period.

NIOSH (1982) conducted a health survey of past and present workers at the Sherwin Williams Company's Coffeyville, Kansas, USA, facility. Work performed at the facility included grinding, blending, and mixing mineral ores. At the time of the study, four processes were in operation: "ozide process," which involved blending several grades of zinc oxide; "ozark process," which involved bagging very pure zinc oxide powder; "bayrite process," which involved grinding and mixing several grades of barium-containing ores; and "sher-tone process," which involved mixing inert clays with animal tallow. A medical evaluation was performed on 61 current workers (91% participation). Information on demographics, frequency of various symptoms occurring during the previous 2 months, chemical exposure, occupational history, and smoking history, as well as history of renal disease, allergies, and hypertension, was obtained from directed questionnaires. In addition, spot urine and blood samples and blood pressure measurements were taken. Exposures to barium, lead, cadmium, and zinc were estimated from 27 personal samples collected over a 2-day period. In the seven personal breathing-zone samples collected from the bayrite area, the levels of soluble barium ranged from 87.3 to 1920.0 mg/m^3 (mean 1068.5 mg/m^3), lead levels ranged from not detected to 15.0 mg/m^3 (mean 12.2 mg/m^3, excluding two samples in which lead was not detected), zinc levels ranged from 22.4 to 132.0 mg/m^3 (mean 72 mg/m^3), and all seven samples had no detectable levels of cadmium. Soluble barium was also detected in breathing-zone samples in the ozark area (10.6–1397.0 mg/m^3, mean 196.1 mg/m^3), ozide area (11.6–99.5 mg/m^3, mean 46.8 mg/m^3), and sher-tone area (114.3–167.5 mg/m^3, mean 70.45 mg/m^3).

Two approaches were used to analyse the results of the health survey (NIOSH, 1982). In the first approach, the workers were divided into five groups based on current job assignments. Of the 61 current workers, 14 worked in the bayrite area (mean duration 3 years). No statistically

significant increases in the incidence of subjective symptoms (e.g., headache, cough, nausea) or differences in mean blood lead levels, number of workers with blood lead levels greater than 39 mg/dl, mean free erythrocyte protoporphyrin (FEP) levels, mean haematocrit levels, mean serum creatinine levels, number of workers with serum creatinine levels greater than 1.5 mg/dl, number of workers with blood urea nitrogen (BUN) levels greater than 20 mg/dl, blood pressure, or mean urine cadmium levels were observed between the different groups of workers. In the second approach, the workers were divided into seven groups based on past job assignments. One group consisted of 12 workers working in barium process areas (bayrite process and other processes no longer in operation at the facility that involved exposure to barium ores and barium carbonate) for at least 5 years; barium exposure levels were not reported for this group of workers. The results of the health survey for the barium-exposed workers were compared with results for 25 workers who stated that they had never worked in barium process areas. No statistically significant differences in mean age, number of years employed, number of current or past smokers, prevalence of subjective symptoms, mean FEP levels, mean haematocrit levels, mean urine cadmium levels, mean *beta*-2-microglobulin levels, or the prevalence of workers with elevated serum creatinine, BUN, or urine protein levels were observed between the two groups. The number of workers with elevated blood pressure (defined as systolic pressure >140 mmHg [>18.7 kPa] or diastolic pressure >90 mmHg [>12 kPa] or taking medication for hypertension) was significantly higher in the barium-exposed group than in the comparison group. The number of workers in the barium group with blood lead levels of >39 mg/dl was lower than in the comparison group; however, the difference was not statistically significant. Additionally, there was no sig nificant difference between mean blood lead levels in the barium-exposed workers (24 mg/dl) and the compar ison group (32 mg/dl).

The health effects associated with occupational exposure to barium during arc welding with barium-containing stick electrodes and flux-cored wires were investigated by Zschiesche et al. (1992). A group of 18 healthy welders not using barium-containing consumables in the past 10 days was divided into three groups: group A (n = 8, mean age 30.4 years) performed arc welding with barium-containing stick electrodes, group B (n = 5, mean age 43.6 years) performed arc welding with barium-containing self-shielded flux-cored wires, and group C (n = 5, mean age 32.0 years) performed arc welding with barium-containing self-shielded flux-cored wires using welding guns with built-in ventilation systems. All welders performed welding with barium-free consumables on Thursday and Friday of the first week of the study. Barium-containing consumables were used during week 2 of the study and on Monday of week 3. The subjects welded for an average of 4 h/day. The average barium concentrations in the breathing zones were 4.4 (range 0.1–22.7), 2.0 (0.3–6.0), and 0.3 (0.1–1.5) mg/m^3 for groups A, B, and C, respectively. No exposure-related subjective adverse health symptoms or neurological signs were found. No significant differences between pre- and post-shift electrocardiogram, pulse rate, whole-blood pH, base excess and standard bicarbonate, or plasma concen trations of sodium, magnesium, and total and ionized calcium were observed. During week 2, decreases in plasma potassium concentrations were observed in groups A and C; the levels returned to the normal range under continuation of barium exposure and were not statistically different from levels during week 1 (no barium exposure). This drop in serum potassium levels was not observed in group B, which had a barium exposure level similar to that of group A.

10. EFFECTS ON OTHER ORGANISMS IN THE LABORATORY AND FIELD

10.1 Aquatic environment

Toxicity of barium to selected aquatic organisms is summarized in Table 2. A 48-h no-observed-effect level (NOEL) of 68 mg/litre was calculated for water fleas (*Daphnia magna*) exposed to various concentrations of barium (LeBlanc, 1980). In contrast, Biesinger &

Christensen (1972) reported 48-h and 21-day LC_{50} values of 14.5 and 13.5 mg/litre, respectively, a 16% impairment of reproduction at 5.8 mg/litre, and a 50% impairment at 8.9 mg/litre during the 21-day tests. Khangarot & Ray (1989) reported 24- and 48-h EC_{50} (the concentration resulting in 50% immobilization) values of 52.8 and 32.0 mg/litre, respectively, for daphnids exposed to barium sulfate. A reported 48-h EC_{50} value for developmental effects in the mussel *Mytilus californianus* was 0.189 mg/litre (Spangenberg & Cherr, 1996). For two aquatic amphipod species (*Gammarus pulex* and *Echinogammarus berilloni*), Vincent et al. (1986) reported 24-, 48-, 72-, and 96-h LC_{50} values of 3980, 395, 255, and 238 mg/litre and 336, 258, 162, and 122 mg/litre, respectively, in eucalcic water; LC_{50} values in oligocalcic water were 1260, 533, 337, and 227 mg/litre and 308, 197, 151, and 129 mg/litre, respectively. The 30-day LC_{50} values for two species of crayfish ranged from 39 to 61 mg/litre; the 96-h values were comparable (Boutet & Chaisemartin, 1973). Heitmuller et al. (1981) reported a NOEL in the sheepshead minnow (*Cyprinodon variegatus*) of 500 mg/litre.

Growth of *Anacystis nidulans* (a cyanobacterium) in an environment containing 50 mg barium chloride/ litre was similar to that of controls. Higher concentrations of barium resulted in a concentration-related increase in growth inhibition; almost complete inhibition was reported at barium chloride concentrations ≥750 mg/litre (Lee & Lustigman, 1996). Wang (1986) reported a 96-h EC_{50} (growth) of 26 mg barium/litre in duckweed (*Lemna minor*) in deionized water. However, in river water, barium showed no toxic effect on growth of duckweed. The lack of an adverse effect in the river water was shown to be due to precipitation of barium from the river water as sulfate. Stanley (1974) investigated the toxic effects of barium on the growth of Eurasian watermilfoil (*Myriophyllum spicatum*). Root weight was the most sensitive parameter measured and showed a 50% reduction, relative to controls, at a barium concentration of 41.2 mg/litre.

Table 2: Toxicity of barium to selected aquatic organisms.[a]

Organism	Static/ flow[b]	Temperature (°C)	pH	Hardness (mg/litre)	Duration	LC_{50}/EC_{50} (mg/litre)	Reference
Water flea (*Daphnia magna*) (fresh water)	static	21–23	7.4–9.4	173	24 h	LC_{50} >530	LeBlanc (1980)
	static	21–23	7.4–9.4	173	48 h	LC_{50} 410 (320–530)	
			7.4–8.2	44–53	48 h	LC_{50} 14.5	Biesinger & Christensen (1972)
			7.4–8.2	44–53	21 days	LC_{50} 13.5[c] (12.2–15.0)	
	static	11.5–14.5	7.2–7.8	235–260	24 h	EC_{50} 52.8[d]	Khangarot & Ray (1989)
	static	11.5–14.5	7.2–7.8	235–260	48 h	EC_{50} 32.0[d]	

Crayfish (*Orconectes limosus*) (fresh water)	flow	15–17	7.0		96 h	LC_{50} 78	Boutet & Chaisemartin (1973)
	flow	15–17	7.0		30 days	LC_{50} 59	
	flow	15–17	7.0		30 days	LC_{50} 61[c]	
Crayfish (*Austropotamobius pallipes pallipes*) (fresh water)	flow	15–17	7.0		96 h	LC_{50} 46	
	flow	15–17	7.0		30 days	LC_{50} 39	
	flow	15–17	7		30 days	LC_{50} 43[c]	
Sheepshead minnow (*Cyprinodon variegatus*) (marine water)	static	25–31		10–31[e]	96 h	LC_{50} >500	Heitmuller et al. (1981)

a Adapted from IPCS (1990).

b static = static conditions (water unchanged for the duration of the test); flow = intermittent flow-through conditions.

c Test conducted with a food source.

d EC_{50} = concentration resulting in 50% immobilization.

e Salinity ($^{0}/_{00}$).

Barium sulfate is the principal constituent of drilling muds used in oil drilling operations. These muds also contain metals other than barium. No deaths occurred in a number of unspecified marine fish, crustaceans, and molluscs exposed to various levels (as high as 7500 mg/kg) of drilling mud for an unspecified period of time (Daugherty, 1951). Other studies reported reduced populations of molluscs and/or annelids exposed to barite in estuarine water, but it could not be determined whether the results were due to larval avoidance of barite or to barite toxicity (Tagatz & Tobia, 1978; Cantelmo et al., 1979).

10.2 Terrestrial environment

In general, barium has been shown to inhibit the growth of bacteria, fungi, mosses, and algae (IPCS, 1990). Other relevant information was not identified.

11. EFFECTS EVALUATION

11.1 Evaluation of health effects

11.1.1 Hazard identification and dose–response assessment

Barium enters the body primarily through the inhalation and ingestion processes. The degree of absorption of barium from the lungs and gastrointestinal tract varies according to animal species, solubility of the compound, and age of the animal. Studies in rats using a soluble salt (barium chloride) have indicated that the absorbed barium ions are distributed via the blood and deposited primarily in the skeleton.

The principal route of elimination for barium following oral, inhalation, or intratracheal administration is in the faeces. Following introduction into the respira tory tract, the appearance of barium sulfate in the faeces represents mucociliary clearance from the lungs and subsequent ingestion.

In humans, ingestion (accidental or intentional) of barium compounds may cause gastroenteritis (vomit ing, diarrhoea, abdominal pain), hypopotassaemia, hypertension, cardiac arrhythmias, and skeletal muscle paralysis (IPCS, 1990; US EPA, 1990, 1998; ATSDR, 1992). The toxicity is dependent on the water solubility of the barium compound; the lack of case reports of systemic toxicity despite the routine oral administration for many years of approximately 450 g barium sulfate as a radiocontrast medium indicates that this practically insoluble barium compound is not toxic by the oral route. Due to its limited absorption by the dermal route, systemic toxicity is not anticipated.

Medium- and long-term oral exposure animal studies (McCauley et al., 1985; NTP, 1994) provide evidence that the kidney is a sensitive target of barium toxicity in rats and mice fed a nutritionally adequate diet. Hypertension has been observed in studies in which rats were fed a marginally adequate diet, particularly one with inadequate calcium levels (Perry et al., 1983, 1985, 1989).

Although limited due to the small population size (2000) and lack of individual measurements of expo sure, longer-term human studies (Brenniman & Levy, 1984; Wones et al., 1990) have not found adverse effects following oral exposure to relatively low concentrations of barium in drinking-water.

Inhalation of barium carbonate powder was associated with hypopotassaemic paralysis in a male worker (Shankle & Keane, 1988).

Several case reports (Pendergrass & Greening, 1953; Seaton et al., 1986) and a cross-sectional examination of workers at a barite grinding facility reported by Doig (1976) indicated reversible baritosis in workers exposed to airborne barite ore or barium sulfate. Upon exposure termination, there was an apparent decrease in barium levels in the lung (Doig, 1976); the barium-related lesions were also potentially reversible (ACGIH, 1992). A NIOSH (1982) survey indicated prevalence of hypertension in workers exposed to an unspecified concentration of barium; these results should be interpreted cautiously, because it is likely that the workers were also exposed to other metals, including lead, which has a known hypertensive effect.

Data on the toxicity of inhaled barium to animals are limited; studies have deficiencies that preclude their usefulness for hazard identification or dose–response assessment.

A reproductive/developmental toxicity study did not find any significant alterations in reproductive end-points or in gestation length, pup survival, or occurrence of external abnormalities in rats and mice exposed to barium chloride in drinking-water (Dietz et al., 1992). The low

pregnancy rates in all groups, including controls, limit the usefulness of this study.

Oral exposure studies in rats and mice (Schroeder & Mitchener, 1975a,b; McCauley et al., 1985; NTP, 1994) did not find significant increases in tumour incidence following long-term exposure. The design of the McCauley et al. (1985) and Schroeder & Mitchener (1975a,b) studies was inadequate for carcinogenicity evaluation. In the McCauley et al. (1985) study, small numbers of animals of one sex were exposed to relatively low concentrations of barium chloride for less than a lifetime. The absence of adverse effects suggests that the maximum tolerated dose (MTD) may not have been achieved in this study. In the Schroeder & Mitchener (1975a) rat study, only the incidence of total gross tumours was reported; the lack of adverse effects suggests that the only dose used was lower than the MTD. The decrease in longevity in the mouse study by Schroeder & Mitchener (1975b) suggests that the MTD may have been achieved in this study. However, it appears that only two types of cancer were examined (leukaemia and lung tumours).

The design of the rat and mouse NTP (1994) oral studies was adequate to assess carcinogenicity. These studies used an adequate number of animals per group, exposed animals for 2 years, tested several dosage levels, and examined an extensive number of tissues. The decreased survival and histological alterations in the kidneys of the mice and the increased kidney weights in the rats suggest that the MTD was achieved in both of these studies. No carcinogenic effects were observed in either species. In fact, significant negative trends in the incidence of leukaemia, adrenal tumours, and mammary gland tumours were observed in the rats.

Available data indicate that barium salts would not be expected to have genotoxic potential, and the weight of evidence from *in vitro* studies is negative.

Topical and ocular applications of barium nitrate caused skin and eye irritation in rabbits. Barium hydroxide and barium oxide irritate the eye, skin, and respiratory tract. Physicochemical properties of barium sulfate and the lack of reports of skin or eye irritation in humans despite its widespread use, particularly for X-ray purposes, suggest that barium sulfate is not irritating or corrosive to either skin or eyes. Similarly, there is a lack of reports of either skin or respiratory tract sensitization, suggesting that barium sulfate is not a sensitizer.

11.1.2 Criteria for setting tolerable intakes/ concentrations or guidance values for barium and barium compounds

No single study is appropriate as the basis for a lifetime tolerable intake for barium. The US EPA (1998) developed a reference dose (RfD) of 0.07 mg/kg body weight per day with a uncertainty factor of 3 applied to a NOAEL of 0.21 mg/kg body weight per day for barium based on a weight-of-evidence approach that focuses on four co-principal studies: the Wones et al. (1990) experimental study in humans, the Brenniman & Levy (1984) epidemiological study, and the medium- and long-term exposure rat studies that employed adequate diets and investigated both cardiovascular and renal end-points (NTP, 1994). The McCauley et al. (1985) study of unilaterally nephrectomized rats was used to support the identification of the kidney as a co-critical target. In addition, the approach includes a consideration of supporting information from single-exposure and mechanistic studies as well as from medium-term and long-term exposure studies of animals on low-mineral diets.

The identification of hypertension as a health end-point of concern is supported by findings of hypertensive effects in humans who ingested acutely high doses of barium compounds, in workers who inhaled dusts of barium ores and barium carbonate, in experimental animals given barium intravenously, and in rats exposed to barium in drinking-water while on restricted diets. Based on these findings, lower-dose human studies were conducted to examine the potential effects on blood pressure in humans and on both blood pressure and kidney function in animals. Although the experimental study by Wones et al. (1990), together with the epidemiological study by Brenniman & Levy (1984), did

not report any significant effects on blood pressure, they establish a NOAEL in humans of 0.21 mg barium/kg body weight per day. The animal data suggest that the kidney may also be a sensitive target for ingested barium from low-level exposure (Schroeder & Mitchener, 1975a; NTP, 1984; McCauley et al., 1985); although the human studies investigated hypertensive effects, the clinical surveillance data did not uncover any renal dysfunction or any other health abnormalities. There fore, 0.21 mg barium/kg body weight per day is used as the basis to derive the tolerable intake for barium. The use of a NOAEL from human studies increases the confidence in the derivation of the tolerable intake value, which is defined as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

Therefore, the tolerable intake can be calculated as the NOAEL of 0.21 mg/kg body weight per day divided by an uncertainty factor of 10 to account for some data base deficiencies and potential differences between adults and children, giving a tolerable intake of 0.02 mg/kg body weight per day.

Regarding inhalation exposure, the human (Pendergrass & Greening, 1953; Doig, 1976; Seaton et al., 1986) and animal inhalation (Muller, 1973; Tarasenko et al., 1977) and intratracheal (Tarasenko et al., 1977; Uchiyama et al., 1995) studies suggest that the respiratory system is a target of barium toxicity. The data also suggest that systemic effects, such as hyper tension, may occur following inhalation exposure (Tarasenko et al., 1977; NIOSH, 1982; Zschiesche et al., 1992). The human studies cannot be used to derive a reference concentration (RfC) for barium because exposure concentrations were not reported. Although the NIOSH (1982) study measured barium breathing-zone levels for some groups of workers, the barium exposure levels were not measured in the group of workers with the increased incidence of hypertension. The deficient reporting of the methods and results of the only animal medium-term/long-term inhalation exposure studies (Muller, 1973; Tarasenko et al., 1977) precludes deriving an RfC for barium from the animal data.

Under EPA's Guidelines for Carcinogen Risk Assessment (US EPA, 1986), barium would be classified as Group D, not classifiable as to human carcinogenicity. Although adequate long-term oral exposure studies in rats and mice have not demonstrated carcinogenic effects, the lack of adequate inhalation studies precludes an assessment of the carcinogenic potential of inhaled barium. Under the Proposed Guidelines for Carcinogen Risk Assessment (US EPA, 1996, 1999), barium is considered not likely to be carcinogenic to humans following oral exposure, and its carcinogenic potential cannot be determined following inhalation exposure. Thus, derivation of slope factors and unit risk values is precluded.

Barium compounds exhibit close relationships with calcium and strontium, which are also alkaline earth metals. Owing to its similarity to calcium in its chemical properties and because it lies below calcium in the periodic table, barium is thought to interact with calcium through biochemical pathways involving calcium binding protein and compete for binding sites (IPCS, 1990). Hypertensive effects of barium in rats (Perry et al., 1989) may have been due to inadequate calcium levels in the diet.

11.1.3 Sample risk characterization

There are a number of different approaches to assessing the risks to human health posed by chemicals. For example, barium sulfate is the most likely substance of occupational concern and is of very low toxicity. Since exposure estimates can vary widely, the risk characterizations below are provided as examples for illustrative purposes.

11.1.3.1 Ingestion

Dog and rat pharmacokinetic studies (Taylor et al., 1962; Cuddihy & Griffith, 1972) suggest that gastrointestinal absorption of barium may be higher in young animals than in older ones. Brenniman & Levy (1984) examined persons 18–75+ years of age living in the community for more than 10 years. It is likely that this study included adult residents who were exposed to elevated barium levels as children, but it may not account for all of the uncertainty. The barium database consists of subchronic and chronic toxicity studies in three species (humans, rats, and mice) and a marginally adequate first-generation reproductive/developmental toxicity study. The rat and mouse study (Dietz et al., 1992) gave no indication that developmental or reproductive end-points are more sensitive than other end-points; interpretation of the study results is limited by very low pregnancy rates in all groups, including controls, and examination of a small number of developmental end-points. No modifying factor is proposed for this assessment.

The US EPA (1998) derived an RfD of 0.07 mg/kg body weight per day for barium, based on the NOAEL of 0.21 mg/kg body weight per day for no adverse health effects identified in the Wones et al. (1990) and Brenniman & Levy (1984) human studies, with an uncertainty factor of 3 to account for some database deficiencies and potential differences between adults and children. The primary route of exposure to barium appears to be ingestion in drinking-water and food. A daily intake of 0.03–0.60 mg barium/kg body weight per day from drinking-water can be estimated using the drinking-water concentration of 1–20 mg/litre, a reference consumption rate of 2 litres/day, and a body weight of 70 kg. IPCS (1990) reported several published estimates of dietary intake of barium by humans, ranging from 300 to 1770 mg barium/day, with wide variations; this is equivalent to a range of 4–25 mg barium/kg body weight per day, assuming a 70-kg adult body weight. Hence, populations consuming high dietary barium levels may have intakes approximating or exceeding the oral RfD value of 0.07 mg/kg body weight per day and the tolerable intake of 0.02 mg/kg body weight per day.

11.1.3.2 Occupational (barium sulfate)

Another sample risk characterization is based on occupational exposure primarily to barium sulfate in the United Kingdom. In general, the highest typical levels of exposure appear to occur in offshore drilling activities. The highest exposures for which measured data are available apparently occur during addition of the barite ore from the bulk hopper to the mud mixing tank. There are no concerns for human health with typical exposures that arise during drilling activities if the machinery is enclosed and LEV used. However, where the machinery is not enclosed and appropriate LEV is not available, modelled data indicate that exposures could be much higher, on the order of several tens of mg/m^3 of total inhalable dust. The consequences for human health of long-term exposures at such high levels are not clear.

Because of the low exposures involved, there are no concerns for human health during the processing of barite ore where LEV is used. A similar conclusion can be drawn regarding its use in the formulation of plastics and coatings, although, from modelled data, exposures could be much higher and the human health picture less reassuring in these industries if LEV is not used. The extremely high personal sampling values for total inhalable dust (55 mg/m^3 8-h TWA) measured at one factory milling barite ore merit further consideration. At present, workers wear powered respirators that should substantially reduce the current level of personal exposure to levels below those measured in the atmos phere.

If occupational exposures are controlled to less than 10 mg/m^3 (total inhalable dust, which is primarily of low toxicity) as an 8-h TWA, it would appear that there are no significant risks to human health.

11.1.4 Uncertainties in the evaluation of health risk

An area of scientific uncertainty concerning the non-cancer hazard assessment for barium is the identification of the most sensitive end-point of barium toxicity in humans. The results of the NTP (1994) medium-term rat study suggest that renal effects may be a more sensitive end-point than hypertension. However, it is not known if a similar relationship would exist following long-term exposure or in humans. The Brenniman & Levy (1984) human study examined the effect of barium on blood pressure but did not investigate sensitive renal end-points (kidney disease was assessed by a health questionnaire only). The long-term rat study (NTP, 1994) did not measure blood pressure. Another area of scientific uncertainty is whether any toxicological or toxicokinetic differences exist between children and adults. Animal data (Taylor et al., 1962; Cuddihy & Griffith, 1972) suggest that gastrointestinal absorption may be higher in children than in adults.

The overall confidence in the tolerable intake value calculated in section 11.1.2 is medium, reflecting medium confidence in the principal studies and in the database. There is medium confidence in the human co-principal studies because LOAELs for hypertension and kidney disease were not identified. The lack of cardiovascular measurements (heart rate, blood pressure, or electrocardiogram recordings) in the long-term animal studies that used adequate diets (NTP, 1994) reduces the confidence in the animal co-principal studies. Confidence in the database is medium because of the existence of medium-term and long-term human studies, medium-term and long-term animal studies in more than one species, and a reproductive/developmental study in rats and mice.

11.2 Evaluation of environmental effects

Barium is present in soil at an average concentration of 500 mg/g (Brooks, 1978). Concentrations ranging from 0.04 to 37 mg/litre (mean approximately 7.1 mg/litre) and from 7.0 to 15 000 mg/litre (average 50 mg/litre) have been measured in ocean and fresh waters, respectively (Anderson & Hume, 1968; Schroeder et al., 1972; Reeves, 1986). Levels of barium in the air are generally æ0.05 mg/m^3 (Tabor & Warren, 1958). In a more recent survey in the USA, ambient barium concentrations ranged from 0.0015 to 0.95 mg/m^3 (US EPA, 1984). Barium salts are no longer used in developing countries as pesticides and rodenticides.

No information was located concerning the potential for toxicity in plants or animals exposed to ambient airborne barium. Based on available studies in laboratory animals exposed to barium in controlled atmospheres, environmentally encountered levels of barium in air would not be expected to pose a toxic threat to wildlife or flora.

Soluble barium compounds are capable of being transported through the environment and absorbed by organisms (IPCS, 1990). Barium may accumulate in different parts of plants (IPCS, 1990). There is no indication that barium is toxic to terrestrial plants.

No studies were located regarding toxic effects in terrestrial animals orally exposed to barium compounds present in the environment. Based on laboratory studies reporting a chronic oral NOAEL of 45 mg/kg body weight per day in rats and measured mean levels of barium in the environment, it is not likely that animals would be adversely affected via oral exposure to typical barium concentrations encountered in the environment. The potential for toxicity might be increased in areas where barium is released to surface waters or in animals feeding on plants that accumulate high levels of barium from barium-rich soils (Robinson et al., 1950).

Although Stanley (1974) found reduced root weight in Eurasian watermilfoil exposed to a barium concentration of 41.2 mg/litre, there is no indication that barium is toxic to aquatic plants at the highest concen tration (15 000 mg/litre) reported from environmental sampling.

Barium concentrations of 5.8 mg/litre have been observed to impair reproduction and growth in daphnids during 21-day tests (Biesinger &

Christensen, 1972). In 96-h tests using amphipods, LC_{50} values in the range of 122–238 mg/litre were reported (Vincent et al., 1986). A 48-h EC_{50} (developmental) value in the mussel *Mytilus californianus* is 0.189 mg/litre (Spangenberg & Cherr, 1996). The 30-day LC_{50} values for freshwater crayfish range from 39 to 61 mg/litre (Boutet & Chaisemartin, 1973).

There is little information on the potential for adverse effects in fish exposed to barium compounds. In the only study located, an LC_{50} value in sheepshead minnows was greater than 500 mg/litre (Heitmuller et al., 1981).

Based on toxic effects observed in daphnids (Biesinger & Christensen, 1972), mussels (Spangenberg & Cherr, 1996), and other aquatic organisms exposed to barium concentrations that were within the upper range of those concentrations measured in surface waters, it appears that aquatic environments with relatively high barium concentrations may represent a risk to some aquatic populations. However, the paucity of information on environmental effects of exposure to barium compounds precludes a critical evaluation of environmental risk.

12. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES

Barium was evaluated in the WHO *Guidelines for drinking-water quality*, and a guideline value of 0.7 mg barium/litre was established (WHO, 1996).

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APPENDIX 1 — SOURCE DOCUMENTS

US Environmental Protection Agency: *Toxicological review of barium and compounds* (US EPA, 1998)

Copies may be obtained from:

US Environmental Protection Agency

National Center for Environmental Assessment

26 West Martin Luther King Drive

Cincinnati, Ohio 45268

USA

The toxicological review document has received peer review both by EPA scientists and by independent scientists external to EPA. External reviewers included Dr M. Goldman (University of California, Davis, USA), Dr A. Gregory (Techto Enterprises, USA), and Mr P. Mushak (PB Associates, USA). Subsequent to external peer review, this assessment has undergone an Agency-wide review process whereby the Integrated Risk Information System (IRIS) Program Manager has achieved a consensus approval among the Office of Research and Development; Office of Air and Radiation; Office of Prevention, Pesticides, and Toxic Substances; Office of Solid Waste and Emergency Response; Office of Water; Office of Policy, Planning, and Evaluation; and Regional Offices.

Agency for Toxic Substances and Disease Registry: *Toxicological profile for barium* (ATSDR, 1992)

Copies may be obtained from:

Agency for Toxic Substances and Disease Registry

Division of Toxicology/Toxicology Information Branch

1600 Clifton Road, NE, E-29

Atlanta, Georgia 30333

USA

The profile has been reviewed by scientists from ATSDR, the Centers for Disease Control and Prevention, the National Toxicology Program, and other federal agencies. It has also been reviewed by a panel of nongovernment peer reviewers, including Dr J. Borowitz (Purdue University, USA), Dr J. Gould (Georgia Institute of Technology, USA), and Dr A. Reeves (Wayne State University, USA).

United Kingdom Health and Safety Executive: *Barium sulphate risk assessment document EH72/9* (Ball et al., 1997)

The authors' draft version is initially reviewed internally by a group of approximately 10 HSE experts, mainly toxicologists but also involving other relevant disciplines, such as epidemiology and occupational hygiene. The toxicology section of the amended draft is then reviewed by toxicologists from the United Kingdom Department of Health. Subsequently, the entire criteria document is reviewed by a tripartite advisory committee to the United Kingdom Health and Safety Commission, the Working Group for the Assessment of Toxic Chemicals (WATCH). This committee comprises experts in toxicology and occupational health and hygiene from industry, trade unions, and academia.

The members of the WATCH committee at the time of the peer review were:

Mr S.R. Bailey (Independent Consultant)

Professor J. Bridges (University of Surrey)

Dr H. Cross (Trades Union Congress)

Mr D. Farrer (Independent Consultant)

Dr A. Fletcher (Trades Union Congress)

Dr I.G. Guest (Chemical Industries Association)

Dr A. Hay (Trades Union Congress)

Dr L. Levy (Institute of Occupational Hygiene, Birmingham)

Dr T. Mallet (Chemical Industries Association)

Mr A. Moses (Independent Consultant)

Dr R. Owen (Trades Union Congress)

Mr J. Sanderson (Independent Consultant)

APPENDIX 2 — CICAD PEER REVIEW

The draft CICAD on barium and barium compounds was sent for review to institutions and organizations identified by IPCS after contact with IPCS national contact points and Participating Institutions, as well as to identified experts. Comments were received from:

M. Ball, Health and Safety Executive, Bootle, Merseyside, United Kingdom

M. Baril, International Programme on Chemical Safety/ Institut de Recherche en Santé et en Sécurité du Travail du Québec, Montreal, Quebec, Canada

D. Bayliss, National Center for Environmental Assessment, US Environmental Protection Agency, Washington, DC, USA

R. Benson, US Environmental Protection Agency, Denver, CO, USA

T. Berzins, National Chemicals Inspectorate, Solna, Sweden

R. Chhabra, Department of Health and Human Services, National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA

P. Edwards, Protection of Health Division, Department of Health, London, United Kingdom

L. Hall, Pharmacokinetics Branch, Environmental Toxicology Division, National Health and Environmental Effects Research Laboratory, US Environmental Protection Agency, Research Triangle Park, NC, USA

H. Nagy, National Institute for Occupational Safety and Health, Washington, DC, USA

E. Ohanian, Office of Water, US Environmental Protection Agency, Washington, DC, USA

B. Sjögren, Toxicology and Risk Assessment, Swedish National Institute for Working Life, Stockholm, Sweden

S. Soliman, Department of Pesticide Chemistry, Faculty of Agriculture, Alexandria University, Alexandria, Egypt

M. Vojtísek, National Institute of Public Health, Srobarova, Prague, Czech Republic

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A. Zitting, Unit of Risk Assessment, Department of Toxicology and Industrial Hygiene, Finnish Institute of Occupational Health, Helsinki, Finland

APPENDIX 3 — CICAD FINAL REVIEW BOARD

Helsinki, Finland, 26–29 June 2000

Members

Mr H. Ahlers, Education and Information Division, National Institute for Occupational Safety and Health, Cincinnati, OH, USA

Dr T. Berzins, National Chemicals Inspectorate (KEMI), Solna, Sweden

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Mr R. Cary, Health and Safety Executive, Liverpool, United Kingdom *(Rapporteur)*

Dr R.S. Chhabra, General Toxicology Group, National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA

Dr H. Choudhury, National Center for Environmental Assessment, US Environmental Protection Agency, Cincinnati, OH, USA

Dr S. Dobson, Centre for Ecology and Hydrology, Monks Wood, Abbots Ripton, United Kingdom *(Chairman)*

Dr H. Gibb, National Center for Environmental Assessment, US Environmental Protection Agency, Washington, DC, USA

Dr R.F. Hertel, Federal Institute for Health Protection of Consumers and Veterinary Medicine, Berlin, Germany

Ms K. Hughes, Priority Substances Section, Environmental Health Directorate, Health Canada, Ottawa, Ontario, Canada

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Dr A. Nishikawa, Division of Pathology, Biological Safety Research Centre, National Institute of Health Sciences, Tokyo, Japan

Dr V. Riihimäki, Finnish Institute of Occupational Health, Helsinki, Finland

Dr J. Risher, Agency for Toxic Substances and Disease Registry, Division of Toxicology, US Department of Health and Human Services, Atlanta, GA, USA

Professor K. Savolainen, Finnish Institute of Occupational Health, Helsinki, Finland *(Vice-Chairman)*

Dr J. Sekizawa, Division of Chem-Bio Informatics, National Institute of Health Sciences, Tokyo, Japan

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Ms D. Willcocks, National Industrial Chemicals Notification and Assessment Scheme, Sydney, NSW, Australia

Observers

Dr R.J. Lewis (representative of European Centre for Ecotoxicology and Toxicology of Chemicals), Epidemiology and Health Surveillance, ExxonMobil Biomedical Sciences, Inc., Annandale, NJ, USA

Secretariat

Dr A. Aitio, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland *(Secretary)*

Dr P.G. Jenkins, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

Dr M. Younes, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

INTERNATIONAL CHEMICAL SAFETY CARDS

BARIUM ICSC:1052

BARIUM CHLORATE ICSC:0613

BARIUM CHLORIDE ICSC:0614

BARIUM CHLORIDE, DIHYDRATE ICSC:0615

BARIUM OXIDE ICSC:0778

BARIUM PEROXIDE ICSC:0381

BARIUM SULFATE ICSC:0827

RÉSUMÉ D'ORIENTATION

Ce CICAD relatif au baryum et à ses composés a été préparé par l'Environmental Protection Agency des Etats-Unis d'Amérique (US EPA) et par le Health and Safety Executive (HSE) du Royaume-Uni afin de mettre à jour la monographie de la série *WHO Environmental Health Criteria* consacrée au baryum (IPCS, 1990). Les documents utilisés sont *Toxicological review of barium and compounds* de l'US EPA (US EPA, 1998), *Toxicological profile for barium* de l'Agency for Toxic Substances and Disease Registry (ATSDR, 1992) et *Barium sulphate risk assessment document* du HSE, qui porte essentiellement sur l'exposition professionnelle (Ball et al., 1997). Le document de l'US EPA (1998) s'appuie sur une recherche des données toxicologiques dans la littérature, effectuée en 1998. Une nouvelle recherche a été effectuée en janvier 1999 sur les bases de données en ligne afin de trouver toutes les références bibliographiques contenant des données toxicologiques ou écologiques sur le baryum, et postérieures à celles citées dans les documents susmentionnés. Le document du HSE couvre les données sur le sulfate de baryum arrêtées au mois de septembre 1997. Une nouvelle recherche documentaire sur la période allant jusqu'en avril 1999 a été effectuée afin d'identifier toutes les informations supplémentaires postérieures à ce document. On trouvera à l'appendice 1 des indications sur les modalités de l'examen par des pairs et sur les sources documentaires. Les renseignements concernant l'examen du CICAD par des pairs font l'objet de l'appendice 2. Ce CICAD a été approuvé en tant qu'évaluation internationale lors d'une réunion du Comité d'évaluation finale qui s'est tenue à Helsinki (Finlande) du 26 au 29 juin 2000. La liste des participants à cette réunion figure à l'appendice 3. Les fiches d'information internationales sur la sécurité chimique pour le baryum (ICSC 1052), le chlorate de baryum (ICSC 0613), le chlorure de baryum (ICSC 0614), le chlorure de baryum dihydraté (ICSC 0615), l'oxyde de baryum (ICSC 0778), le peroxyde de baryum (ICSC 0381) et le sulfate de baryum (ICSC 0827) établies par le Programme international sur la Sécurité chimique (IPCS, 1993, 1999a-f) sont également reproduites dans ce document.

Le baryum est un métal alcalino-terreux dense qui se trouve dans la nature à l'état de cation divalent en combinaison avec d'autres éléments. Outre sa présence naturelle dans l'écorce terrestre et par conséquent dans la plupart des eaux de surface, il est aussi libéré dans l'environnement par les rejets industriels. Son temps de séjour dans l'atmosphère peut atteindre plusieurs jours.

Le sulfate de baryum se présente sous forme de poudre ou de cristaux orthorhombiques. La barytine, minerai à partir duquel est produit le sulfate de baryum, est un solide cristallin blanc de dureté moyenne, opaque à transparent. Ses impuretés les plus importantes sont l'oxyde ferrique, l'oxyde d'aluminium, la silice et le sulfate de strontium.

La barytine est principalement utilisée comme constituant des boues de forage dans l'industrie pétrolière. On l'utilise également comme charge dans divers revêtements industriels, comme charge dense dans certains plastiques et produits du caoutchouc, dans les garnitures de freins et dans certains produits de scellement et adhésifs. La granulométrie de la barytine après broyage est déterminée par l'usage auquel elle est destinée. Par exemple, pour les boues de forage, le diamètre moyen des particules doit être de 44 µm, avec un maximum de 30 % de particules de moins de 6 µm.

Rien ne montre que le baryum subisse une bio transformation autre que celle d'un cation divalent. La toxicocinétique des ions baryum devrait être la même que celle des sels solubles de baryum. Des études chez le rat portant sur un sel soluble (chlorure de baryum) indiquent que les ions baryum absorbés sont distribués dans l'organisme via la circulation sanguine et se déposent principalement au niveau du squelette. L'élimination du baryum après administration par voie orale, par inhalation ou par voie intratrachéale se fait essentiellement par voie fécale. Après introduction dans les voies respiratoires, l'apparition de sulfate de baryum dans les fèces traduit une évacuation mucociliaire depuis les poumons suivie d'une ingestion.

Chez l'homme, l'ingestion en grande quantité de composés solubles du baryum peut provoquer une gastro-entérite (vomissements, diarrhée, douleurs abdominales), une hypokaliémie, de l'hypertension, des arythmies cardiaques et une paralysie des muscles squelettiques. Le sulfate de baryum insoluble est largement utilisé en doses importantes (450 g) par voie orale comme milieu de contraste radiologique sans que des effets indésirables généraux soient signalés. On ne dispose pas de données expérimentales sur le sulfate de baryum mais, du fait de sa faible absorption au niveau des voies digestives ou de la peau, il est peu probable qu'il donne lieu à des effets généraux notables.

La toxicité orale aiguë des composés du baryum chez l'animal d'expérience est faible à modérée. La perfusion intraveineuse de chlorure de baryum entraîne une hypertension et des arythmies cardiaques.

L'hydroxyde de baryum est fortement alcalin et donc corrosif. Le nitrate de baryum provoque une irritation modérée de la peau et une forte irritation oculaire chez le lapin. L'absence d'observations d'irritation cutanée ou oculaire chez l'homme malgré un usage répandu montre que le sulfate de baryum, souvent utilisé comme milieu de contraste, n'est pas un irritant puissant. On n'a pas trouvé d'informations utiles sur le potentiel de sensibilisation des composés du baryum.

Le rein semble l'organe cible le plus sensible chez les rats et souris exposés de façon répétée à du chlorure de baryum dans l'eau de boisson. Lors d'études de toxicité chronique chez l'animal d'expérience, les effets du baryum sur la tension artérielle, la fonction cardiaque et les muscles squelettiques, observés chez l'homme et chez l'animal après exposition orale aiguë, n'ont pas été confirmés.

L'exposition humaine par inhalation à des formes insolubles de baryum entraîne des manifestations radiologiques de barytose sans signes d'atteinte de la fonction pulmonaire ni de pathologie pulmonaire. On ne dispose que de données limitées à ce sujet chez l'animal. L'exposition répétée à l'oxyde de baryum par inhalation peut provoquer l'apparition d'une bronchite avec toux, expectoration muqueuse et/ou dyspnée. Dans une étude limitée, des altérations histopathologiques mineures ont été observées dans les poumons de rats exposés au sulfate de baryum à raison de 40 mg/m^3 pendant 5 heures par jour, 5 jours par semaine, mais sans indication de potentiel fibrogène. Des études sur l'animal avec instillation de sulfate de baryum dans les voies respiratoires ont montré une réponse inflamma toire et la formation de granulomes pulmonaires, mais ce type de réponse s'observe en cas d'exposition à des quantités importantes de n'importe quelles poussières de faible solubilité, qui entraîne des modifications de la clairance pulmonaire et des effets sur le poumon.

D'après les données disponibles, le baryum ne semble pas comporter de risques pour la reproduction ou le développement, même si les études chez l'animal sont limitées. Lors des essais biologiques standard du National Toxicology Program sur des rongeurs, le baryum ne s'est pas montré cancérogène. Malgré l'absence de données *in vivo*, les résultats obtenus *in vitro* indiquent que les composés du baryum sont dépourvus de potentiel mutagène.

L'ingestion avec l'eau de boisson et les aliments est la voie la plus fréquente d'exposition aux composés du baryum dans la population

générale. En ce qui concerne l'environnement professionnel, les données en provenance de l'industrie au Royaume-Uni et les prévisions réalisées avec le modèle EASE (Estimation and Assessment of Substance Exposure) indiquent que l'exposition pourrait être abaissée jusqu'à moins de 10 mg/m^3 en moyenne pondérée sur une durée de 8 heures (total des poussières inhalables). Dans certains cas, les taux pourront être abaissés à des valeurs encore plus faibles. L'exposition à court terme pourra dépasser 10 mg/m^3 pour certains travaux.

Les critères de toxicité chez l'homme pour l'expo sition au baryum et à ses composés sont l'hypertension et les troubles de la fonction rénale. En prenant dans le présent document une dose sans effet indésirable observé (NOAEL) chez l'homme de 0,21 mg de baryum par kg de poids corporel par jour, on est parvenu à une dose tolérable de 0,02 mg/kg de poids corporel par jour pour le baryum et les composés du baryum.

Le baryum dissous dans les environnements aquatiques peut constituer un risque pour des organismes aquatiques comme les daphnies, mais apparemment dans une moindre mesure pour les poissons et les plantes aquatiques, même si on ne dispose que de données limitées. Aucun effet indésirable n'a été observé lors de bilans écologiques réalisés sur la flore et la faune terrestres, bien que l'on connaisse chez certaines plantes une bioaccumulation du baryum présent dans le sol.

RESUMEN DE ORIENTACIÓN

Este CICAD sobre el bario y los compuestos de bario fue preparado por la Agencia para la Protección del Medio Ambiente de los Estados Unidos (EPA) y la Dirección de Salud y Seguridad del Reino Unido (HSE) para actualizar la monografía de los Criterios de Salud Ambiental de la OMS correspondiente al bario (IPCS, 1990). Los documentos originales fueron el *Examen toxicológico del bario y sus compuestos* de la EPA (US EPA, 1998), el *Perfil toxicológico del bario* de la Agencia para el Registro de Sustancias Tóxicas y Enfermedades (ATSDR, 1992) y el documento de *Evaluación del riesgo del sulfato de bario* de la HSE, que se concentra en la exposición ocupacional (Ball et al., 1997). En la preparación del examen de la US EPA (1998) se realizó una búsqueda de datos toxicológicos actualizados (1998) en la bibliografía. En enero de 1999 se hizo una búsqueda bibliográfica en las bases de datos en línea actualizadas para identificar cualquier referencia con información toxicológica o ecológica sobre el bario publicada después de las incorporadas a los documentos originales enumerados más arriba. Los datos sobre el sulfato de bario localizados hasta septiembre de 1997 figuraban en el documento de la HSE. Se realizó una búsqueda bibliográfica ulterior hasta abril de 1999 para determinar cualquier información adicional publicada antes de la conclusión de este examen. La información relativa al carácter del examen colegiado y a la disponibilidad de los documentos originales se presenta en el apéndice 1. La información sobre el examen colegiado de este CICAD aparece en el apéndice 2. Este CICAD se aprobó como evaluación internacional en una reunión de la Junta de Evaluación Final, celebrada en Helsinki (Finlandia) del 26 al 29 de junio de 2000. La lista de participantes en esta reunión figura en el apéndice 3. Las Fichas internacionales de seguridad química para el bario (ICSC 1052), el clorato de bario (ICSC 0613), el cloruro de bario (ICSC 0614), el dihidrato de cloruro de bario (ICSC 0615), el oxido de bario (ICSC 0778), el peróxido de bario (ICSC 0381) y el sulfato de bario (ICSC 0827), preparadas por el Programa Internacional de Seguridad de las Sustancias Químicas (IPCS, 1993, 1999a-f), se reproducen en este documento.

El bario es un metal alcalinotérreo denso que se encuentra en la naturaleza como catión divalente en combinación con otros elementos. Además de su presencia natural en la corteza terrestre y, por consiguiente, en la mayor parte de las aguas superficiales, el bario también se libera al medio ambiente a través de las emisiones industriales. Su tiempo de permanencia en la atmósfera puede durar hasta varios días.

El sulfato de bario existe como polvo o cristales ortorrómbicos de color blanco. La barita, mineral del cual se obtiene el sulfato de bario, es un

mineral cristalino moderadamente blando de color blanco entre opaco y transparente. Las impurezas más importantes son el óxido de hierro (III), el óxido de aluminio, la sílice y el sulfato de estroncio.

La barita (sulfato de bario) se utiliza fundamentalmente como elemento constitutivo de los lodos de perforación en la industria del petróleo. También se emplea como relleno en una serie de revestimientos industriales, como relleno denso en algunos plásticos y productos de caucho, en los cojinetes del embrague y en algunos selladores y adhesivos. El tamaño de las partículas al que hay que triturar la barita depende del uso. Por ejemplo, los lodos de perforación se trituran hasta un diámetro medio de las partículas de 44 μm, con un máximo del 30% de las partículas con un diámetro inferior a 6 μm.

No hay pruebas de que el bario sufra biotransformación distinta de la de catión divalente. Cabe suponer que la toxicocinética de los iones de bario es la misma que la de las sales solubles de bario. Los estudios en ratas utilizando una sal soluble (cloruro de bario) han puesto de manifiesto que los iones de bario absorbidos se distribuyen a través de la sangre y se depositan fundamentalmente en el esqueleto. La vía principal de eliminación del bario tras la administración oral, la inhalación o la instilación intratraqueal son las heces. Tras la introducción en el tracto respiratorio, la aparición de sulfato de bario en las heces se debe a una elimina ción mucociliar de los pulmones y la posterior ingestión.

En las personas, la ingestión de concentraciones elevadas de compuestos de bario solubles puede provocar gastroenteritis (vómitos, diarrea, dolor abdominal), hipopotasemia, hipertensión, arritmias cardíacas y parálisis de los músculos esqueléticos. El sulfato de bario insoluble se ha utilizado ampliamente en dosis elevadas (450 g) como medio de radiocontraste oral y no se han notificado efectos sistémicos adversos. No se dispone de datos experimentales sobre el sulfato de bario; sin embargo, debido a su absorción limitada a partir del tracto gastrointestinal o la piel, es poco probable que pueda tener un efecto sistémico significativo.

La toxicidad aguda por vía oral de los compuestos de bario en animales experimentales es de ligera a moderada. La infusión intravenosa de cloruro de bario produce un aumento de la presión sanguínea y arritmias cardíacas.

El hidróxido de bario es fuertemente alcalino, y por consiguiente corrosivo. El nitrato de bario provocó una irritación cutánea leve e irritación ocular grave en conejos. La falta de información acerca de la irritación cutánea u ocular en las personas, a pesar de su uso generalizado, parece indicar que el sulfato de bario, utilizado con frecuencia como medio de contraste, no es un irritante fuerte. No se encontró información útil sobre el potencial de sensibilización de los compuestos de bario.

El riñón parece ser el órgano destinatario más sensible en las ratas y los ratones expuestos repetidamente a cloruro de bario en el agua de bebida. En estudios de exposición crónica al bario con animales de laboratorio no se han confirmado los efectos en la presión sanguínea y los músculos cardíacos y esqueléticos observados en las personas y en los animales de laboratorio tras la exposición oral a concentraciones muy elevadas.

La exposición de las personas a formas insolubles de bario por inhalación da lugar a resultados radiológi cos de baritosis, sin pruebas de alteración de la función y la histología pulmonares. La información sobre la toxicidad del bario inhalado en los animales es limitada. La exposición repetida al oxido de bario por inhalación puede provocar bronquitis, acompañada de tos, flemas y/o disnea. En un estudio limitado se observaron cambios histopatológicos pequeños en los pulmones de ratas expuestas a sulfato de bario en concentraciones de 40 mg/m^3 durante cinco horas al día, cinco días a la semana, pero no se obtuvieron pruebas del potencial fibrogénico. En los estudios en animales

utilizando la instilación de sulfato de bario en las vías respiratorias se han puesto de manifiesto respuestas inflamatorias y formación de granulomas en los pulmones; cabe esperar este efecto de la exposición a cantidades importantes de cualquier polvo de baja solubilidad, debido a un cambio en la eliminación pulmonar y el consiguiente efecto en los pulmones.

Los datos actualmente disponibles indican que el bario no parece representar un peligro para la reproducción o el desarrollo, aunque los estudios en animales son limitados. El bario no fue carcinógeno en las biovaloraciones normalizadas realizadas con roedores en el marco del Programa Nacional de Toxicología. Aunque no se dispone de datos *in vivo*, los datos obtenidos *in vitro* indican que los compuestos de bario no tienen potencial mutagénico.

La ingesta oral con el agua de bebida y los alimentos es la vía más frecuente de exposición a los compuestos de bario para la población general. En el entorno ocupacional, los datos de la industria británica y los pronósticos realizados mediante el modelo de Estimación y evaluación de la exposición a sustancias (EASE) parecen indicar que las exposiciones se pueden mantener a un nivel inferior a 10 mg/m^3 en un promedio ponderado por el tiempo de ocho horas (polvo inhalable total). En algunas situaciones se podrá contener a niveles muy inferiores a éste. En algunas tareas se pueden producir exposiciones breves a concentraciones superiores a 10 mg/m^3.

Los efectos finales críticos en las personas para la toxicidad derivada de la exposición al bario y los compuestos de bario parecen ser la hipertensión y la disfunción renal. Utilizando una concentracione sin efectos adversos observados (NOAEL) en las personas de 0,21 mg de bario/kg de peso corporal al día, se ha obtenido en este documento un valor de la ingesta tolerable de 0,02 mg/kg de peso corporal al día para el bario y los compuestos de bario.

El bario disuelto en el entorno acuático puede representar un riesgo para organismos acuáticos como los dáfnidos, pero al parecer el riesgo es menor para los peces y las plantas acuáticas, aunque los datos son limitados. No se han notificado efectos adversos en evaluaciones ecológicas de plantas terrestres o de flora y fauna silvestres, aunque se conocen algunas plantas capaces de bioacumular bario del suelo.

ENDNOTES:

1. International Programme on Chemical Safety (1994) *Assessing human health risks of chemicals: derivation of guidance values for health-based exposure limits.* Geneva, World Health Organization (Environmental Health Criteria 170).

2. Toxic Chemical Release Inventory (TRI) database, Office of Toxic Substances, US Environmental Protection Agency, Washington, DC, 1998.

3. EASE is a general-purpose predictive model for workplace exposure assessments. It is an electronic, knowledge-based, expert system that is used where measured exposure data are limited or not available. The model is in use across the European Union for the occupational exposure assessment of new and existing substances.

See Also:
Toxicological Abbreviations