TOXICOLOGICAL PROFILE FOR
BARIUM AND COMPOUNDS

Agency for Toxic Substances and Disease Registry
U.S. Public Health Service

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DISCLAIMER

The use of company or product name(s) is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry.

FOREWORD

The Superfund Amendments and Reauthorization Act of 1986 (Public Law 99-499) extended and amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law (also known as SARA) directed the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare toxicological profiles for hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List and which pose the most significant potential threat to human health, as determined by ATSDR and the Environmental Protection Agency (EPA). The list of the 200 most significant hazardous substances was published in the Federal Register on April 17, 1987 and on October 20, 1988.

Section 110 (3) of SARA directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list. Each profile must include the following content:

(A) An examination, summary, and interpretation of available toxicological information and epidemiological evaluations on the hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects,

(B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, or chronic health effects, and

(C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

This toxicological profile is prepared in accordance with guidelines developed by ATSDR and EPA. The original guidelines were published in the Federal Register on April 17, 1987. Each profile will be revised and republished as necessary, but no less often than every three years, as required by SARA.

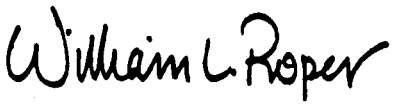
The ATSDR toxicological profile is intended to characterize succinctly the toxicological and health effects information for the hazardous substance being described. Each profile identifies and reviews the key literature that describes a hazardous substance's toxicological properties. Other literature is presented but described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

Foreword

Each toxicological profile begins with a public health statement, which describes in nontechnical language a substance's relevant toxicological properties. Following the public health statement is information concerning levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Data needs that are of significance to protection of public health will be identified by ATSDR, the National Toxicology Program (NTP) of the Public Health Service, and EPA. The focus of the profiles is on health and toxicological information; therefore, we have included this information in the beginning of the document.

The principal audiences for the toxicological profiles are health professionals at the federal, state, and local levels, interested private sector organizations and groups, and members of the public.

This profile reflects our assessment of all relevant toxicological testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, the Centers for Disease Control, the NTP, and other federal agencies. It has also been reviewed by a panel of nongovernment peer reviewers. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.



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1. PUBLIC HEALTH STATEMENT

This Statement was prepared to give you information about barium and to emphasize the human health effects that may result from exposure to it. The Environmental Protection Agency (EPA) has identified 1,177 sites on its National Priorities List (NPL). Barium has been found at 154 of these sites. However, we do not know how many of the 1,177 NPL sites have been evaluated for barium. As EPA evaluates more sites, the number of sites at which barium is found may change. The information is important for you because barium may cause harmful health effects and because these sites are potential or actual sources of human exposure to barium.

When a chemical is released from a large area such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment as a chemical emission. This emission, which is also called a release, does not always lead to exposure. You can be exposed to a chemical only when you come into contact with the chemical. You may be exposed to it in the environment by breathing, eating, or drinking substances containing the chemical or from skin contact with it.

If you are exposed to a hazardous substance such as barium, several factors will determine whether harmful health effects will occur and what the type and severity of those health effects will be. These factors include the dose (how much), the duration (how long), the route or pathway by which you are exposed (breathing, eating, drinking, or skin contact), the other chemicals to which you are exposed, and your individual characteristics such as age, sex, nutritional status, family traits, life style, and state of health.

1.1 WHAT IS BARIUM?

Barium is a silvery-white metal that occurs in nature in many different forms called compounds. These compounds are solids and they do not burn well. Two forms of barium, barium sulfate and barium carbonate, are often found in nature as underground ore deposits. Barium is sometimes found naturally in drinking water and food. Because certain forms of barium (barium sulfate and barium carbonate) do not mix well with water, the amount of barium usually found in drinking water is of a small quantity. Other barium compounds, such as barium chloride, barium nitrate, and barium hydroxide, are manufactured from barium sulfate. Barium compounds such as barium acetate, barium carbonate, barium chloride, barium hydroxide, barium nitrate, and barium sulfide dissolve more easily in water than barium sulfate and barium carbonate.

Barium and barium compounds are used for many important purposes. Barium sulfate ore is mined and used in several industries. It is used mostly by the oil and gas industries to make drilling muds. Drilling muds make it easier to drill through rock by keeping the drill bit lubricated. Barium sulfate is also used to make paints, bricks, tiles, glass, rubber, and other barium compounds. Some barium compounds, such as barium carbonate, barium

chloride, and barium hydroxide, are used to make ceramics, insect and rat poisons, additives for oils and fuels, and many other useful products. Barium sulfate is sometimes used by doctors to perform medical tests and take x-ray photographs of the stomach and intestines.

The length of time that barium will last in the environment following release to air, land, and water depends on the form of barium released. Barium compounds that do not dissolve well in water, such as barium sulfate and barium carbonate, can last a long time in the environment. Barium compounds that dissolve easily in water usually do not last a long time in the environment. Barium that is dissolved in water quickly combines with sulfate or carbonate ions and becomes the longer lasting forms (barium sulfate and barium carbonate). Barium sulfate and barium carbonate are the forms of barium most commonly found in the soil and water. If barium sulfate and barium carbonate are released onto land, they will combine with particles of soil. More information on the chemical and physical properties, use, and environmental fate of barium is found in Chapters 3, 4, and 5.

1.2 HOW MIGHT I BE EXPOSED TO BARIUM?

Background levels of barium in the environment are very low. The air that most people breathe contains about 0.0015 parts of barium per billion parts of air (ppb). The air around factories that release barium compounds into the air has only about 0.33 ppb or less of barium. Most surface water and public water supplies contain only about 0.38 parts of barium per million parts of water (ppm) or less. In some areas that have underground water wells, drinking water may contain more barium than the 1 ppm limit set by EPA. The highest amount measured from these water wells has been 10 ppm. The highest amount of barium found in soil is about 100 to 3,000 ppm. Some foods, such as Brazil nuts, seaweed, fish, and certain plants, may contain high amounts of barium. The amount of barium found in food and water usually is not high enough to be a health concern. However, information is still being collected to find out if long-term exposure to low levels of barium causes any health problems.

Barium waste may be released to air, land, and water during industrial operations. Barium is released into the air during the mining and processing of ore and during manufacturing operations. Some industries dump wastes containing barium compounds onto land or into the ocean and other bodies of water. Barium compounds are found in more than 150 hazardous waste sites in the,United States. We do not know the exact number of hazardous waste sites containing barium because not all waste sites have been examined for barium.

People with the greatest known risk of exposure to high levels of barium are those working in industries that make or use barium compounds. Most of these exposed persons breathe air that contains barium sulfate or barium carbonate. Sometimes they are exposed to one of the more harmful forms of barium (for example, barium chloride or barium hydroxide) by breathing the

dust from these compounds or by getting them on their skin. Many hazardous waste sites contain barium compounds, and these sites may be a source of exposure for people living and working near them. Exposure near hazardous waste sites may occur by breathing dust, eating soil or plants, or drinking water that is polluted with barium. People near these sites may also get soil or water that contains barium on their skin. More information on how you might be exposed to barium is found in Chapter 5.

1.3 HOW CAN BARIUM ENTER AND LEAVE MY BODY?

Barium enters your body when you breathe air, eat food, or drink water containing barium. It may also enter your body to a small extent when you have direct skin contact with barium compounds. Barium that you breathe seems to enter the bloodstream very easily. Barium does not seem to enter the bloodstream as well from the stomach or intestines. How much barium actually gets into your bloodstream depends on how much barium you breathe, eat, or drink and how easily the form of barium you breathe dissolves in the fluids in your body. Some barium compounds (for example, barium chloride) can enter your body through your skin, but this is very rare and usually occurs in industrial accidents at factories where they make or use barium compounds. Barium at hazardous waste sites may enter your body if you breathe dust, eat soil or plants, or drink water polluted with barium. Barium can also enter your body if polluted soil or water touches your skin.

Barium that enters your body by breathing, eating, or drinking is removed mainly in feces and urine. Most of the barium that enters your body is removed within a few days, and almost all of it is gone within l-2 weeks. Most barium that stays in your body goes into the bones and teeth. We do not know the long-term health effects of the barium that stays in your body. More information on how barium enters and leaves your body is found in Chapter 2.

1.4 HOW CAN BARIUM AFFECT MY HEALTH?

The health effects of the different barium compounds depend on how well the specific barium compound dissolves in water. For example, barium sulfate does not dissolve well in water and has few adverse health effects. Doctors sometimes give barium sulfate orally or by placing it directly in the rectum of patients for purposes of making x-rays of the stomach or intestines. The use of this particular barium compound in this type of medical test is not harmful to people. Barium compounds such as barium acetate, barium carbonate, barium chloride, barium hydroxide, barium nitrate, and barium sulfide that dissolve in water can cause adverse health effects. Most of what we know comes from studies in which a small number of individuals were exposed to fairly large amounts of barium for short periods. Eating or drinking very large amounts of barium compounds that dissolve in water may cause paralysis or death in a few individuals. Some people who eat or drink somewhat smaller amounts of barium for a short period may potentially have difficulties in breathing, increased blood pressure, changes in heart rhythm, stomach

irritation, minor changes in blood, muscle weakness, changes in nerve reflexes, swelling of the brain, and damage to the liver, kidney, heart, and spleen. One study showed that people who drank water containing as much as 10 ppm of barium for 4 weeks did not have increased blood pressure or abnormal heart rhythms. We have no reliable information about the possible health effects in humans who are exposed to barium by breathing or by direct skin contact. However, many of the health effects might be similar to those seen after eating or drinking barium. We have no information about the ability of barium to cause birth defects or affect reproduction in humans. Barium has not been shown to cause cancer in humans.

The health effects of barium have been studied more often in experimental animals than in humans. Rats that ate or drank barium over short periods had build-up of fluid in the trachea (windpipe), swelling and irritation of the intestines, changes in organ weights, decreased body weight, and increased numbers of deaths. Rats that ate or drank barium over long periods had increased blood pressure and changes in the function and chemistry of the heart. Mice that ate or drank barium over a long period had a shorter life span. We have no reliable information about the health effects in experimental animals that are exposed to barium by breathing or by direct skin contact. We also have no reliable information to tell whether barium causes cancer or birth defects in experimental animals.

The Department of Health and Human Services, the International Agency for Research on Cancer, and EPA have not classified barium as to its carcinogenicity.

More information on the health effects of barium can be found in Chapter 2.

1.5 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO BARIUM?

There is no routine medical test to determine whether you have been exposed to barium. Doctors can measure barium in body tissues and fluids, such as blood, bones, urine, and feces, using very complex instruments. This is normally done only for cases of severe barium poisoning and for medical research. More information on testing for barium exposure is found in Chapters 2 and 6.

1.6 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

To protect individuals from the possible harmful health effects of barium, the federal government regulates the amount of barium in the environment. EPA estimates that for an adult of average weight, exposure to 1.5 ppm of barium in water each day for a lifetime (70 years) is unlikely to result in harmful health effects. For a long-term but less than lifetime

exposure (about 7 years), 1.8 ppm is estimated to be a level unlikely to result in harmful health effects for an adult. EPA has established a maximum level of 1 ppm for barium in drinking water. The Food and Administration (FDA) has set the quality standard for barium in bottled water at 1.0 ppm. Similarly, EPA has set the maximum barium concentration for groundwater protection at 1.0 ppm. EPA reportable quantity regulations require that a spill of 10 pounds or more of barium cyanide be reported to the Federal Government National Response Center.

The Occupational Safety and Health Administration (OSHA) has a legally enforceable occupational exposure limit of 0.5 milligrams (mg) of soluble barium compounds per cubic meter (m^3) of air averaged over an 8-hour work day. The OSHA 8-hour exposure limit for barium dust in air is 5-10 mg/m^3. The National Institute for Occupational Safety and Health (NIOSH) has classified barium exposures of 250 mg/m^3 as immediately dangerous to life or health.

More information on government regulations can be found in Chapter 7.

1.7 WHERE CAN I GET MORE INFORMATION?

If you have any more questions or concerns not covered here, please contact your state health or environmental department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road, E-29
Atlanta, Georgia 30333

This agency can also provide you with information on the location of the nearest occupational and environmental health clinic. Such clinics specialize in recognizing, evaluating, and treating illnesses that result from exposure to hazardous substances.

2. HEALTH EFFECTS

2.1 INTRODUCTION

The primary purpose of this chapter is to provide public health officials, physicians, toxicologists, and other interested individuals and groups with an overall perspective of the toxicology of barium and a depiction of significant exposure levels associated with various adverse health effects. It contains descriptions and evaluations of studies and presents levels of significant exposure for barium based on toxicological studies and epidemiological investigations.

When evaluating the health effects of barium compounds, it is important to keep in mind that different barium compounds have different solubilities in water and body fluids and therefore serve as variable sources of the Ba^{2+} ion. The Ba^{2+} ion and the soluble compounds of barium (notably chloride, nitrate, hydroxide) are generally highly toxic to humans and experimental animals. The insoluble barium compounds (notably sulfate and carbonate) are inefficient sources of the Ba^{2+}, ion and therefore are generally nontoxic. Throughout the following section (2.2), the health effects by route of exposure of both soluble and insoluble barium compounds are discussed.

2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

To help public health professionals address the needs of persons living or working near hazardous waste sites, the information in this section is organized first by route of exposure--inhalation, oral, and dermal--and then by health effect--death, systemic, immunological, neurological, developmental, reproductive, genotoxic, and carcinogenic effects. These data are discussed in terms of three exposure periods--acute (less than 15 days), intermediate (15-364 days), and chronic (365 days or more).

Levels of significant exposure for each route and duration are presented in tables and illustrated in figures. The points in the figures showing noobserved-adverse-effect levels (NOAELS) or lowest-observed-adverse-effect levels (LOAELs) reflect the actual doses (levels of exposure) used in the studies. LOAELs have been classified into "less serious" or "serious" effects. These distinctions are intended to help the users of the document identify the levels of exposure at which adverse health effects start to appear. They should also help to determine whether or not the effects vary with dose and/or duration, and place into perspective the possible significance of these effects to human health.

The significance of the exposure levels shown in the tables and figures may differ depending on the user's perspective. For example, physicians concerned with the interpretation of clinical findings in exposed persons may be interested in levels of exposure associated with "serious" effects. Public health officials and project managers concerned with appropriate actions to take at hazardous waste sites may want information on levels of exposure

associated with more subtle effects in humans or animals (LOAEL) or exposure levels below which no adverse effects (NOAEL) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels, MRLs) may be of interest to health professionals and citizens alike.

Estimates of exposure levels posing minimal risk to humans (MRLs) have been made, where data were believed reliable, for the most sensitive noncancer effect for each exposure duration. MRLs include adjustments to reflect human variability from laboratory animal data to humans.

Although methods have been established to derive these levels (Barnes et al. 1988; EPA 1989c), uncertainties are associated with these techniques. Furthermore, ATSDR acknowledges additional uncertainties inherent in the application of the procedures to derive less than lifetime MRLs. As an example, acute inhalation MRLs may not be protective for health effects that are delayed in development or are acquired following repeated acute insults, such as hypersensitivity reactions, asthma, or chronic bronchitis. As these kinds of health effects data become available and methods to assess levels of significant human exposure improve, these MRLs will be revised.

2.2.1 Inhalation Exposure

Studies evaluating the effects of barium following acute, intermediate, and chronic inhalation exposure are limited to several case reports of humans exposed occupationally (Doig 1976; Essing et al. 1976; Seaton et al. 1986; Shankle and Keane 1988) and to two experimental studies with animals (Hicks et al. 1986; Tarasenko et al. 1977). These case reports and animal studies are not adequate for firmly establishing the health effects of barium by inhalation because of a number of significant study limitations. The case reports are generally inadequate because data were available for a limited number of exposed subjects and because exposure conditions (duration, frequency, dose) were not well characterized (Doig 1976; Essing et al. 1976; Seaton et al. 1986; Shankle and Keane 1988). One of the two animal studies was limited in that apparently no control animals were used, an inhalation chamber providing a controlled dose and environment was not used, and there was a lack of information regarding the vehicle used, the purity of the test material, the duration and frequency of exposure, and the number of animals tested (Hicks et al. 1986). The second animal study consisted of several experiments but was generally limited in that the authors provided few details regarding experimental methods, exposure conditions, and test results, and no information as to the number of animals tested, the purity of the test material, or the statistical methods used; furthermore, in some experiments it was not clear whether or not control animals were used (Tarasenko et al. 1977). In view of the major limitations associated with the available case reports and animal studies, results from these reports should be regarded as providing only preliminary and/or suggestive evidence that acute, intermediate, and chronic inhalation exposure to barium may potentially be associated with adverse health effects. No reliable information was available

from any of the inhalation studies to identify NOAELs or LOAELs. Findings from the various case reports and animal studies are briefly described below.

2.2.1.1 Death

No studies were located regarding death in humans or animals after inhalation exposure to barium.

2.2.1.2 Systemic Effects

No studies were located regarding dermal/ocular effects in humans or animals after inhalation exposure to barium.

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Respiratory Effects. Two studies of workers exposed chronically to dust from barium sulfate demonstrated that this exposure had a minor effect on the lungs. In one study, a benign pneumonoconiosis was observed in several factory workers (Doig 1976). In a second study in which workers were exposed by mining barium sulfate, silicosis was observed but was attributed to inhalation of quartz (Seaton et al. 1986). In contrast, a study of workers chronically exposed to barium carbonate dust reported no respiratory symptoms attributable to barium exposure (Essing et al. 1976). X-ray analysis of the lungs also showed no abnormalities attributable to barium dust.

Studies regarding respiratory effects in animals following inhalation exposure to barium are limited to two reports (Hicks et al. 1986; Tarasenko et al. 1977). Pulmonary lesions (perivascular and peribronchial sclerosis and focal thickening of the interalveolar septa) were observed in rats following intermediate inhalation exposure to 3.6 mg barium/m3 as barium carbonate dust (Tarasenko et al. 1977). Bronchoconstriction was reportedly noted in guinea pigs following inhalation for an unspecified period of time to 0.06 mg barium/m3/min as aerosolized barium chloride solution (Hicks et al. 1986).

Cardiovascular Effects. Three of 12 workers chronically exposed to barium carbonate dust had elevated blood pressure and 2 workers had ECG abnormalities (Essing et al. 1976). However, it is unknown whether this represented an increased incidence because no comparison with a control population was performed. Increased blood pressure and cardiac irregularities were reportedly observed in guinea pigs exposed by inhalation for an unspecified period of time to 0.06 mg barium/m3/min as aerosolized barium chloride solution (Hicks et al. 1986).

Gastrointestinal Effects. Abdominal cramps, nausea, and vomiting were experienced by a 22-year-old factory worker accidentally exposed by acute inhalation to a large but unspecified amount of barium carbonate powder (Shankle and Keane 1988). No animal studies were located regarding gastrointestinal effects in animals after inhalation exposure to barium.

Hematological Effects. Low serum potassium level was observed in a 22-year-old factory worker accidentally exposed by acute inhalation to barium carbonate powder (Shankle and Keane 1988). Altered hematological parameters were observed in rats following inhalation for an intermediate exposure period to 3.6 mg barium/m^3 as barium carbonate dust (Tarasenko et al. 1977). Reported changes included decreased blood hemoglobin, decreased thrombocyte count, decreased blood glucose, decreased albumin, increased leukocyte count, and increased blood phosphorus.

Musculoskeletal Effects. After accidental exposure to a large amount of barium carbonate powder by acute inhalation, a 22-year-old factory worker developed progressive muscle weakness and paralysis of the extremities and neck (Shankle and Keane 1988). X-ray analysis of the bones and skeletal muscles of the pelvis and thighs of workers chronically exposed to barium carbonate dust revealed no apparent build up of barium in these tissues (Essing et al. 1976). No studies were located regarding musculoskeletal effects in animals after inhalation exposure to barium.

Hepatic Effects. No studies were located regarding hepatic effects in humans after inhalation exposure to barium. Impaired detoxifying function of the liver was noted in one study in which rats were treated by intermediate inhalation exposure to 3.6 mg barium/m^3 as barium carbonate dust (Tarasenko et al. 1977). No other details were reported.

Renal Effects. Renal failure occurred in a 22-year-old worker accidentally exposed by acute inhalation to barium carbonate powder (Shankle and Keane 1988). No studies were located regarding renal effects in animals after inhalation exposure to barium.

Other Systemic Effects. No studies were located regarding other systemic in humans after inhalation exposure to barium. Decreased body weight and decreased urinary calcium developed in rats following inhalation for an intermediate exposure period to 3.6 mg barium/m^3 as barium carbonate dust (Tarasenko et al. 1977).

2.2.1.3 Immunological Effects

No studies were located regarding immunological effects in humans or animals after inhalation exposure to barium.

2.2.1.4 Neurological Effects

Absence of deep tendon reflexes was observed in a 22-year-old man accidentally exposed by acute inhalation to barium carbonate powder (Shankle and Keane 1988). No studies were located regarding neurological effects in animals after inhalation exposure to barium.

2.2.1.5 Developmental Effects

No studies were located regarding developmental effects in humans after inhalation exposure to barium. Only one limited report was available regarding developmental effects in animals after intermediate inhalation to barium (Tarasenko et al. 1977). Reduced survival, underdevelopment, lowered weight gain, and various hematologic alterations (erythropenia, leukocytosis, eosinophilia, neutrophilia) were reportedly noted in the offspring of female rats exposed by inhalation for an intermediate period to 2.2 or 9.4 mg barium/m^3 as barium carbonate dust (Tarasenko et al. 1977). No other significant details regarding this developmental study were reported.

2.2.1.6 Reproductive Effects

No studies were located regarding reproductive effects in humans after inhalation exposure to barium. Only one limited report was available regarding reproductive effects in animals following intermediate inhalation exposure to barium carbonate (Tarasenko et al. 1977). Disturbances in spermatogenesis, including decreased number of sperm, decreased percentage of motile sperm, and decreased osmotic resistance of sperm, were reportedly observed in male rats exposed by inhalation for one cycle of spermatogenesis to 15.8 mg barium/m^3 as barium carbonate dust. The testicles of these treated rats reportedly had an increase in the number of ducts with desquamated epithelium and a reduced number of ducts with 12^{th}-stage meiosis. The condition of the testicles of treated rats returned to normal 30 days after cessation of barium carbonate treatment (Tarasenko et al. 1977). Similar observations were noted in a second experiment in which male rats were exposed by inhalation for an intermediate period to 3.6 mg barium/m^3 as barium carbonate dust. In a third experiment by the same authors, female rats exposed by inhalation for an intermediate period to 2.2 or 9.4 mg barium/m^3 as barium carbonate dust reportedly developed a shortened estrous cycle and alterations in the morphological structure of the ovaries.

2.2.1.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans or animals after inhalation exposure to barium. Genotoxicity studies are discussed in Section 2.4.

2.2.1.8 Cancer

No studies were located regarding cancer in humans or animals after inhalation exposure to barium.

2.2.2 Oral Exposure

The majority of studies evaluating the health effects of barium are oral exposure studies. The available oral studies include numerous case reports of humans exposed orally to barium through accidental or intentional ingestion, several epidemiological and statistical investigations of humans exposed to drinking water containing barium, and various experimental animal studies involving acute, intermediate, or chronic exposure to barium either by gavage or by drinking water. In contrast to the limited inhalation studies that provide no reliable data to identify NOAELs and LOAELs, the available oral studies are more adequate for assessing the health effects of barium and provide reliable information to identify NOAEL and LOAEL values. Findings from the various oral studies are .summarized below.

2.2.2.1 Death

Death occurred in six cases of accidental or intentional ingestion of barium salts. Two deaths were due to cardiac arrest, one was due to severe gastrointestinal hemorrhage, and in three cases the specific cause was not determined (Das and Singh 1970; Diengott et al. 1964; McNally 1925; Ogen et al. 1967; Talwar and Sharma 1979). Doses in these cases were not known.

In addition to case reports of death in humans, several studies have examined mortality rates in humans exposed to drinking water contaminated with barium (Brenniman and Levy 1985; Brenniman et al. 1979a, 1979b, 1981; Elwood et al. 1974; Schroeder and Kraemer 1974). Two of these studies examined the statistical correlation between barium concentrations in drinking water and total mortality and/or cardiovascular mortality rates in exposed populations (Elwood et al. 1974; Schroeder and Kraemer 1974). Negative correlations between barium and these mortality rates were found in both studies. These two particular studies are of limited use in assessing barium-induced mortality because of a number of study limitations, including a lack of information on exposure conditions (dose, duration, frequency) and the number of people exposed. Results of a third study indicated that relative to communities with little or no barium in drinking water, communities with elevated concentrations of barium in their drinking water had significantly higher mortality rates for all causes, heart disease, arteriosclerosis, and all cardiovascular disease (Brenniman and Levy 1985; Brenniman et al. 1979a, 1979b, 1981). This epidemiological study had a number of confounding variables, including possible use in the study population of home water softeners that would remove barium from the drinking water, inclusion of communities that had significant changes in population, lack of a way to control-for length of time an individual lived in a community, and widely varying concentrations of other contaminants (calcium, sodium, magnesium) in the drinking water. The human studies are not reliable for identifying NOAELs or LOAELs for death because of the limitations associated with these studies.

Mortality has been observed in experimental animals following acute and chronic oral exposure to barium chloride and barium acetate (Borzelleca et al. 1988; Schroeder and Mitchener 1975b; Tardiff et al. 1980). The acute oral LD_{50} was determined in one study to be 269 and 277 mg/kg (expressed as elemental barium) for female and male rats, respectively (Borzelleca et al. 1988). The acute oral LD_{50} in a second study was determined to be 132 and 220 mg/kg (expressed as elemental barium) for adult and weanling rats, respectively (Tardiff et al. 1980). These LD_{50} values (132 to 277 mg/kg) indicate that barium is toxic by acute oral gavage exposure to small experimental animals.

The studies evaluating mortality during intermediate and chronic oral exposure of experimental animals have provided mixed results. Reduced lifespan (approximately 11 percent) has been noted in male mice but not in female mice treated chronically with 0.95 mg barium/kg/day as barium acetate in drinking water (Schroeder and Mitchener 1975b). No significant effects *on* mortality were noted in an intermediate exposure study in which rats were treated with 35 mg barium/kg/day as barium chloride in drinking water (Tardiff et al. 1980). In a chronic study in which rats were treated with 0.7 mg barium/kg/day as barium acetate in drinking water, there were no significant effects on mortality (Schroeder and Mitchener 1975a). These mixed results may possibly be due to species differences.

The highest NOAEL values and all reliable LOAEL values for death in each species and duration category are recorded in Table 2-1 and plotted in Figure 2-1. LD_{50} values have also been recorded in Table 2-1 and Figure 2-1.

2.2.2.2 Systemic Effects

The highest NOAEL values and all reliable LOAEL values for systemic effects in each species and duration category are recorded in Table 2-1 and plotted in Figure 2-1.

Respiratory Effects. Respiratory weakness and paralysis requiring mechanical ventilation were frequently observed in cases of acute ingestion of barium salts by humans (Das and Singh 1970; Gould et al. 1973; Lewi and Bar-Khayim 1964; Morton 1945; Ogen et al. 1967; Phelan et al. 1984; Wetherill et al. 1981).

Limited data are available regarding respiratory effects in animals following oral barium exposure. Acute gavage exposure of rats to 198 mg barium/kg/day as barium chloride has been associated with accumulation of fluid in the trachea; however, no pulmonary lesions upon gross necropsy and no changes in pulmonary weight were observed (Borzelleca et al. 1988). No changes in pulmonary weight were observed in a study in which rats were exposed for an intermediate period to doses less than 35 mg barium/kg/day as barium chloride in drinking water (Tardiff et al. 1980). Gross and

TABLE 2-1. Levels of Significant Exposure to Barium - Oral

Key to figure[a]	Species	Route	Exposure frequency/ duration	System	NOAEL (mg Ba/kg/day)	LOAEL (effect) Less serious (mg Ba/kg/day)	LOAEL (effect) Serious (mg Ba/kg/day)	Reference	Form
ACUTE EXPOSURE									
Death									
1	Rat	(GW)	1 d 1x/d				132 (LD_{50}, adult) 220 (LD_{50}, weanling)	Tarditf et al. 1980	$BaCl_2$
2	Rat	(GW)	1 d 1x/d				277 (LD_{50}, males) 269 (LD_{50}, females)	Borzelleca et al. 1988	$BaCl_2$
3	Rat	(GW)	1 d 1x/d				198 (death in 15/20 rats)	Borzelleca et al. 1988	$BaCl_2$
4	Rat	(GW)	10 d 1x/d				198 (death in 3/10 rats)	Borzelleca et al. 1988	$BaCl_2$
Systemic									
5	Rat	(GW)	1 d 1x/d	Resp		198 (fluid in trachea)		Borzelleca et al. 1988	$BaCl_2$
				Cardio	198				
				Gastro	66	198 (inflammation of intestines)			
				Hemato	198				
				Hepatic	66	198 (decreased liver/ brain weight ratio; darkened liver)			
				Renal	66	198 (increased kidney/ body weight ratio)			
				Other	66	198 (decreased body weight)			
Immunological									
6	Rat	(GW)	1 d 1x/d		198			Borzelleca et al. 1988	$BaCl_2$
7	Rat	(GW)	10 d 1x/d		198			Borzelleca et al. 1988	$BaCl_2$

TABLE 2-1 (Continued)

Key to figure[a]	Species	Route	Exposure frequency/ duration	System	NOAEL (mg Ba/kg/day)	LOAEL (effect) Less serious (mg Ba/kg/day)	LOAEL (effect) Serious (mg Ba/kg/day)	Reference	Form
Neurological									
8	Rat	(GW)	1 d 1x/d		198			Borzelleca et al. 1988	$BaCl_2$
9	Rat	(GW)	10 d 1x/d		198			Borzelleca et al. 1988	$BaCl_2$
Reproductive									
10	Rat	(GW)	1 d 1x/d		198			Borzelleca et al. 1988	$BaCl_2$
11	Rat	(GW)	10 d 1x/d		138	198 (decreased ovaries weight and ovaries/ brain weight ratio)		Borzelleca et al. 1988	$BaCl_2$
INTERMEDIATE EXPOSURE									
Death									
12	Rat	(W)	13 wk 7d/wk		35			Tardiff et al. 1980	$BaCl_2$
Systemic									
13	Human	(W)	4 wk 7d/wk	Cardio	0.21			Wones et al. 1990	$BaCl_2$
14	Rat	(W)	1 mo 7d/wk	Cardio	0.71	7.1 (increased blood pressure)		Perry et al. 1983, 1985, 1989	$BaCl_2$
15	Rat	(W)	4 mo 7d/wk	Cardio	0.643	6.43 (increased blood pressure)		Perry et al. 1983, 1985, 1989	$BaCl_2$
16	Rat	(W)	13 wk 7d/wk	Resp	35			Tardiff et al. 1980	$BaCl_2$
				Cardio	35				
				Hemato	35				
				Musc/skel	35				
				Hepatic	35				
				Renal	35				
				Other	35				

TABLE 2-1 (Continued)

Key to figure[a]	Species	Route	Exposure frequency/ duration	System	NOAEL (mg Ba/kg/day)	LOAEL (effect) Less serious (mg Ba/kg/day)	LOAEL (effect) Serious (mg Ba/kg/day)	Reference	Form
17	Rat	(W)	16 wk 7d/wk	Cardio Renal	15 15			McCauley et al. 1985	N.S.
Neurological									
18	Rat	(W)	13 wk 7d/wk		35			Tardiff et al. 1980	$BaCl_2$
CHRONIC EXPOSURE									
Death									
19	Rat	(W)	2 yr 7d/wk		0.7			Schroeder and Mitchener 1975a	$Ba(C_2H_3O_2)_2$
20	Mouse	(W)	2 yr 7d/wk				0.95 (reduced lifespan in males)	Schroeder and Mitchener 1975b	$Ba(C_2H_3O_2)_2$
Systemic									
21	Rat	(W)	2 yr 7d/wk	Resp Cardio Hepatic Renal	0.7 0.7 0.7 0.7			Schroeder and Mitchener 1975a	$Ba(C_2H_3O_2)_2$
22	Rat	(W)	16 mo 7d/wk	Cardio		5.4 (myocardial pathophysiologic and metabolic changes)		Kopp et al. 1985; Perry et al. 1983, 1985, 1989	$BaCl_2$
23	Rat	(W)	16 mo 7d/wk	Cardio	0.054	0.54 (increased blood pressure)		Perry et al. 1983, 1985, 1989	$BaCl_2$

TABLE 2-1 (Continued)

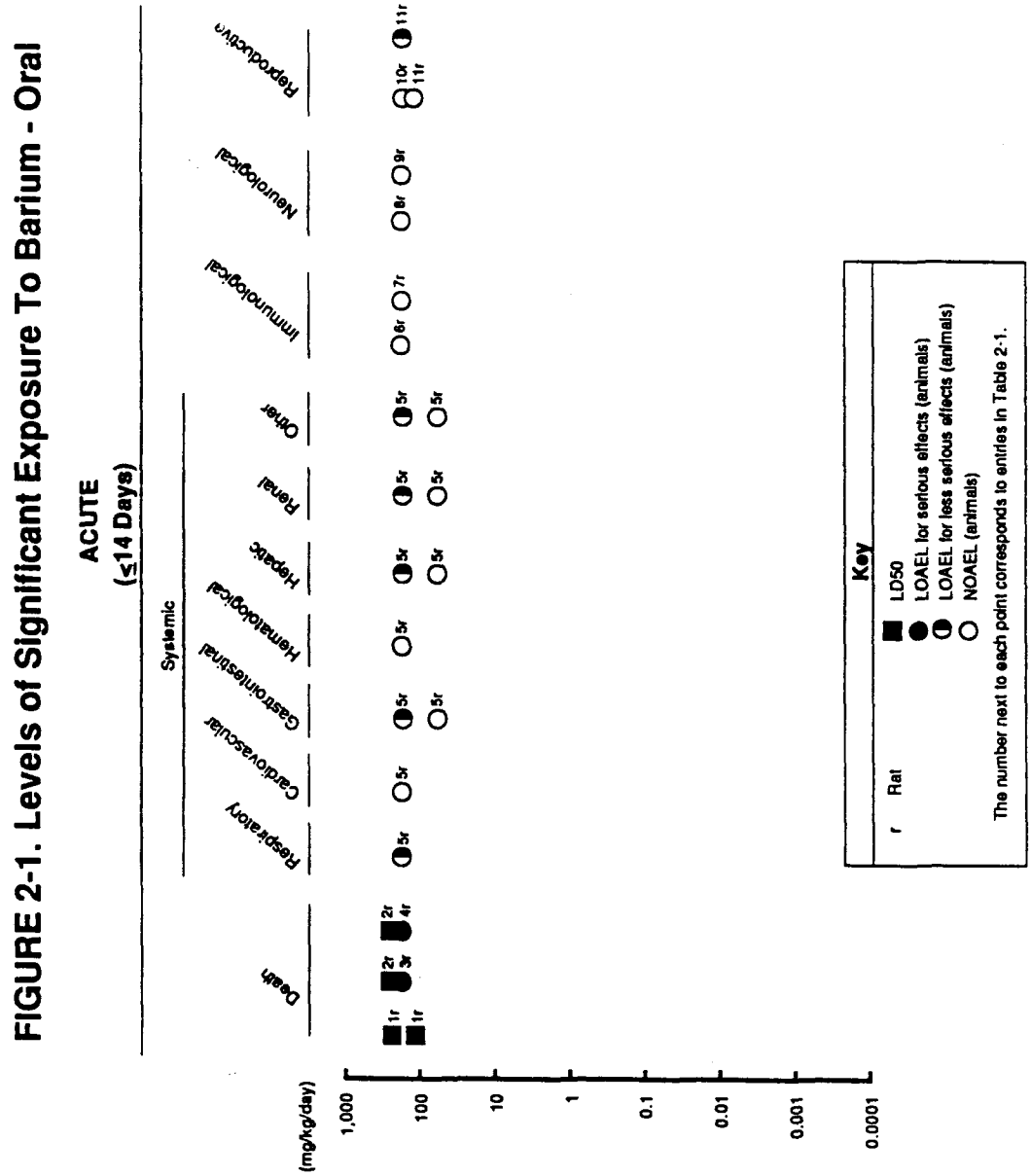
Key to figure[a]	Species	Route	Exposure frequency/ duration	System	NOAEL (mg Ba/kg/day)	LOAEL (effect) Less serious (mg Ba/kg/day)	LOAEL (effect) Serious (mg Ba/kg/day)	Reference	Form
24	Mouse	(W)	2 yr 7d/wk	Other	0.95			Schroeder and Mitchener 1975b	$Ba(C_2H_3O_2)_2$

[a]The number corresponds to entries in Figure 2-1.

$Ba(C_2H_3O_2)_2$ = barium acetate; $BaCl_2$ = barium chloride; Cardio = cardiovascular; d = day; Gastro = gastrointestinal; GW = gavage-water; Hemato = hematological; LD_{50} = lethal dose, 50% kill; *mo* = *month*; Musc/skel = musculoskeletal; N.S. = not specified; Resp = respiratory; W = drinking water; wk = week; x = time(s); yr = year

2. HEALTH EFFECTS

FIGURE 2-1. Levels of Significant Exposure to Barium - Oral



2. HEALTH EFFECTS

FIGURE 2-1 (Continued)

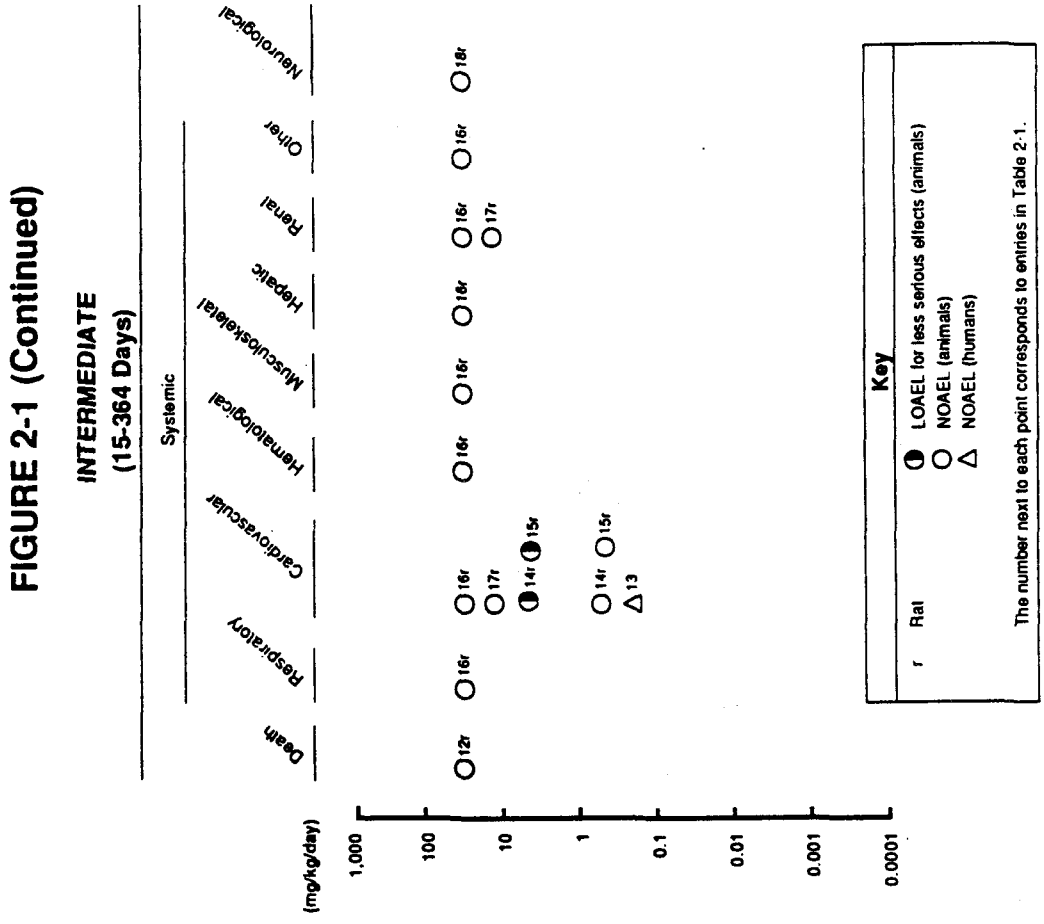
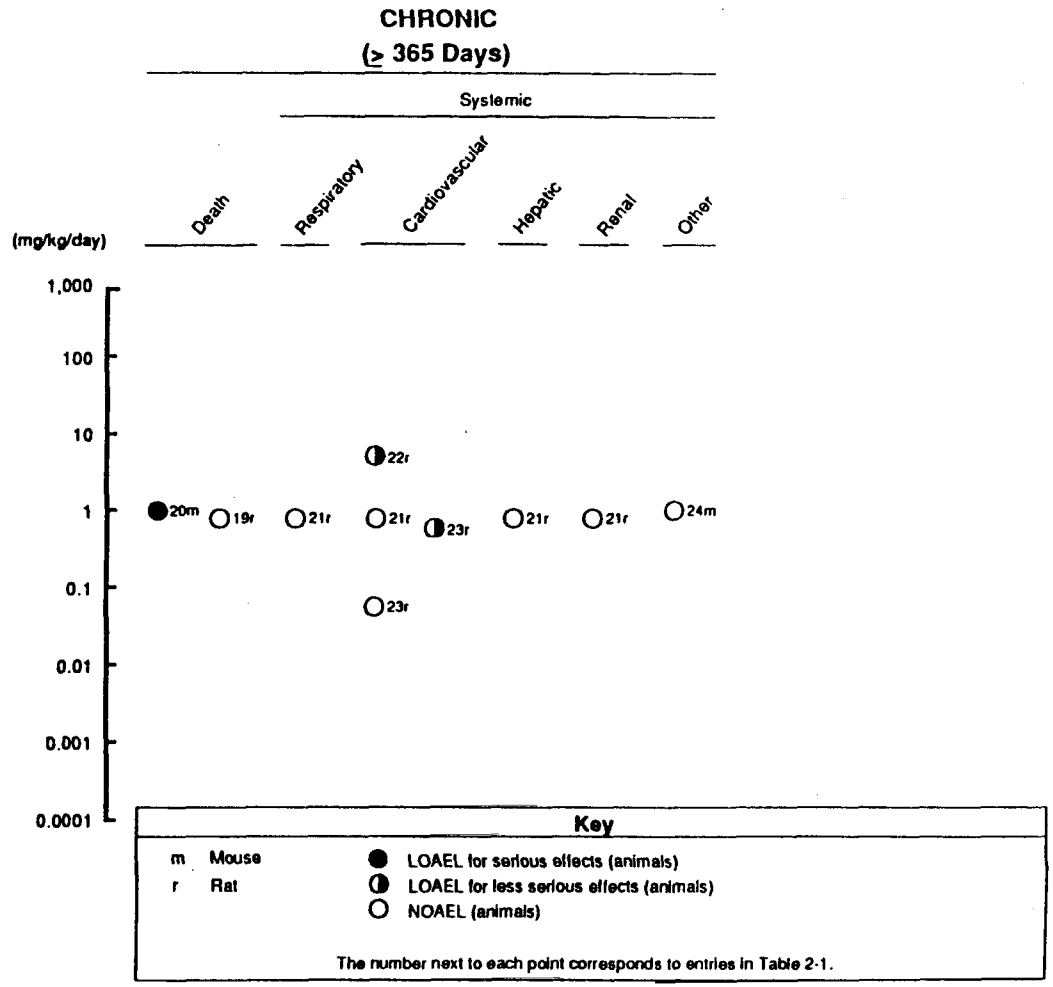


FIGURE 2-1 (Continued)



histopathological lesions of the lung have not been observed in rats exposed to 0.7 mg barium/kg/day as barium acetate in drinking water for lifetime (Schroeder and Mitchener 1975a).

Cardiovascular Effects. The most commonly observed cardiovascular effects in cases of acute ingestion of barium compounds are hypertension and abnormalities in heart rhythm (Das and Singh 1970; Diengott et al. 1964; Gould et al. 1973; Wetherill et al. 1981). Myocardial damage was observed in a few cases (Lewi and Bar-Khayim 1964; McNally 1925; Talwar and Sharma 1979). Ln one atypical case, hypotension was observed (Talwar and Sharma 1979).

No adverse effects on blood pressure or cardiac rhythms were observed in a study in which volunteers consumed 0.21 mg barium/kg/day for 4 weeks (Wones et al. 1990). In this study, the subjects' preexposure blood pressure and cardiac rhythm served as the control for comparison with postexposure values. This study is somewhat limited in that the number of subjects evaluated was small (n=11) and the absorption and/or serum levels of barium were not assessed. An epidemiological study of communities consuming drinking water containing elevated barium levels also did not provide evidence that chronic exposure to barium in drinking water was associated with increased blood pressure, hypertension, stroke, heart disease, *or* altered electrocardiograms (Brenniman and Levy 1985; Brenniman et al. 1979a, 1979b, 1981). However, this study is limited in that blood pressure was determined in a single 20-minute session and not followed over a longer period (e.g., months, years), exposure conditions were not well-characterized (duration, frequency), individual exposure doses were not determined, and the incidence of hypertension, stroke, and heart disease was determined by responses to a survey questionnaire and not by testing and/or diagnosis.

Cardiovascular effects have been evaluated in acute, intermediate, and chronic oral studies with experimental animals. Acute studies have been limited to histological examination of the heart following 1-day or 10-day gavage exposure of rats to doses as high as 198 mg barium/kg/day as barium chloride (Borzelleca et al. 1988). No microscopic lesions of the heart were observed. Other cardiovascular parameters were not evaluated.

Results from several studies with experimental animals indicate that intermediate and chronic oral exposure to barium is associated with adverse cardiovascular effects (Kopp et al. 1985; Perry et al. 1983, 1985, 1989). In a series of experiments, rats were administered barium chloride in drinking water either for 1, 4, or 16 months (Perry et al. 1983, 1985, 1989). Elemental barium doses in the l-month study were either 0, 0.071, 0.71, or 7.1 mg/kg/day. Elemental barium doses in the 4-month study were either 0, 0.0643, 0.643, or 6.43 mg/kg/day. Elemental barium doses in the 16-month study were either 0, 0.054, 0.54, or 5.4 mg/kg/day. In the l-month study, significant increases in blood pressure were noted in rats treated with 7.1 mg/kg/day; no change in blood pressure was noted in rats treated with

either 0.071, or 0.71 mg/kg/day. In the 4-month study, significant increases in blood pressure were observed in rats treated with 6.43 mg/kg/day; no change in blood pressure was observed in rats treated with either 0.0643 or 0.643 mg/kg/day. Significant increases in blood pressure also were noted in the 16-month study in rats treated with 0.54 and 5.4 mg/kg/day; however, no effects on blood pressure were noted in the 16-month experiment at 0.054 mg/kg/day. The high-dose group (5.4 mg/kg/day) exposed for 16 months also had depressed cardiac contraction, depressed cardiac electrical conductivity, and decreased cardiac ATP, phosphocreatine, and phosphorylation potential (Kopp et al. 1985; Perry et al. 1983, 1985, 1989).

In contrast to the studies by Perry et al. (1983, 1985, 1989), increased blood pressure was not observed in one study in which barium was administered to normotensive rats for an intermediate period at doses up to 15 mg/kg/day in either drinking water or in 0.9% saline (McCauley et al. 1985). The reason for the discrepancy between the results of the studies by Perry et al. (1983, 1985, 1989) and the study by McCauley et al. (1985) is not known. As in the Perry et al. (1983, 1985, 1989) studies, the rats in the study by McCauley et al. (1985) were maintained on a diet low in barium content. However, it was not reported by McCauley et al. (1985) whether or not this low barium diet contained certain other trace metals. Certain metals such as sodium and potassium can potentially influence blood pressure.

In other studies with rats, intermediate and chronic oral exposure to barium chloride and barium acetate in drinking water have not been associated with any changes in heart weight or with any gross or microscopic Lesions of the heart (Schroeder and Mitchener 1975a; Tardiff et al. 1980).

Additional experiments using uninephrectomized and specially bred Dahl salt-sensitive and salt-resistant strains of rats revealed no adverse effects on blood pressure resulting from 16 weeks of exposure to barium doses as high as 150 mg/kg/day (McCauley et al. 1985). However, no untreated controls were used in these experiments; thus, these results must be interpreted with caution. Interestingly, Dahl salt-sensitive rats treated with 15 or 150 mg barium/kg/day did not experience the normal hypertensive response when given 0.9% NaCl-containing drinking water. Experiments assessing the effect of a 5-month exposure to barium on the cardiac response to an arrythmagenic challenge with 1-norepinephrine demonstrated a significant increase in reflex bradycardia when rats were given 37.5 mg barium/kg/day in their drinking water (McCauley et al. 1985). However, this experiment was confounded by the presence of barium in the diet of both control and treated animals (estimated barium intake from diet consumption = 1 mg/kg/day). Without adequate controls these experiments are difficult to interpret.

Gastrointestinal Effects. All cases of acute oral barium poisoning in adults exhibit gastrointestinal disturbances as the initial symptoms. These include gastric pain, vomiting, and diarrhea (Das and Singh 1970; Diengott et

al. 1964; Gould et al. 1973; Lewi and Bar-Khayim 1964; McNally 1925; Morton 1945; Ogen *et* al. 1967; Phelan et al. 1984; Talwar and Sharma 1979; Wetherill et al. 1981). In one case, severe gastrointestinal hemorrhage occurred in an adult male victim (Diengott et al. 1964).

Gastrointestinal effects also have been observed in animals, but the reliable animal data are limited. Inflammation of the intestines was noted in rats acutely exposed by gavage to doses of 198 mg barium/kg/day as barium chloride (Borzelleca et al. 1988). Stomach rupture, bowel obstruction, and gastrointestinal hemorrhage have been observed in rats in a separate study involving acute oral exposure to barium sulfate; however, those adverse effects were most likely due to the massive doses used in the study (25%-40% of body weight) and not necessarily to barium sulfate toxicity (Boyd and Abel 1966). No gross or microscopic lesions of the esophagus, stomach, pancreas, small intestines, or colon were noted in several intermediate and chronic experiments in which rats were exposed to doses as high as 37.5 mg barium/kg/day of an unspecified barium compound in drinking water; however, interpretation of these experiments is confounded by the presence of barium as a contaminant in the rat chow and the resulting lack of an "untreated" control group (McCauley et al. 1985). Actual oral exposure doses cannot be reliably determined from these particular intermediate and chronic studies but may be estimated at up to 38.5 mg barium/kg/day by adding the estimated intake from the contaminated chow (1 mg barium/kg/day) to the dose in the drinking water.

Hematological Effects. In human case studies of oral barium poisoning, a decrease in serum potassium is frequently observed in the subjects (Diengott et al. 1964; Gould et al. 1973; Lewi and Bar-Khayim 1964; Phelan et al. 1984; Talwar and Sharma 1979; Wetherill et al. 1981).

The effect of oral barium exposure on various blood chemistry parameters that are important for cardiovascular function has been evaluated in only one experimental study with humans (Wones et al. 1990). In this study, 0.2 mg barium/kg/day as barium chloride was supplied in the drinking water of subjects for 4 weeks. No clinically significant changes were noted in any of the blood chemistry parameters monitored (total plasma cholesterol; plasma triglycerides; plasma HDL and LDL cholesterol; plasma apolipoproteins; and serum glucose, potassium, calcium, and albumin). However, this study is limited in that the number of subjects evaluated was small (n-11) and absorption and/or serum levels of barium were not assessed.

Results of animal studies indicate that acute, intermediate, and chronic oral exposure to barium is not associated with any adverse hematological effects. In an acute study in which groups of rats were exposed by gavage to four doses ranging from 66 to 198 mg barium/kg/day as barium chloride, hematological and blood chemistry parameters did not significantly change or could not be attributed to barium exposure (erythrocyte, leukocyte, platelet, and differential leukocyte count; hematocrit; hemoglobin; prothrombin time;

plasma fibrinogen; serum protein, albumin, globulin, bilirubin. creatine, calcium, phosphorus, chloride, 5'-nucleotidase, glutamic pyruvic transaminase, glutamic oxaloacetic transaminase, and alkaline phosphatase) (Borzelleca et al. 1988). Intermediate and chronic oral exposure of rats to barium acetate and barium chloride in drinking water has not been associated with any significant or treatment-related changes in a variety,of hematological parameters (Schroeder and Mitchener 1975a; Tardiff et al. 1980). Elemental barium doses in these intermediate and chronic drinking water studies ranged from 0.7 mg/kg/day to 35 mg/kg/day.

Musculoskeletal Effects. The predominant musculoskeletal effect observed in cases of barium toxicity in humans is progressive muscle weakness, often leading to partial or total paralysis (Das and Singh 1970; Diengott et al. 1964; Gould et al. 1973; Lewi and Bar-Khayim 1964; McNally 1925; Morton 1945; Ogen et al. 1967; Phelan et al. 1984; Wetherill et al. 1981). In severe cases, the paralysis affects the respiratory system (Das and Singh 1970; Gould et al. 1973; Lewi and Bar-Khayim 1964; Morton 1945; Ogen et al. 1967; Phelan et al. 1984; Wetherill et al. 1981).

Very limited animal data are available regarding the musculoskeletal effects of barium following oral exposure. No changes in femur weight and no gross or microscopic lesions of the femur were observed in rats following intermediate exposure to doses of 35 mg barium/kg/day as barium chloride in drinking water (Tardiff et al. 1980). Gross and microscopic lesions of the sternebrae and femur were not observed in several intermediate and chronic experiments in which rats were exposed to an unspecified barium compound in drinking water (McCauley et al. 1985). However, these experiments were flawed in that barium was detected as a contaminant in the rat chow of both control and treated animals; consequently, no true "untreated" controls were available for comparison. Thus, the results should be interpreted with caution.

Hepatic Effects. In one case study involving accidental acute ingestion of barium carbonate in an adult female, some degeneration of the liver was noted post-mortem .(McNally 1925). Adverse hepatic effects in animals following oral barium exposure have been minor or have not been observed. Decreased liver/brain weight ratio and darkened liver were observed in rats exposed acutely by gavage to 198 mg barium/kg/day as barium chloride; however, these changes were not associated with any microscopic hepatic lesions (Borzelleca et al. 1988). Acute gavage exposure of rats to four doses ranging from 66 to 198 mg barium/kg/day as barium chloride was not associated with any significant changes in the activities of serum glutamic pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), or alkaline phosphatase (ALP) (Borzelleca et al. 1988). Changes in these enzyme levels in blood can be indicative of liver damage. Significantly reduced blood urea nitrogen was noted at all exposure doses. A reduction in this particular blood chemistry parameter is a potential sign of altered liver function. However, insufficient information was presented in the published study to

determine if the reduced blood urea nitrogen was an adverse liver effect. Results of intermediate and chronic studies involving oral exposure of rats to barium in drinking water have been negative for hepatic effects (Schroeder and Mitchener 1975a; Tardiff et al. 1980). In these intermediate and chronic studies, hepatic effects were assessed by determining hepatic weight and by performing gross and histopathological examinations of the liver.

Renal Effects. Toxic effects on the kidneys have been observed in several adult cases of acute barium poisoning. Effects include hemoglobin in the urine (Gould et al. 1973), renal insufficiency (Lewi and Bar-Khayim 1964; Phelan et al. 1984), degeneration of the kidneys (McNally 1925), and acute renal failure (Wetherill et al. 1981).

Renal effects observed in animals following oral barium exposure have been minor. Increased kidney/body weight ratios have been noted in rats exposed acutely by gavage to 198 mg barium/kg/day as barium chloride; however, this change was not associated with gross or microscopic renal lesions (Borzelleca et al. 1988).

Results of intermediate and chronic studies in which rats have been exposed orally to barium drinking water have been negative for renal effects (McCauley et al. 1985; Schroeder and Mitchener 1975a; Tardiff et al. 1980). In these intermediate and chronic studies, renal effects were evaluated by determining kidney weight and by performing gross and/or histopathologic examination of the kidney. Lesions of the renal glomeruli were reportedly observed in several experiments involving oral exposure of uninephrectomized rats and salt-sensitive and salt-resistant rats to 150 mg barium/kg/day of an unspecified barium compound for 16 weeks; however, these particular experiments are inconclusive regarding renal toxicity because no control animals were used (McCauley et al. 1985).

Dermal/Ocular Effects. No studies were located regarding dermal/ocular effects in humans after oral exposure to barium. In studies with Sprague-Dawley rats, both ocular discharge following acute oral exposure to barium chloride (Borzelleca et al. 1988) and a nonsignificant increase in retinal dystrophy following intermediate and chronic oral exposure to an unspecified barium compound (McCauley et al. 1985) have been observed. Although the retinal dystrophy was statistically insignificant, a dose-related trend was observed if different duration exposure groups were combined (McCauley et al. 1985). Both ocular discharge and retinal dystrophy are commonly observed in Sprague-Dawley rats; consequently, the ocular lesions noted in these animal studies can not necessarily be attributed to oral barium exposure.

Other Systemic Effects. In one human case study involving accidental acute ingestion of barium carbonate by an adult female, some degeneration of the spleen was noted post-mortem (McNally 1925). Body weight has been monitored in a number of acute, intermediate, and chronic studies in which

rats and mice were exposed orally to barium compounds (Borzelleca et al. 1988; Perry et al. 1983, 1985, 1989; Schroeder and Mitchener 1975a, 1975b; Tardiff et al. 1980). A change in body weight was observed in only one of these studies (Borzelleca et al. 1988). In this one study, decreased body weight was noted in rats given a single gavage dose of 198 mg barium/kg/day as barium chloride (Borzelleca et al. 1988). Limited data are available on other systemic effects of barium. In one intermediate drinking water study with rats, no gross or microscopic lesions of the adrenals were noted at doses up to 35 mg barium/kg/day as barium chloride (Tardiff et al. 1980).

2.2.2.3 Immunological Effects

No studies were located regarding immunological effects in humans after oral exposure to barium. Animal data regarding immunological effects following oral exposure are very limited. Acute gavage exposure of rats to doses less than 198 mg barium/kg/day as barium chloride was not associated with any changes in thymus weight or any gross lesions of the thymus (Borzelleca et al. 1988). Intermediate and chronic oral exposure of rats to nominal concentrations of barium in drinking water of 37.5 and 15 mg/kg/day, respectively, was not associated with lesions of the lymph nodes or thymus upon gross and histopathologic examination (McCauley et al. 1985). However, this latter study is of limited value for evaluating the effects of barium because the barium compound tested was not specified and the chow used to feed the rats was contaminated with 12 ppm barium; thus, no true "untreated" control group was available for comparison.

The highest NOAEL values for immunological effects in each species and duration category are recorded in Table 2-1 and plotted in Figure 2-1.

2.2.2.4 Neurological Effects

Numbness and tingling around the mouth and neck were sometimes among the first symptoms of barium toxicity in humans (Lewi and Bar-Khayim 1964; Morton 1945). Occasionally, these neurological symptoms extended to the extremities (Das and Singh 1970; Lewi and Bar-Khayim 1964). Partial and complete paralysis occurred in severe cases, often accompanied by an absence of deep tendon reflexes (Das and Singh 1970; Diengott et al. 1964; Gould et al. 1973; Lewi and Bar-Khayim 1964; Morton 1945; Ogen et al. 1967; Phelan et al. 1984; Wetherill et al. 1981). Post-mortem examination in one case of poisoning by ingestion of barium sulfide revealed brain congestion and edema (McNally 1925).

Animal studies evaluating the neurological effects of barium following oral exposure are limited to three reports (Borzelleca et al. 1988; McCauley et al. 1985; Tardiff et al. 1980). Acute gavage exposure of rats to doses as high as 198 mg barium/kg/day as barium chloride was not associated with changes in brain weight or with any gross lesions of the brain (Borzelleca et al. 1988). Intermediate oral exposure of rats to nominal doses less than

37.5 mg barium/kg/day in drinking water was not associated with lesions of the brain upon gross and microscopic examination (McCauley et al. 1985; Tardiff et al. 1980), or with any changes in brain weight (Tardiff et al. 1980). No lesions of the brain were observed in rats following chronic oral exposure to nominal doses of 15 mg barium/kg/day in drinking water (McCauley et al. 1985). The intermediate and chronic drinking water studies are of limited value for assessing the effects of barium on the brain because the barium compound tested was not specified and because the chow used to feed the rats was contaminated with 12 ppm barium; thus, no true "untreated" control group was available for comparison.

The highest NOAEL values for neurological effects in each species and duration category are recorded in Table 2-1 and plotted in Figure 2-1.

2.2.2.5 Developmental Effects

Studies regarding developmental effects of barium following oral exposure are limited to one human study (Morton et al. 1976) and one animal study (Tarasenko et al. 1977). A statistically significant negative correlation was found between barium concentrations in drinking water and human congenital malformation rates of the central nervous system in South Wales (Morton et al. 1976). A negative correlation implies that as the barium concentration in drinking water increased, the rate of central nervous system malformations decreased. This statistical study is of limited value in identifying a NOAEL for developmental effects because exposure conditions (duration and frequency of exposure, dose, number of subjects exposed) were not characterized.

Developmental effects were reported in one study in which female rats were treated orally during conception and pregnancy with approximately 18.3 mg barium/kg/day as barium carbonate (Tarasenko et al. 1977). Reported effects in offspring included increased mortality, increased leukocyte count, disturbances in liver function, and increased urinary excretion of hippuric acid. The latter study is inadequate for evaluating developmental effects of oral barium exposure because of major study limitations. These limitations include a general lack of information provided by the authors regarding experimental methods, exposure conditions, and test results, and no information as to the number of animals tested, the purity of the test material, the statistical methods used, and whether or not controls were used. No other animal studies evaluating developmental effects were available.

2.2.2.6 Reproductive Effects

No studies were located regarding reproductive effects in humans after oral exposure to barium. However, limited data are available from acute, intermediate, and chronic animal studies in which certain reproductive organs were weighed and examined grossly and microscopically following oral barium exposure. Acute gavage exposure of rats to doses as low as 198 mg

barium/kg/day as barium chloride has been associated with decreased ovary weight and decreased ovary/brain weight ratio; however, no changes in testicular weight and no gross lesions of the ovaries or testes were observed at this dose (Borzelleca et al. 1988). No adverse effects in these parameters were noted at doses as high as 135 mg barium/kg/day. Intermediate and chronic oral exposure of rats to nominal concentrations of barium in drinking water of 37.5 or 15 mg/kg/day, respectively, was not associated with any gross or histopathologic lesions of the uterus, ovaries, or testes (McCauley et al. 1985). However, this latter study is of limited value for identifying a NOAEL for barium because the barium compound tested was not specified and because the chow used to feed the rats was contaminated with 12 ppm barium; thus, no true "untreated" control group was available for comparison. No animal studies were available that assessed reproductive function following oral barium exposure.

The highest NOAEL values and all reliable LOAEL values for reproductive effects in each species and duration category are recorded in Table 2-1 and plotted in Figure 2-1.

2.2.2.7 Genotoxic Effects

No studies were located regarding genotoxicity in humans or animals after oral exposure to barium. Genotoxicity studies are discussed in Section 2.4.

2.2.2.8 Cancer

No studies were located regarding cancer in humans after oral exposure to barium. Only two animal studies evaluated the induction of tumors following chronic oral exposure to barium (Schroeder and Mitchener 1975a, 1975b). In these two studies, rats and mice were exposed to 0.7 and 0.95 mg barium/kg/day, respectively, as barium acetate in drinking water for lifetime. Organs and tissues were examined grossly and microscopically; organs examined microscopically were limited to heart, lung, liver, kidney, and spleen. No differences in the incidence of tumors were noted between treated animals and vehicle controls in either study. These two studies are inadequate for evaluating the carcinogenic potential of barium because insufficient numbers of animals were used for a carcinogenicity study, it was not determined whether or not a maximum tolerated dose was achieved, a complete histological examination was not performed, the purity of the test material was not specified, and only one exposure dose was used in each study.

2.2.3 Dermal Exposure

Limited information is available regarding the health effects of barium following dermal exposure. Barium salts would be expected to have a local effect on skin surfaces and would not likely be absorbed systematically to any great extent. Available studies include a case report of an individual exposed

dermally to molten barium chloride (Stewart and Hummel 1984), a skin irritation study evaluating barium carbonate in experimental animals (Tarasenko et al. 1977), and a skin-painting study in which mice were exposed dermally to a barium hydroxide extract of tobacco leaf (Van Duuren et al. 1968). No reliable information was available from any of these dermal studies to identify study NOAELs or LOAELs for barium. In the case report (Stewart and Hummel 1984), the dermal burns that developed in the individual exposed to molten barium chloride may potentially have contributed to some of the reported health effects, which are described briefly in Section 2.2.3.2 (Systemic Effects).

2.2.3.1 Death

No studies were located regarding death in humans or animals after dermal exposure to barium.

2.2.3.2 Systemic Effects

No studies were located regarding respiratory, musculoskeletal, hepatic, or renal effects in humans or animals after dermal exposure to barium.

Cardiovascular Effects. An abnormal electrocardiogram was observed in a 62-year-old man burned by molten barium chloride (Stewart and Hummel 1984). No studies were located regarding cardiovascular effects in animals after dermal exposure to barium.

Gastrointestinal Effects. A 62-year-old man experienced vomiting after he was accidentally burned by molten barium chloride (Stewart and Hummel 1984). No studies were located regarding gastrointestinal effects in animals after dermal exposure to barium.

Hematological Effects. A 62-year-old victim accidentally exposed to molten barium chloride had a depressed plasma potassium level and an increased plasma barium level when admitted to the hospital (Stewart and Hammel 1984). No studies were located regarding hematological effects in animals after dermal exposure to barium.

Dermal/Ocular Effects. Molten barium chloride induced burns on the skin of a 62-year-old man who was accidentally exposed through an explosion. The dermal burns, however, were very probably due to the molten nature of the material and not necessarily to barium chloride (Stewart and Hammel 1984).

The dermal and ocular effects of barium carbonate were examined in a study with rats and rabbits (Tarasenko et al. 1977). When barium carbonate in lanolin was applied to the skin, ulcers developed. These dermal lesions reportedly disappeared within a month when dermal treatment was discontinued. When barium carbonate powder was introduced into the conjunctival sac,

purulent discharge, conjunctivitis, and slight opacity of the cornea developed. Although these findings suggest that barium carbonate may be a dermal and ocular irritant, these particular investigations are inadequate for establishing the dermal and ocular effects of barium because of a number of significant study limitations. The authors provided few details regarding experimental methods and results, and no information as to the concentration of barium carbonate used, the number of animals used, and whether or not controls were used. Furthermore, rats are not typically used to evaluate the skin and eye irritating effects of compounds.

No studies were located regarding the following health effects in humans or animals after dermal exposure to barium:

2.2.3.3 Immunological Effects
2.2.3.4 Neurological Effects
2.2.3.5 Developmental Effects
2.2.3.6 Reproductive Effects
2.2.3.7 Genotoxic Effects

Genotoxicity studies are discussed in Section 2.4.

2.2.3.8 Cancer

No studies were located regarding cancer in humans after dermal exposure to barium. Dysplasia of the cervical epithelium was reportedly induced in a woman who had a barium chloride solution applied to her cervix (Ayre 1966). The use of dimethyl sulfoxide in combination with the barium chloride solution reportedly enhanced the ability of barium chloride to induce dysplasia. Dysplasia can be regarded as a potential precancerous lesion. The significance of the observations reported in this study are difficult to assess, since only one subject was exposed and because there have been no reports of similar findings in other human or animal studies. Also, the vehicle used was not specified in this study.

No studies were located regarding cancer in animals after dermal exposure to barium. However, results of one skin-painting study with mice suggest that barium hydroxide extract derived from tobacco leaf may act as a tumor-promoting agent (Van Duuren et al. 1968). In this study, mice were treated dermally for an unspecified period of time with either barium hydroxide extract alone, 7,12-dimethylbenz(a)anthracene (DMBA) alone (an initiating agent), or a combination of DMBA and barium hydroxide extract. After 1 year, none of the mice treated with barium hydroxide extract developed skin tumors. However, 3 out of 20 mice treated with DMBA alone and 7 out of 20 mice treated with a combination of both barium hydroxide extract and DMBA developed skin papillomas and carcinomas. These results provide limited, but suggestive evidence that barium hydroxide extract of tobacco leaf acted as a tumor-promoting agent. However, it can not be determined whether or not this

apparent positive tumorigenic response was due to barium hydroxide or some other component of the barium hydroxide tobacco leaf extract.

2.3 TOXICOKINETICS

2.3.1 Absorption

2.3.1.1 Inhalation Exposure

No studies were located regarding absorption of barium in humans following inhalation exposure: However, results of studies with experimental animals suggest that the rate and extent of absorption of barium from the respiratory tract depends on the exposure level, how much barium reaches the alveolar spaces, the clearance rate from the upper respiratory tract, and the solubility of the particular form of barium that was administered.

The results of a hamster study indicated that after inhalation of barium chloride, 65% of the administered dose was deposited in the nasal region and was eventually absorbed into the body (Cuddihy and Ozog 1973b). Radioactive barium sulfate that is injected directly into the trachea of rats can be taken up into the epithelium membranes, and remain in these membranes for at least a few weeks (Gore and Patrick 1982; Takahashi and Patrick 1987). These studies have also shown that barium in the trachea can be cleared to the lymphatic system (Takahashi and Patrick 1987).

Results of experiments with dogs have indicated that, following inhalation of barium chloride or barium sulfate, approximately half of the barium chloride dose and three-fourths of the barium sulfate dose are deposited in the pulmonary region (Cuddihy et al. 1974). About one-fourth of the absorbed barium is transported to the skeleton, the remainder is excreted in the urine and feces within 2 weeks. The biological half life of radioactive barium sulfate in the pulmonary region has been calculated to be 8 days in the dog (Morrow et al. 1964) and 10 days in the rat (Cember et al. 1961). Total body deposition in dogs that inhaled radioactive barium chloride was found to be 51% of the total inhaled activity, indicating that at least this much was absorbed (Morrow et al. 1964). Experiments in rats exposed to barium sulfate via intratracheal injection have shown that about 7% of the initial lung burden was finally cleared to the blood (Spritzer and Watson 1964).

2.3.1.2 Oral Exposure

As with other metals, barium is probably very poorly absorbed from the gastrointestinal tract. The International Commission for Radiation Protection (ICRP) estimates that the gastrointestinal absorption of barium is less than 5% (ICRP 1973). This percentage is supported by studies of two men whose daily input and fecal excretion were monitored for 50 weeks (Tipton et al. 1969).

Experiments in rats have shown that younger animals (22 days old or less) absorb about 10 times more barium chloride from the gastrointestinal tract (63%-84%) than do older animals (about 7%) (Taylor et al. 1962). Starved adult rats absorb a bit more (20%). Gastrointestinal absorption in dogs has been calculated to be about 7% (Cuddihy and Griffith 1972). Measurements of barium in the serum indicate that the peak absorption from the gastrointestinal system is within 1 hour in dogs (Chou and Chin 1943). Similar results were seen in rats given various barium compounds (McCauley and Washington 1983).

2.3.1.3 Dermal Exposure

No studies were located regarding absorption of barium in humans after dermal exposure. One animal study showed that barium applied to the skin of piglets was found in the various layers of the skin (Shvydko et al. 1971). Barium is not expected to cross the intact skin because of the high polarity of the forms in which it is most commonly encountered.

2.3.2 Distribution

2.3.2.1 Inhalation Exposure

Studies in humans indicate that barium distributes predominantly to the skeleton and teeth. The route of exposure is not always known, but it is presumed to be mostly oral; therefore, the studies are discussed below in Section 2.3.2.2.

Dogs that inhaled radiolabeled barium chloride had about 70% of the initial body burden in the lungs and internal organs. Of this, most was in the skeleton (44%), and urine and feces (13% each). Very little was found in the blood (1%) and muscle (4%) (Cuddihy and Griffith 1972).

2.3.2.2 Oral Exposure

Humans can be exposed to barium in the air, water, or food. Numerous studies exist that discuss the distribution of barium in the human body, but they do not always specify route of exposure. It is presumed that the majority of the barium intake is from the oral route. Barium occurs mostly (over 93%) in the bones and teeth of humans. Very little is found in blood plasma or soft tissues; but, when it is detected in the organs, it is found in the eye, lungs, skin, and adipose tissue in humans at less than 1% of total body weight (Schroeder et al. 1972). This information is supported by a number of studies (Bauer et al. 1957; Losee et al. 1974; Miller et al. 1985; Moloukhia and Ahmed 1979; Sowden 1958; Sowden and Stitch 1957; Sowden and Pirie 1958).

Rats that ate barium chloride as a component of Brazil nuts showed an accumulation in the skeleton (Stoewsand et al. 1988). Rats that were given

various barium compounds in the drinking water showed distribution to the heart > eye > skeletal muscle > kidney > blood > liver. The skeleton was not examined (McCauley and Washington 1983).

2.3.2.3 Dermal Exposure

No studies were located regarding distribution of barium in humans or animals after dermal exposure.

2.3.3 Metabolism

Barium is not metabolized in the body, but it may be metabolically transported or incorporated into complexes or tissues.

2.3.4 Excretion

2.3.4.1 Inhalation Exposure

No studies have been located regarding excretion of barium following inhalation exposure in humans. In dogs that inhaled radiolabeled barium chloride, less than 1% of the initial body burden remained in the body after 5 days. Fecal excretion was about twice that of urinary excretion (Cuddihy and Griffith 1972).

2.3.4.2 Oral Exposure

Barium taken by mouth is poorly absorbed; therefore, most of the dose is excreted in the feces. Case studies have shown that excretion of oral doses of humans is about 3% in the urine, and most of the remainder in the feces (Tipton et al. 1966).

Dogs that received barium by gavage excreted most of the dose within a few days and less than 3% of the initial body burden remained in the body after 2 weeks (Cuddihy and Griffith 1972).

2.3.4.3 Dermal Exposure

No studies were located regarding excretion of barium in humans or animals after dermal exposure.

2.3.4.4 Other Routes of Exposure

Humans who have had intravenous injections of barium excrete barium in the feces. A man who was injected with barium intravenously excreted most of the dose in the feces (Newton et al. 1977). Another case study showed that about 9% of an intravenous dose of barium was excreted in the urine, and about 84% in the feces (Harrison et al. 1967).

Animal studies have also shown secretion of radioactive barium into the stomach and intestines following intravenous injection (Syed et al. 1981). The plasma clearance of barium following intravenous injection over 9 days has been demonstrated in rabbits to be 62 ml/hour in the urine and 170 ml/hour in the feces (Liniecki 1971). The total excretion after 9 days was about 50%.

2.4 RELEVANCE TO PUBLIC HEALTH

No acute-, intermediate-, or chronic-duration inhalation MRLs were derived for barium because studies evaluating the effects of barium in humans and animals following acute, intermediate, and chronic inhalation exposure were inadequate for establishing the exposure concentrations associated with adverse health effects. The human studies (Doig 1976; Easing et al. 1976; Seaton et al. 1986; Shankle and Keane 1988) were limited by the small number of subjects and the lack of quantitative exposure information. The animal studies (Hicks et al. 1986; Tarasenko et al. 1977) were limited by inadequate descriptions of the experimental design.

No acute-, intermediate-, or chronic-duration oral MRLs were derived for barium because of limitations of the studies evaluating oral exposure to barium for such durations. Case studies of acute exposures in humans did not provide adequate characterization of the doses associated with adverse health effects and acute-duration animal studies did not provide sufficient data to identify a target organ.

Intermediate-duration oral studies in humans either did not provide adequate characterization of doses associated with adverse health effects (Brenniman and Levy 1985; Brenniman et al. 1979a, 1981) or the number of subjects examined was too small (Wanes et al. 1990). The observation of increased blood pressure in an intermediate-duration oral study in rats (Perry et al. 1983, 1985, 1989) was not used to set an MRL because the resulting MRL would be approximately 1.5-4-fold lower than the estimated daily intake of barium from air, water, and dietary sources combined.

No chronic-duration oral KRL was established for barium, despite the observation of a NOAEL and a LOAEL for blood pressure effects in a ChrOniC rat study by Perry et al. (1983, 1985, 1989), because the resulting MRL would have been approximately 19-50-fold lower than the estimated daily intake of barium from air, water, and dietary sources combined.

No acute-, intermediate-, or chronic-duration dermal MRLs were derived for barium because of the lack of an appropriate methodology for the development of dermal MRLs.

Barium is naturally present to some extent in water and food. Consequently, the general population is exposed normally to barium through the ingestion of drinking water or food. The general population also is exposed by inhalation to low levels of barium in ambient air. Exposure to barium

through public drinking water supplies, food, or ambient air generally should not pose a significant health risk to humans because of the very low levels of barium that would typically be associated with these types of exposures.

Since barium is a frequent contaminant at hazardous waste sites, humans living or working near these sites may potentially become exposed to barium. Concentrations of barium in soil or groundwater may be significantly elevated over background levels at hazardous waste sites, thereby posing a potential health risk to humans. Soil contaminated with barium is of concern because airborne dusts generated from contaminated surface soil through the action of wind may potentially expose individuals by inhalation. Airborne barium dusts generated from contaminated surface soil could potentially form residues on foods that are ingested. There is also the potential that children may ingest barium through hand to mouth contact following playing in contaminated soil. Groundwater contaminated with barium is of concern because of the potential for humans to ingest such water. Contaminated soil and groundwater also are of concern because individuals may directly become exposed dermally through airborne dusts, through direct contact with contaminated soil from construction, excavation, or recreational activities, and/or through direct contact by showering with contaminated water.

There is little quantitative information regarding the extent of barium absorption following inhalation, oral, or dermal exposure. Available evidence indicates that barium is absorbed to some extent following inhalation, oral, and dermal exposure; however, absorption in some cases is expected to be limited. For example, there is some evidence that gastrointestinal absorption of barium in humans is less than 5-30% of the administered dose. These latter data suggest that although individuals may become exposed orally to high levels of barium, adverse health effects may not necessarily develop because of the limited gastrointestinal absorption. Another important factor affecting the development of adverse health effects in humans is the solubility of the barium compound to which the individual is exposed. Soluble barium compounds would generally be expected to be of greater health concern than insoluble barium compounds because of the greater potential of soluble barium compounds to be absorbed by the body.

The different barium compounds have different solubilities in water and body fluids and therefore they serve as variable sources of the Ba^{2+} ion. The Ba^{2+} ion and the soluble compounds of barium (notably chloride, nitrate, hydroxide) are toxic to humans. The insoluble compounds of barium (notably sulfate and carbonate) are inefficient sources of Ba^{2+} ion because of limited solubility and are therefore generally nontoxic to humans (IL0 1983). The insoluble, nontoxic nature of barium sulfate has made it practical to use this particular barium compound in medical applications such as enema procedures and in x-ray photography of the gastrointestinal tract. Barium provides an opaque contrasting medium when ingested or given by enema prior to x-ray examination. Under these routine medical situations, barium sulfate is generally safe. However, barium sulfate or other insoluble barium compounds

may potentially be toxic when it is introduced into the gastrointestinal tract under conditions where there is colon cancer (Princenthal et al. 1983) or perforations of the gastrointestinal tract and barium is allowed to enter the blood stream.

Barium has been associated with a number of adverse health effects in both humans and experimental animals. Both human and animal evidence suggests that the cardiovascular system may be one of the primary targets of barium toxicity. In addition to cardiovascular effects, exposure of humans and/or animals to barium has been associated with respiratory, gastrointestinal, hematological, musculoskeletal, hepatic, renal, neurological, developmental, and reproductive effects. No data or insufficient data are available to draw conclusions regarding the immunological, genotoxic, or carcinogenic effects of barium. Death has been observed in some individuals following acute oral exposure to high concentrations of barium. The following section evaluates the significance of existing toxicity data on barium with regard to human health.

Death. No studies were available regarding death in humans or animals after inhalation or dermal exposure to barium. However, mortality has been reported to occur in a number of cases where humans have been exposed acutely to barium through accidental or intentional ingestion (Das and Singh 1970; Diengott et al. 1964; McNally 1925; Ogen et al. 1967; Talwar and Sharma 1979). The observations from human case reports are supported by findings from acute studies with rodents that indicate barium is toxic by the oral route (Borzelleca et al. 1988; Tardiff et al. 1980). Reduced lifespan also has been observed in chronic oral studies with mice (Schroeder and Mitchener 1975b). The results from human case studies and animal studies suggest that humans who are exposed orally to high levels of barium may be at increased risk for mortality.

One death in an adult female due to acute intravasation of barium sulfate during a barium enema was found in the literature. Direct entry of barium sulfate into the circulatory system apparently resulted in cardiorespiratory failure (Cove and Snyder 1974). Acute parenteral administration of barium compounds to animals has resulted in death. Rate of administration, total dose, species, and individual differences are all factors affecting the ability of barium and its compounds to cause death. Major symptoms leading to death are hypokalemia (Jalinski et al. 1967; Roza and Berman 1971; Schott and McArdle 1974), muscle paralysis (Roza and Berman 1971; Schott and McArdle 1974), cardiorespiratory failure (Cove and Snyder 1974; Roza and Berman 1971), and convulsions (Segreti et al. 1979; Welch et al. 1983). Parenteral administration is not a normal route of barium exposure in humans and only on the rare occurrence of intravasation during barium enema would it be expected to be a problem. However, many of the symptoms experienced are the same as those experienced by humans and animals exposed to acute doses by inhalation and ingestion.

Systemic Effects

Respiratory Effects. Studies evaluating the respiratory effects of barium following inhalation, oral, and dermal exposure are limited. Benign pneumonoconiosis has been observed in workers exposed occupationally by inhalation to barium (Doig 1976). However, no respiratory effects were observed in another study of workers exposed to barium carbonate dust by inhalation (Essing et al. 1976). There are case reports of individuals who developed respiratory weakness and paralysis following acute ingestion of barium (Das and Singh 1970; Gould et al. 1973; Lewi and Bar-Khayim 1964; Morton 1945; Ogen et al. 1967; Phelan et al. 1984; Wetherill et al. 1981). Respiratory effects have not been evaluated in humans following dermal exposure. Accumulation of fluid in the trachea has been noted in acute oral studies with rats (Borzelleca et al. 1988). The results from human case and occupational studies and from acute oral studies with rats suggest that humans who are exposed orally or by inhalation to barium may be at increased risk for minor respiratory effects.

Acute intravasation of barium sulfate into the circulatory system of an adult female patient following a barium enema procedure caused the compound to be deposited in blood vessels throughout the body, including the lungs, and resulted in respiratory failure (Cove and Snyder 1974). Acute parenteral administration of barium compounds to animals has been shown to result in paralysis of the respiratory muscles (Roza and Berman 1971). Similar respiratory paralysis is frequently encountered in cases of acute exposure in humans and animals by ingestion or inhalation. Intratracheal administration of barium sulfate into rat lungs produced a mild inflammatory reaction (Huston et al. 1952). Barium sulfate could not be removed by either polymorphonuclear leukocytes or monocytes. A tissue reaction followed; however, no fibrosis was observed. Since this mode of entry is similar to inhalation, these results may be significant for cases of inhalation exposure.

Cardiovascular Effects. No reliable information is available regarding cardiovascular effects in humans or animals for inhalation or dermal exposure. However, case reports of humans exposed orally by acute ingestion and results of acute, intermediate, and chronic oral studies with experimental animals indicate that barium induces a number of cardiovascular effects. These effects include increased blood pressure, changes in heart rhythm, myocardial damage, and changes in heart physiology and metabolism (Das and Singh 1970; Diengott et al. 1964; Gould et al. 1973; Kopp et al. 1985; Lewi and Bar-Khayim 1964; McNally 1925; Perry et al. 1983, 1985, 1989; Talwar and Sharma 1979; Wetherill et al. 1981). The results from this study suggest that humans who are exposed orally to barium may be at increased risk for cardiovascular effects.

In addition to cardiovascular effects following oral exposure, cardiovascular effects have been observed in humans following intravasation of barium and in animals following parenteral barium exposure. During a barium

sulfate enema procedure on an adult female, the patient developed cardiorespiratory failure (Cove and Snyder 1974). On necropsy, barium sulfate was found throughout the circulatory system, including the heart. The authors attributed the death of the woman to barium intravasation. In animals, parenteral administration of barium compounds has been shown to cause hypertension and dysrhythmias (Foster et al. 1977; Mattila et al. 1986; Roza and Berman 1971). Although parenteral exposure is not a common exposure route for humans, similar symptoms are observed in cases of acute oral and inhalation exposure in humans and animals.

In vitro research in mammalian systems indicated barium induces both contraction and automaticity in isolated hearts and heart muscles (Delfino et al. 1988; Ehara and Inazawa 1980; Hiraoka et al. 1980; Katzung and Morgenstern 1976; Mascher 1973; Munch et al. 1980; Saeki et al. 1981; Slavicek 1972; Toda 1970). Electrical and mechanical effects caused by barium appear to be primarily calcium dependent, although barium could still induce contractions and pacemaker activity in calcium deficient media (Ebeigbe and Aloamaka 1987; Ehara and Inazawa 1980; Hiraoka et al. 1980; Slavicek 1972; Toda 1970). Barium has also been shown to cause significant alterations of most myocyte components and degeneration of mitochondria and the contractile apparatus (Delfino et al. 1988). Repeated exposures to barium in isolated heart systems resulted in tachycardia (Ebeigbe and Aloamaka 1987). These in vitro findings offer some possible explanations for the heart abnormalities seen in barium toxicity in humans and animals.

Gastrointestinal Effects. Reliable human and animal studies evaluating the gastrointestinal effects of barium following inhalation and dermal exposure were not available. Data from case reports of humans suggest that gastrointestinal hemorrhage and gastrointestinal disturbances, including gastric pain, vomiting, and diarrhea, have been associated with acute oral exposure to barium (Das and Singh 1970; Diengott et al. 1964; Gould et al. 1973; Lewi and Bar-Khayim 1964; McNally 1925; Morton 1945; Ogen et al. 1967; Phelan et al. 1984; Talwar and Sharma 1979; Wetherill et al. 1981). Inflammation of the intestines has been noted in acute oral studies with rats (Borzelleca et al. 1988). No data were available from intermediate or chronic exposure studies. Results from human case studies and acute studies with rats suggest that humans exposed orally to barium for acute periods may develop gastrointestinal effects.

Two case studies of acute intrusion of barium sulfate into the peritoneal space during barium enema examination of four men showed barium sulfate caused an acute inflammatory tissue response (Kay 1954; Yamamura et al. 1985), and in one case resulted in formation of a fibrous granuloma (Kay 1954). This is an extremely rare mode of entry and not of significant concern for individuals exposed at a hazardous waste site. Increased fluid accumulation in the intestinal lumen of rats was observed after intraperitoneal injection of barium chloride (Hardcastle et al. 1983b, 1985); however, this observation is not significant for individuals exposed at

hazardous waste sites because of the route of exposure and because there has been no documentation of this effect occurring in humans following normal exposure routes.

Limited studies have been done in vitro on mammalian gastrointestinal systems. Generally, they indicated that barium induced intestinal secretion by releasing intracellular calcium, which combined with calmodulin to stimulate the secretory process (Hardcastle et al. 1983a, 1983b, 1985). Barium also increased gastrointestinal tissue sugar accumulation and decreased mucosal to serosal galactose fluxes. The two proposed mechanisms for this are (1) activation of the calcium-calmodulin complex or (2) direct action of barium on smooth muscle tone (Alcalde and Ilundain 1988). The relevance of these effects on the gastrointestinal tract is unknown.

Hematological Effects. No reliable studies were available regarding hematological effects in humans or animals following inhalation or dermal exposure to barium. There is suggestive evidence from case reports that acute inhalation, oral, and dermal exposure of humans is associated with lowered blood potassium levels (Diengott et al. 1964; Gould et al. 1973; Lewi and Bar-Khayim 1964; Phelan et al. 1984; Shankle and Keane 1988; Stewart and Hummel 1984; Talwar and Sharma 1979; Wetherill et al. 1981). These findings suggest that humans exposed to barium by various routes may be at increased risk for minor hematological effects.

Several studies of animals exposed to barium by parenteral routes indicate that barium decreases in serum potassium (Foster et al. 1977; Jaklinski et al. 1967; Roza and Berman 1971; Schott and McArdle 1974). In one study, dogs intravenously administered barium chloride demonstrated a decrease in serum potassium accompanied by an increase in red blood cell potassium concentration (Roza and Berman 1971). The authors concluded that the observed hypokalemia was due to a shift of potassium from extracellular to intracellular compartments and not to excretion. Additional intravenous studies have linked the observed hypokalemia to muscle paralysis in rats (Schott and McArdle 1974) and cardiac arrhythmias in dogs (Foster et al. 1977). These experiments in animals strongly support the suggestive human case study evidence indicating hypokalemia is an important effect of acute barium toxicity.

Musculoskeletal Effects. No studies were available in humans or animals regarding musculoskeletal effects of barium following dermal exposure. Case reports of humans indicate that acute inhalation and acute oral exposure to barium has been associated with muscle weakness and paralysis (Das and Singh 1970; Diengott et al. 1964; Gould et al. 1973; Lewi and Bar-Khayim 1964; McNally 1925; Morton 1945; Ogen et al. 1967; Phelan et al. 1984; Shankle and Keane 1988; Wetherill et al. 1981). Occupational exposure has not, however, been found to result in radiologically apparent barium deposits in skeletal muscle or bone (Essing et al. 1976). Very limited animal data are available regarding musculoskeletal effects. No adverse effects on the musculoskeletal

system were reported in an intermediate oral study with rats (Tardiff et al. 1980). The findings from human case reports suggest that humans having acute oral or inhalation exposure to barium may develop musculoskeletal effects.

No data on musculoskeletal involvement in cases of barium exposure by other than oral or inhalation modes have been reported for humans. In animals receiving acute doses of barium compounds parenterally, both muscle twitching and paralysis have been reported. Muscle twitching usually occurred within minutes of injection with flaccid paralysis following (Roza and Berman 1971; Schott and McArdle 1974). Parenteral administration is a very rare route of barium exposure, but once barium has entered the bloodstream and has been systemically distributed, it will have the same effects on the same organ. Similar symptoms are expected to occur in humans acutely exposed to barium via inhalation and oral routes.

Barium induced smooth muscle contractions in a variety of in vitro mammalian systems (Antonio et al. 1973; Breuing et al. 1987; Clement 1981; Ebeigbe and Aloamaka 1987; Ehara and Inazawa 1980; Karaki et al. 1967; Mishra et al. 1988; Munch et al. 1980; Saeki et al. 1981; Saito et al. 1972; Slavicek 1972). Contraction appears to be calcium dependent (Antonio et al. 1973; Breuing et al. 1987; Clement 1981; Karaki et al. 1967; Saito et al. 1972), although the exact mechanism is unknown (Breuing et al. 1987; Clement 1981; Mishra et al. 1988).

Hepatic Effects. No reliable human or animal data were available regarding hepatic effects following inhalation or dermal exposure. Degeneration of the liver following acute oral exposure to barium has been noted in one human case report (McNally 1925). Increased liver/brain weight ratio and darkened liver were observed in rats following acute oral exposure to barium (Borzelleca et al. 1988). Decrease blood urea nitrogen, a potential sign of altered hepatic activity, was also noted in this study (Borzelleca et al. 1988). The available data are too limited to conclusively determine whether or not oral exposure to barium is associated with increased risk of hepatic effects in humans.

Renal Effects. No dermal studies evaluating renal effects in humans or animals were available. Renal failure was reported in one case study of a human exposed by acute inhalation to barium (Shankle and Keane 1988). Case studies of humans developing renal failure, renal insufficiency, and renal degeneration following acute oral barium poisoning have been reported (Gould et al. 1973; Lewi and Bar-Khayim 1964; McNally 1925; Phelan et al. 1984; Wetherill et al. 1981). Increased kidney/body weight ratio has been observed in rats following acute oral exposure to barium (Borzelleca et al. 1988). Renal effects have not been observed in intermediate or chronic oral studies with rats (Schroeder and Mitchener 1975a; Tardiff et al. 1980). Together, the findings from human case reports and animal studies suggest that individuals exposed to barium by acute inhalation or ingestion may be at increased risk of developing minor renal effects.

One in vitro study on rat renal tissue homogenate showed barium weakly inhibited the sodium-potassium-adenosine triphosphatase enzyme system (Kramer et al. 1986). A second study on mouse kidney tubules showed barium chloride could depolarize the membrane and inhibit potassium transport (Valkl et al. 1987). A similar defect in cell membrane transport in humans could be responsible for the renal involvement observed in some cases of acute barium poisoning.

Dermal/Ocular Effects. Few inhalation or dermal studies evaluating dermal/ocular effects in humans or animals are available. Results of one limited study suggested that barium carbonate was a dermal and ocular irritant when applied to the skin and eye of animals; however, it was not clear whether or not control animals were used (Tarasenko et al. 1977). In studies with Sprague-Dawley rats, both ocular discharge following acute oral exposure (Borzelleca et al. 1988) and nonsignificant increases in retinal dystrophy following intermediate and chronic oral exposure (McCauley et al. 198.5) have been observed. Although the retinal dystrophy was not statistically significant, a dose-related trend was noted in several groups of rats if different duration exposure groups were combined. Both ocular discharge and retinal dystrophy are commonly observed in Sprague-Dawley rats; consequently, these ocular lesions cannot necessarily be attributed to oral barium exposure. Together, these results from animal studies provide unreliable information to draw firm conclusions about dermal/ocular effects in humans following barium exposure.

Other Systemic Effects. Other systemic effects have been observed. Barium sulfate was observed to act as an appendocolith in two cases following barium enema procedures (Palder and Dalessandri 1988). This is a rare occurrence and probably not significant in cases of human barium toxicity. Intravenous injection of barium sulfate into pigs increased calcitonin secretion from the thyroid (Pento 1979). This is probably not a significant effect for humans since intravenous exposure is not a common route and the dose required was so high (1.7 mg/kg/minute for 20 minutes) it caused cardiotoxicity.

Limited data are available on In vitro effects of barium on the endocrine system. Studies done with isplated pancreatic islet cells from mice show barium is transported across the cell membrane and incorporated into organelles, especially the mitochondria and secretory granules (Berggren et al. 1983). Barium was found to increase cytoplasmic calcium: consequently, the insulin-releasing action of barium may be mediated by calcium. Barium has also been found capable of stimulating the calcitonin secretion system of the thyroid in pigs (Pento 1979).

Immunological Effects. No information was available regarding immunotoxicity in humans following exposure to barium. Acute oral exposure of rats to barium failed to induce changes in thymus weight or gross or

microscopic lesions of the thymus (Borzelleca et al. 1988). Information from this study is too limited to draw any conclusions regarding relevance to human health.

An in vitro immunological study indicated that barium sulfate in low doses for relatively short periods posed no serious toxic hazard to phagocytic cells (Rae 1977).

Neurological Effects. No data were available regarding neurological effects in humans and/or animals following dermal exposure. One case study of a human accidentally exposed by acute inhalation to barium noted the absence of deep tendon reflexes (Shankle and Keane 1988). Case studies of humans having acute oral exposure to barium have reported such effects as numbness and tingling of the mouth and neck, partial and complete paralysis, and brain congestion and edema (Das and Singh 1970; Diengott et al. 1964; Gould et al. 1973; Lewi and Bar-Khayim 1964; McNally 1925; Morton 1945; Ogen et al. 1967; Phelan et al. 1984; Wetherill et al. 1981). Acute and intermediate oral exposure of rats to barium has not been associated with changes in brain weight or with gross or microscopic changes of the brain (Borzelleca et al. 1988; Tardiff et al. 1980). Based on the limited, but suggestive evidence from human case studies, there is the potential that individuals exposed by acute inhalation or acute oral exposure to barium may be at increased risk of developing neurological effects.

There are no cases of neurological effects in humans following parenteral exposure to barium compounds. In a few animal studies where barium chloride was injected intracerebroventricularly, insensitivity to pain occurred within minutes (Welch et al. 1983) followed by fatal convulsions if the dose was sufficient (Segreti et al. 1979; Welch et al. 1983). The significance of these data is difficult to assess since this unusual mode of entry would not occur in humans, and could be partially responsible for the rapid and extreme effects. Intraperitoneal injection of barium sulfate into mice produced an immediate increase in electroshock sensitivity followed by a decrease in sensitivity 24 hours later (Peyton and Borowitz 1978). These results are also difficult to assess in terms of effects observed in cases of human exposure, but suggest that barium in sufficient amounts may potentially influence brain function.

In most in vitro studies of nerve fibers, barium prolonged the action potential and caused rhythmic discharges (de No and Feng 1946; Greengard and Straub 1959). Barium released catecholamines in the absence of calcium both after nerve stimulation and in the absence of stimulation (Boullin 1965, 1967; Douglas and Rubin 1964a; Nakazato and Onoda 1980; Shanbaky et al. 1978). Barium also inhibited potassium flux in glial cells (Walz et al. 1984). These in vitro effects provide clues to the possible mechanism by which barium induces toxic effects on the cardiovascular and musculoskeletal systems. Barium had only a weak effect in blocking activation of spinal cord neurons by

excitatory amino acids (Ault et al. 1980). Barium was also taken up by mitochondria in bovine adrenal medulla (Shanbaky et al. 1982). These organelles therefore maybe more susceptible to the toxic effects of barium.

Developmental Effects. Little information is available regarding developmental effects in humans and/or animals following inhalation, oral, or dermal exposure to barium. One study reported reduced survival, underdevelopment, lowered weight, decreased lability of the peripheral nervous system, and various blood disorders in offspring of female rats exposed by intermediate inhalation to barium (Tarasenko et al. 1977). The same study also reportedly observed increased mortality, increased leukocyte count, disturbances in liver function, and increased urinary excretion of hippuric acid in offspring of female rats treated orally with barium during conception and pregnancy (Tarasenko et al. 1977). These studies are inadequate for evaluating the developmental effects of barium because of a number of significant study limitations (see Sections 2.2.1.2 and 2.2.2.5). In view of the major study limitations, and until verified by further tests, results from these studies should be regarded as providing only preliminary and/or suggestive evidence that inhalation and oral exposure to barium is potentially associated with adverse developmental effects.

Reproductive Effects. No studies were available regarding reproductive effects in humans following inhalation, oral, or dermal exposure. Disturbances in spermatogenesis, shortened estrous cycle, and alterations in the morphological structure of the ovaries and testes were reportedly observed in intermediate exposure experiments in which rats were treated by inhalation with barium carbonate dust (Tarasenko et al. 1977). However, these experiments suffered from a number of major limitations (see Section 2.2.1.2). Acute oral exposure of rats to barium has been associated with decreased ovary/brain weight ratio and decreased ovary weight (Borzelleca et al. 1988). These latter animal findings suggest that humans exposed orally to barium may be at increased risk of reproductive effects.

Genotoxic Effects. No data on in vivo studies of barium genotoxicity were available. In vitro studies were limited and primarily involve prokaryotic test systems, Tests of the fidelity of DNA synthesis using an avian myeloblastosis virus (AMV) DNA polymerase system showed that neither barium acetate nor barium chloride affect the accuracy of DNA replication (Sirover and Loeb 1976a; Sirover and Loeb 1976b). Barium chloride produced negative test results for its ability to inhibit growth in wild and recombination deficient strains of Bacillus subtilis. These results indicate that barium chloride is not mutagenic (Nishioka 1975). However, studies with a DNA polymerase I system from Micrococcus luteus, demonstrated that concentrations of barium ion less than or equal to 0.1 mM stimulated DNA polymerase activity while concentrations greater than this inhibited polymerase activity (Korman et al. 1978). The significance of the inhibitory and stimulatory effects has not been determined. Results from an experiment

designed to test the effect of barium chloride on sporulation frequency, recombination frequency, and meiotic failures in Saccharomyces cerevisiae demonstrated a definite inhibition of sporulation. Effects on recombination frequency and meiotic failures were ambiguous. Barium chloride may have caused a marginal increase in recombination frequencv and information of diploid clones (Sora et al. 1986), but the data are inconclusive. The data available to date are insufficient to support a conclusive statement regarding the genotoxicity of barium and barium compounds.

Cancer. No adequate human studies were available that evaluated the carcinogenic potential of barium. Two chronic oral studies were available that examined the incidence of tumors in rats and mice exposed to barium acetate in drinking water for lifetime (Schroeder and Mitchener 1975a, 1975b). Although results of these oral studies were negative for carcinogenicity, they were inadequate for evaluating carcinogenic effects because insufficient numbers of animals were used, it was not determined whether or not a maximum tolerated dose was achieved, a complete histological examination was not performed, and only one exposure dose was evaluated. Precancerous lesions (dysplasia) were reported in one study in which a woman was treated on the cervix with a barium chloride solution; however, the relevance of this limited observation cannot be determined because only one subject was treated and because the vehicle solution was not specified (Ayre 1966). Results of one skin-painting study with mice suggest that barium hydroxide extract derived from tobacco leaf acted as a tumor-promoting agent; however, it cannot be determined whether or not this apparent positive tumorigenic response was due to barium hydroxide or some other component of the tobacco leaf extract (Van Duuren et al. 1968). Barium has not been evaluated by EPA for human carcinogenic potential (IRIS 1991).

2.5 BIOMARKERS OF EXPOSURE AND EFFECT

Biomarkers are broadly defined as indicators signaling events in biologic systems or samples. They have been classified as markers of exposure, markers of effect, and markers of susceptibility (NAS/NRC 1989).

A biomarker of exposure is a xenobiotic substance or its metabolite(s) or the product of an interaction between a xenobiotic agent and some target molecule(s) or cell(s) that is measured within a compartment of an organism (NAS/NRC 1989). The preferred biomarkers of exposure are generally the substance itself or substance-specific metabolites in readily obtainable body fluid(s) or excreta. However, several factors can confound the use and interpretation of biomarkers of exposure. The body burden of a substance may be the result of exposures from more than one source. The substance being measured may be a metabolite of another xenobiotic substance (e.g., high urinary levels of phenol can result from exposure to several different aromatic compounds). Depending on the properties of the substance (e.g., biologic half-life) and environmental conditions (e.g., duration and route of

exposure), the substance and all of its metabolites may have left the body by the time biologic samples can be taken. It may be difficult to identify individuals exposed to hazardous substances that are commonly found in body tissues and fluids (e.g., essential mineral nutrients such as copper, zinc, and selenium). Biomarkers of exposure to barium are discussed in Section 2.5.1.

Biomarkers of effect are defined as any measurable biochemical, physiologic, or other alteration within an organism that, depending on magnitude, can be recognized as an established or potential health impairment or disease (NAS/NRC 1989). This definition encompasses biochemical or cellular signals of tissue dysfunction (e.g., increased liver enzyme activity or pathologic changes in female genital epithelial cells), as well as physiologic signs of dysfunction such as increased blood pressure or decreased lung capacity. Note that these markers are often not substance specific. They also may not be directly adverse, but can indicate potential health impairment (e.g., DNA adducts). Biomarkers of effects caused by barium are discussed in Section 2.5.2.

A biomarker of susceptibility is an indicator of an inherent or acquired limitation of an organism's ability to respond to the challenge of exposure to a specific xenobiotic substance. It can be an intrinsic genetic or other characteristic or a preexisting disease that results in an increase in absorbed dose, biologically effective dose, or target tissue response. If biomarkers of susceptibility exist, they are discussed in Section 2.7, "POPULATIONS THAT ARE UN-USUALLY SUSCEPTIBLE."

At present, there are no‘well-established biomarkers of exposure and effect for barium. Data suggesting possible biomarkers are presented below.

2.5.1 Biomarkers Used to Identify and/or Quantify Exposure to Barium

Barium can be measured in bone, blood, urine, and feces. It has been shown to be sequestered in bone and teeth and excreted in feces and urine. Background levels of barium in bone are approximately 2 μg/g wet weight (ICRP 1974; Scroeder et al. 1972). Background levels of barium in blood, urine, and feces will vary with daily intake of barium. However, the following levels have been reported: bone, 2 ppm (ICRP 1974; Scroeder et al. 1972); feces, 690-1,215 μg/day (ICRP 1974; Scroeder et al. 1972; Tipton et al, 1969); and urine, 17-50 μg/day (ICRP 1974; Scroeder et al. 1972; Tipton et al. 1969). There are no data correlating bone, blood, urine, or feces levels of barium with specific exposure levels. For more detailed information on the toxicokinetics of barium, see Section 2.3.

Hypokalemia and hypertension are effects usually found in cases of acute and intermediate exposures to relatively high doses of barium. While it is reasonable to expect the dose level to influence the presence of these effects, there are no data supporting a correlation between dose level and

either appearance of or degree of hypokalemia and hypertension. Observation of hypokalemia and hypertension together is indicative of barium exposure, however, other toxicants and disease states can produce these effects.

2.5.2 Biomarkers Used to Characterize Effects Caused by Barium

The organs most sensitive to the toxic effects of barium are the organs of the cardiovascular and gastrointestinal systems, muscles, and nerves. Gastrointestinal disturbances are usually the first symptoms of acute barium exposure. Hypokalemia, hypertension, and abnormalities in heart rhythm frequently occur. General muscle weakness is a frequent symptom, sometimes followed by paralysis. Nerve conduction is often affected, resulting in numbness and tingling of the mouth, neck and extremities. Loss of deep tendon reflexes may also occur. Not all symptoms appear in every case of acute barium poisoning. The presence of other toxicants and disease states may also cause these effects. More information on the specific effects of barium toxicity can be found in Section 2.2.

2.6 INTERACTIONS WITH OTHER CHEMICALS

There are no data regarding the interaction between barium and various chemicals potentially found at hazardous waste sites. However, there are data that suggest that barium may interact with other cations and certain prescription drugs. Drug interactions are of relevance because individuals exposed to barium by living or working near hazardous waste sites contaminated with this substance may also be taking prescription drugs.

The cations potassium, calcium, and magnesium also interact with barium. Barium exposure, for example, may cause a buildup of potassium inside the cell resulting in extracellular hypokalemia which is believed to mediate bariuminduced paralysis. In fact, potassium is a powerful antagonist of the cardiotoxic and paralyzing effects of barium in animals (Foster et al. 1977; Jaklinski et al. 1967; Roza and Berman 1971; Schott and McArdle 1974) and is used as an antidote in cases of acute barium poisoning. Calcium and magnesium suppress uptake of barium in vitro in pancreatic islets. Conversely, barium, in low concentrations, stimulate calcium uptake in these cells. Although the data are insufficient to determine the significance of these findings to human health effects, displacement of calcium may be the mechanism by which barium stimulates insulin release (Berggren et al. 1983).

Among the drugs which are known to interact with barium, the barbiturates sodium pentobarbital and phenobarbital were found to have an increased depressive effect on the hearts of rats exposed to barium (Kopp et al. 1985; Perry et al. 1983, 1989). This hypersensitivity of the cardiovascular system to anesthesia was not observed in similarly treated animals that were anesthetized with xylazine plus ketamine. Results of the study indicated that the hypersensitivity was specific .to the barbiturates and not a generalized effect of anesthesia (Kopp et al. 1985).

Other medically prescribed drugs interact with barium. Experiments with mice indicated that atropine significantly antagonized antinociception and death induced by intracerebroventricular injection of barium chloride (Segreti et al. 1979; Welch et al. 1983). These same studies also found that naloxone, a narcotic antagonist, inhibited the lethal toxicity of barium (Segreti et al. 1979; Welch et al. 1983). Propranolol had no effect 'on barium-induced paralysis in rats (Schott and McArdle 1974). Verapamil rapidly abolished cardiac dysrhythmias in rabbits injected with barium chloride (Mattila et al. 1986). In the same study, pretreatment with the tricyclic antidepressant, doxepin, was found to offer some protection against barium-induced dysrhythmias (Mattila et al. 1986). Cuabain which is an inhibitor of Na^+-K^+ ATPase, while not widely prescribed, has been shown to rapidly reverse the paralyzing effects of barium. it has been hypothesized that ouabain works by reducing barium-induced hypokalemia thereby allowing some intracellular potassium to escape. However, this hypothesis has not yet been proved or disproved because of the complexity of the mechanism involved (Schott and McArdle 1974).

Other substances can affect barium pharmacokinetics. One study showed that sodium alginate could reduce retention of orally administered barium, possibly by inhibiting reabsorption in the gut (Sutton et al. 1972). This could be useful in treating cases of acute barium ingestion. Lysine and lactose increase absorption of barium and could increase the toxic effects of oral exposure (Lengemann 1959).

A human study involving one adult female was performed by applying barium chloride, alone and in combination, with dimethyl sulfoxide to the cervical epithelium. Dimethyl sulfoxide significantly enhanced the ability of barium chloride to induce dysplasia with unusual cell formation in the cervical epithelium (Ayre 1966). The significance of this is difficult to determine since there was only one subject, there were no controls, and few details of the experiment were provided.

2.7 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

The limited data available suggest that certain subgroups of the population may be more susceptible to barium exposure than the general population. These include people with cardiovascular problems, those taking certain prescription drugs, children, pregnant women, smokers, and people with lung disease.

A consistent toxic effect of barium in humans and animals is increased blood pressure. Therefore, humans with hypertension could be at increased risk from either chronic, intermediate, or acute barium exposure. In addition, the cardiotoxic effects of barium exposure could increase the risk for those individuals suffering from other heart problems.

Barbiturates have been shown to have an enhanced depressant effect on the heart in barium-exposed animals (Kopp et al. 1985; Ferry et al. 1983, 1989). Individuals on this type of medication may experience an increased risk of heart problems on exposure to barium.

Children may be at an increased risk since animal studies have demonstrated a higher absorption rate among younger animals than older animals (Taylor et al. 1962). However, a study of an epidemic of oral barium poisoning in Poland indicated that children did not react as adversely as adults even when they had ingested the same amount or more of barium (Lewi and Bar-Khayim 1964; Ogen et al. 1967).

One study showed an increase in barium absorption in the presence of lysine and lactose and could indicate an increased risk in individuals who drink large quantities of milk (Lengemann 1959). These would include young children and pregnant women.

People who smoke and those who have a history of lung disease may be at an increased risk of exposure by inhalation. Studies show that inhalation of dust from barium salts produces a mild, but lengthy, inflammatory response in the lungs of rats (Huston et al. 1952). A benign pneumoconiosis has been noted in cases of chronic, low-level exposure in humans (Doig 1976). Smoking and lung diseases may increase the intensity of this response in affected individuals.

Since barium toxicity has been repeatedly demonstrated to significantly decrease serum potassium in both humans and animals (Foster et al. 1977; Gould et al. 1973; Phelan et al. 1984; Roza and Berman 1971), individuals taking diuretics may have a more severe hypokalemic reaction to barium toxicity.

2.6 MITIGATION OF EFFECTS

This section will describe clinical practice and research concerning methods for reducing toxic effects of exposure to barium. However, because some of the treatments discussed may be experimental and unproven, this section should not be used as a guide for treatment of exposures to barium. When specific exposures have occurred, poison control centers and medical toxicologists should be consulted for medical advice.

General recommendations for reducing absorption of barium following exposure have included removing the exposed individual from the contaminated area and removing contaminated clothing, followed by washing with mild soap and water. If the eyes and skin were exposed, they are flushed with water. Lavage or emesis has also been suggested; however, high concentrations of barium cause nausea and emesis should not be induced in cases where substantial vomiting has already occurred (Haddad and Winchester 1990). Furthermore, there is a risk of aspiration of vomitus during emesis. Administration of soluble sulfates orally will also limit absorption of barium

by causing precipitation of an insoluble form of barium (barium sulfate) (Dreisbach and Robertson 1987; Haddad and Winchester 1988). Intravenous administration of sulfate salts should be avoided because barium precipitate in the kidneys will cause renal failure (Dreisbach and Robertson 1987). Removal of barium from the bloodstream may be facilitated by infusing with saline and inducing saline diuresis (Dreisbach and Robertson 1987).

Hypokalemia is commonly seen in cases of acute barium toxicity and may be responsible for some of the symptoms of barium poisoning (Proctor et al. 1988). Plasma potassium should be monitored and hypokalemia may be relieved by intravenous infusion of potassium (Dreisbach and Robertson 1987; Haddad and Winchester 1990; Proctor et al. 1988).

2.9 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA as amended directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of barium is available. Where adequate information is not available, ATSDR, in conjunction with the National Toxicology Program (NTP), is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of barium.

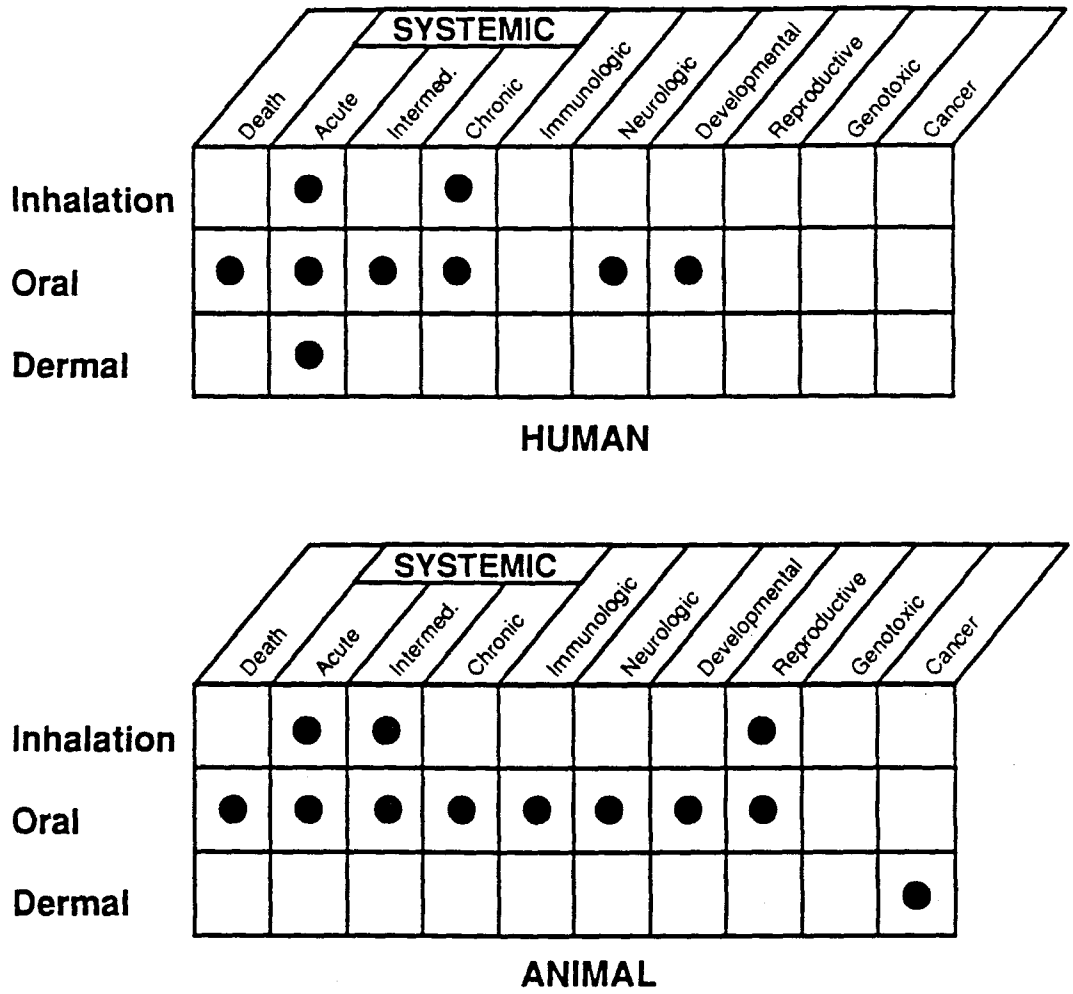
The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that, if met, would reduce or eliminate the uncertainties of human health assessment. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

2.9.1 Existing Information on Health Effects of Barium

The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to barium are summarized in Figure 2-2. The purpose of this figure is to illustrate the existing information concerning the health effects of barium. Each dot in the figure indicates that one or more studies provide information associated with that particular effect. The dot does not imply anything about the quality of the study or studies. Gaps in this figure should not be interpreted as "data needs" information.

There is little information regarding health effects in humans following inhalation, oral, or dermal exposure to barium (Figure 2-2). Inhalation studies are limited to several case reports of individuals exposed acutely or. chronically through occupational exposure (Doig 1976; Essing et al. 1976; Seaton et al. 1986; Shankle and Keane 1988). Oral studies are limited to a number of case reports of individuals exposed through acute ingestion (Das and

FIGURE 2-2. Existing Information on Health Effects of Barium



Singh 1970; Diengott et al. 1964; McNally 1925; Ogen et al. 1967; Talwar and Sharma 1979), a single intermediate-duration experimental study (Wones et al. 1990), and several human epidemiological studies or statistical studies examining mortality and morbidity rates in communities having exposure to barium through drinking water supplies (Brenniman and Levy 1985; Brenniman et al. 1979a, 1979b, 1981; Elwood et al. 1974; Schroeder and Kraemer 1974). Dermal studies are limited to one case report of an exposed individual (Stewart and Hummel 1984).

The majority of studies conducted on animals have been oral exposure studies (Figure 2-2). These oral studies have focused on examining mortality or various systemic effects following acute (Borzelleca et al. 1988; Boyd and Abel 1966; Tardiff et al. 1980), intermediate (McCauley et al. 1985; Perry et al. 1983, 1985, 1989; Tarasenko et al. 1977; Tardiff et al. 1980), and chronic exposure (Kopp et al. 1985; McCauley et al. 1985; Perry et al. 1983, 1985, 1989; Schroeder and Mitchener 1975a, 1975b). Available inhalation studies with experimental animals (Hicks et al. 1986; Tarasenko et al. 1977) can only suggest information on the health effects of barium because these studies have a number of limitations and deficiencies. Dermal studies with experimental animals are limited to one skin irritation study (Tarasenko et al. 1977) and one study evaluating the tumor-promoting activity of barium (Van Duuren et al. 1968).

2.9.2 Data Needs

Acute-Duration Exposure. The majority of experimental studies involving acute.exposure to barium chloride have focused on oral exposure of rats (Borzelleca et al. 1988; Tardiff et al. 1980). These studies have determined acute oral LD_{50} values, as well as evaluated systemic effects. Systemic effects were evaluated primarily by monitoring body weights, selected organ weights, and various hematological and blood chemistry parameters, and by performing gross and microscopic examinations of selected organs and tissues. These studies have provided evidence that barium chloride is lethal by oral ingestion (LD_{50}s range from 132 to 277 mg/kg). The study by Borzelleca et al. (1988) has also provided evidence that acute oral barium exposure is associated with reduced blood urea nitrogen, inflammation of the intestines, accumulation of fluid in the trachea, decreased liver/brain weight ratio, darkened liver, increased kidney/body weight ratio, decreased body weight, decreased ovary weight, and decreased ovaries/brain weight ratio. This study has also provided information as to the barium levels inducing these effects in experimental animals. In the only available acute inhalation study, limited evidence was provided suggesting that barium exposure is potentially associated in rats with increased blood pressure and bronchoconstriction (Hicks et al. 1986). However, this inhalation study was limited in that no controls were used, Limited acute testing of experimental animals also has provided suggestive evidence that barium carbonate is both a dermal and ocular irritant (Tarasenko et al. 1977). Given the available data from acute

exposure studies, additional acute oral studies that focus on mechanisms of toxicity useful.and that further establish and/or refine effect thresholds would be Additional studies of barium following inhalation and dermal exposure would be useful because the potential adverse effects of these two routes have not been thoroughly studied. This information is important because populations exposed to barium from hazardous waste sites may be exposed for a similar duration.

Intermediate-Duration Exposure. The majority of available intermediate-duration studies have focused on oral exposure of experimental animals (McCauley et al. 1985; Perry et al. 1983, 1985, 1989; Tarasenko et al. 1977; Tardiff et al. 1980). Several intermediate oral studies with rats have evaluated mortality and systemic effects (McCauley et al. 1985; Tardiff et al. 1980). Systemic effects were evaluated by monitoring body weight, selected organ weights, food consumption, clinical signs of toxicity, and a variety of hematological and blood chemistry parameters, and by performing gross and microscopic examinations on a wide variety of organs and tissues. Generally, no toxicologically significant adverse effects were noted in any of these parameters. Other intermediate oral studies (Perry et al. 1983, 1985, 1989) have provided evidence that barium induces increased blood pressure. The mechanism of action of this cardiovascular effect has not been established. Various renal lesions have been observed in two intermediate oral experiments with rats (McCauley et al. 1985); however, these studies were of limited value because control rats were not used. Nonsignificant increases in retinal dystrophy have been observed in several intermediate oral experiments with rats (McCauley et al. 1985). It is particularly noteworthy that when these various experiments are combined, a dose-related increase in this ocular lesion is observed. No intermediate dermal studies were available. In the only available intermediate inhalation study (Tarasenko et al. 1977), barium exposure was associated in rats with decreased body weight, altered hematological and blood chemistry parameters, impaired hepatic detoxifying function, and pulmonary lesions. However, this study was of limited value because the number of rats evaluated was not specified. Given the available data, additional intermediate oral studies focusing on the association between barium exposure and hypertension in animals ingesting a normal diet, the mechanism by which barium increases blood pressure, and the potential of barium to induce renal lesions, ocular lesions and various cardiovascular effects would be useful. Because the potential adverse effects of barium following inhalation exposure have not been well characterized and dermal exposure have not been studied, additional intermediate-duration exposure studies involving these two routes of exposure would also be useful. This information is important because there are populations surrounding hazardous waste sites that may be exposed to barium for an intermediate duration.

Chronic-Duration Exposure and Cancer. Chronic studies in which rats and mice were exposed to barium in drinking water for lifetime have evaluated both mortality and systemic effects (Schroeder and Mitchener 1975a, 1975b).

Reduced lifespan but no toxicologically significant systemic effects were observed. Systemic effects were evaluated primarily by monitoring body weight and selected organ weights, and by examining selected organs both grossly and microscopically. Tests for organ function and complete histological examinations were not performed. Further, the fact that no systemic effects were observed may be due to the fact that a single relatively low exposure dose was provided. Another chronic drinking water study with rats provided information on the effects of barium on blood pressure and heart physiology and metabolism (Kopp et al. 1985; Perry et al. 1983, 1985, 1989). Both increased blood pressure and myocardial pathophysiologic and metabolic changes were observed in this chronic study; however, the mechanism of action of barium in inducing these cardiovascular effects was not determined. Therefore. additional chronic studies focusing on organ function, histopathological examination of a wider variety of organs and tissues? multiple exposure doses including a maximum tolerated dose, the association between exposure and cardiovascular effects, and mechanism of action in inducing cardiovascular effects would be useful. In all of these studies, it is important to determine whether the divalent cation Ba+2 is responsible for the toxic effects, or if they are caused by the associated anion.

Another consideration for estimating the toxicity of barium, as well *as* other compounds, is that the toxicity may well be altered by interactions with other toxicants. Specifically, barium would be expected to have reciprocal interactions with other trace metals found in the environment and in human tissues (Berggren et al. 1983; Foster et al. 1977; Jaklinski et al. 1967; Roza and Berman 1971; Schott and McArdle 1974). Considerations of these interactions should be made when designing future tests of barium and other compounds.

EPA and IARC have not evaluated barium for human carcinogenic potential. NTP (1990) is in the process of conducting carcinogenicity bioassays with rats and mice (see Section 2.9.3) on barium chloride. No significant differences in tumor incidence between controls and treated rats and mice have been observed in two published chronic oral studies (Schroeder and Mitchener 1975a, 1975b); however, these two studies were not necessarily designed as carcinogenicity bioassays because maximum tolerated doses were not used, single exposure doses were used, complete histological examinations were not performed, the number of animals was too small for oncogenicity testing, and/or the exposure was less than lifetime. One long-term skin-painting study involving dermal exposure of mice to barium hydroxide extract derived from tobacco leaf provided evidence suggesting that this extract may act as a tumor-promoting agent when applied with a tumor initiating agent (Van Duuren et al. 1968); however, it cannot be determined if this tumor-promoting activity was due to barium hydroxide or some other component of the tobacco leaf extract. There also was one case study of a woman who developed dysplasia of the cervix, a potential precancerous lesion, following cervical treatment with a barium chloride solution (Ayre 1966). Given the available information, lifetime studies in which multiple exposure doses are used

(including a maximum tolerated dose) and complete histopathological examinations are performed would provide useful information on the potential carcinogenic effects of barium. A dermal tumor promotion/tumor initiation study evaluating barium hydroxide and other barium compounds would be useful to clear up concerns as to whether or not barium hydroxide is a tumor-promoting agent.

Genotoxicity. The genotoxicity of barium has not been well characterized. The available data relating to the genotoxic effects of barium are derived from in vitro studies only (Korman et al. 1978; Nishioka 1975; Sirover and Loeb 1976a, 1976b; Sora et al. 1986); there were no available data regarding the genotoxicity of barium in vivo. A single recombination assay in which Bacillus subtilis was exposed to barium was negative for mutagenicity (Nishioka 1975). Results of a test evaluating the fidelity of DNA synthesis in an avian myeloblastosis virus DNA polymerase system indicates that barium did not affect the accuracy of DNA replication (Sirover and Loeb 1976a, 1976b). Results of a study with Micrococcus luteus suggested that DNA polymerase activity was stimulated and inhibited at low and high barium concentrations, respectively (Korman et al. 1978). In a study with Saccharomyces cerevisiae, inhibition of sporulation and marginal increases in recombination frequency and diploid clones were observed following barium treatment (Sora et al. 1986). Additional studies evaluating the genotoxic effects of barium in a variety of in vivo and in vitro systems would be useful because there is limited evidence suggesting barium may affect DNA polymerase activity in bacteria and sporulation, meiotic failures, and recombination frequency in yeast. The limited genotoxicity database for barium supports the need for additional genotoxic studies.

Reproductive Toxicity. The reproductive effects of barium have not been thoroughly studied. There are no studies regarding reproductive effects in humans following barium exposure. However, two animal studies have provided limited information suggesting that humans exposed to barium may be at increased risk for developing reproductive effects (Borzelleca et al. 1988; Tarasenko et al. 1977). Decreased ovary weight and decreased ovary/brain weight ratio have been noted in rats following acute oral exposure to barium (Borzelleca et al. 1988). Intermediate inhalation exposure to barium has been associated with disturbances in spermatogenesis, shortened estrous cycle, and alterations in the morphological structure of the ovaries and testes in rats (Tarasenko et al. 1977). Since limited animal evidence suggests a potential for adverse reproductive effects, epidemiological or occupational studies with humans and/or additional experimental studies with animals would be useful to fully characterize the reproductive toxicity of barium. Experimental animal studies evaluating a wide variety of reproductive parameters through multigenerations would be particularly useful because of the limited number of parameters evaluated in the available single-generation studies.

Developmental Toxicity. The developmental effects of barium have not been studied extensively in either humans or animals. One limited statistical study evaluated the degree of correlation between barium concentrations in drinking water and human congenital malformation rates of the central nervous system (Morton et al. 1976). Results of the study indicated there was a negative statistical correlation between these parameters. However, another limited report provided suggestive evidence that exposure to barium may potentially be associated with adverse developmental effects (Tarasenko et al. 1977). Reduced survival, underdevelopment, lowered body weight, decreased lability of the peripheral nervous system, and various blood disorders were reportedly noted in the offspring of rats following inhalation to barium for an intermediate exposure period. In the same report, increased mortality, increased leukocyte count, disturbances in liver function, and increased urinary excretion of hippuric acid were reportedly noted in the offspring of rats treated orally to barium during conception and pregnancy. Epidemiological or occupational studies with humans and/or additional experimental studies with animals would be useful to better characterize the potential developmental and teratogenic effects of barium since the evidence of one animal study suggests that barium exposure may be associated with developmental toxicity.

Immunotoxicity. The effect of barium on the immune system has not been well studied. No studies were available regarding immunological effects in humans or animals following inhalation or dermal exposure to barium. Data regarding immunological effects following oral exposure are limited to two investigations with rats (Borzelleca et al. 1988; McCauley et al. 1985). Results of these studies suggested that acute, intermediate, and chronic oral exposure to barium was not associated with any changes in thymus weight or with any gross or microscopic lesions of the thymus or lymph nodes. Additional studies evaluating a variety of immunological parameters following various routes of barium exposure would be useful because of the limited nature of the immunotoxicity database for barium.

Neurotoxicity. Data regarding the neurological effects of barium are derived primarily from case studies of exposed humans. One case study of a human provided information suggesting that acute inhalation exposure to barium may be associated with absence of deep tendon reflexes (Shankle and Keane 1988). Numerous other case studies of humans has provided information suggesting that acute oral exposure to barium may be associated with numbness and tingling of the mouth, partial or complete paralysis, and brain congestion and edema (Das and Singh 1970; Diengott et al. 1964; Gould et al. 1973; Lewi and Bar-Khayim 1964; McNally 1925; Morton 1945; Ogen et al. 1967; Phelan et al. 1984; Wetherill et al. 1981). However, acute and intermediate oral exposure of rats to barium has not been associated with changes in brain weight or gross or microscopic lesions of the brain (Borzelleca et al. 1968; Tardiff et al. 1980). No data were available regarding neurological effects in humans and/or animals following dermal exposure. Based on the suggestive

evidence from human case studies, there is the potential that individuals exposed to barium at hazards waste sites may be at increased risk for developing neurological effects. Because of this potential for adverse neurological effects and because the majority of the neurotoxicity database consists primarily of uncontrolled human case studies involving acute oral exposure, additional neurotoxicity data derived from controlled experimental studies and involving various routes of exposure and exposure periods would be useful.

Epidemiological and Human Dosimetry Studies. A limited number of epidemiological and human dosimetry studies evaluating the health effects of barium are available (Brenniman and Levy 1985; Brenniman et al. 1979a, 1979b, 1981; Elwood et al. 1974; Schroeder and Kraemer 1974; Wones et al. 1990). However, all of the available human studies on barium have limitations and/or confounding variables that make it difficult to draw firm conclusions regarding the health effects of barium (see Sections 2.2.2.1 and 2.2.2.2 for discussions on the specific limitations associated with available epidemiological and human dosimetry studies). Two epidemiological studies evaluated mortality and morbidity rates in communities having elevated barium concentrations in drinking water and communities having little or no barium in drinking water (Brenniman and Levy 1985; Brenniman et al. 1979a, 1979b, 1981). Results suggested that relative to low-barium communities, elevated-barium communities had significantly higher mortality rates for all cardiovascular disease, heart disease, arteriosclerosis, and for all causes. No differences between these types of communities were observed with respect to blood pressure, hypertension, stroke, or electrocardiograms. Two statistical studies found negative correlations between barium concentrations in drinking water and rates of cardiovascular mortality and total mortality (Elwood et al. 1974; Schroeder and Kraemer 1974). Results of one human dosimetry study involving a small number of subjects suggested that intermediate exposure to barium in drinking water was not associated with clinically significant changes in blood pressure, electrocardiograms, urinalyses, or hematological parameters (Wones et al. 1990). It is noteworthy that the available epidemiological and human dosimetry studies provide suggestive evidence that barium has no effect on blood pressure. In contrast, results of case studies of humans having acute ingestion exposure (Das and Singh 1970; Diengott et al. 1964; Gould et al. 1973; Wetherill et al. 1981) and experimental studies with animals having intermediate and chronic oral exposure (Perry et al. 1983, 1985, 1989) indicate that barium induces hypertension and increased blood pressure. Therefore, additional epidemiological and/or human dosimetry studies would be useful to determine the effects of barium on blood pressure and other cardiovascular parameters. However, these additional studies may only be useful to the extent that they can control confounding variables and limit study deficiencies that are problematic in currently available studies. Since there are no data or very limited human data regarding the developmental, reproductive, immunotoxic, neurotoxic, and carcinogenic effects

of barium, well-conducted epidemiological studies evaluating these health effects would be useful.

Biomarkers of Exposure and Effect. There are no established biomarkers of exposure for barium. Analytical methods exist for measuring barium in blood, urine, feces, and biological tissues (Mauras and Allain 1979; Schramel 1988; Shiraishi et al. 1987); however, there are no data correlating levels of barium in these tissues and fluids with exposure.

Symptoms of barium toxicity, such as hypokalemia (Diengott *et* al. 1964; Gould et al. 1973; Lewi and Bar-Khayim 1964; Phelan et al. 1984; Shankle and Keane 1988; Stewart and Hummel 1984; Talwar and Sharma 1979; Wetherill et al. 1981) hypertension (Das and Singh 1970; Diengott et al. 1964; Gould et al. 1973; Wetherill et al. 1981), and heart (Lewi and Bar-Khayim 1964; McNally 1925; Talwar and Sharma 1979), muscle (Das and Singh 1970; Diengott et al. 1964; Gould et al. 1973; Lewi and Bar-Khayim 1964; McNally 1925; Morton 1945; Ogen et al. 1967; Phelan et al. 1984; Wetherill et al. 1981), and nerve effects (Das and Singh 1970; Diengott et al. 1964; Gould et al. 1973; Lewi and Bar-Khayim 1964; Morton 1945; Ogen et al. 1967; Phelan et al. 1984; Wetherill et al. 1981), are well documented. However, there are no quantitative studies correlating these effects with dose. For purposes of facilitating medical surveillance, studies to determine useful biomarkers of exposure and effect for barium would be useful.

Absorption, Distribution, Metabolism, and Excretion. The database *on* absorption, distribution, metabolism, and excretion of barium is limited. Existing studies indicate that barium is absorbed more efficiently from the respiratory tract (Cuddihy and Ozog 1973b) than from the digestive system (ICRP 1973; Tipton et al. 1969), primarily deposited in the bones and teeth (Bauer et al. 1957; Cuddihy and Griffith 1972; Losee et al. 1974; Miller et al. 1985; Moloukhia and Ahmed 1979; Sowden 1958; Sowden and Pirie 1958; Sowden and Stitch 1957), and excreted mostly in feces and urine (Cuddihy and Griffith 1972; Tipton et al. 1966). Deposition in bones and teeth and excretion in feces and urine appear to be independent of the route of exposure. Essentially no data exist on dermal absorption, distribution, or excretion; however, this route is not considered to be a significant source of exposure to barium. Because barium is an element, it is not metabolized. No significant data exist on the metabolism of barium compounds in the body. Additional studies evaluating the binding and/or complexing of barium and barium compounds with biological macromolecules or organic molecules in the body would be useful. Studies quantifying the extent of absorption following inhalation, oral, and dermal exposure also would be useful because of limited absorption data.

Comparative Toxicokinetics. Based on available data, there do not appear to be significant differences in the toxicokinetics of barium between species (Chou and Chin 1943; Cuddihy and Griffith 1972; McCauley and

Washington 1983). However, there are not enough similar studies on different species to determine this with certainty. Studies on different species would increase confidence in the reliability of the existing database.

Mitigation of Effects. Methods have been reported for limiting oral and dermal absorption of barium compounds (Bronstein and Currance 1988; Dreisbach and Robertson 1987; Haddad and Winchester 1990) and for counteracting the hypokalemia that is produced by barium in acute high-level exposure situations (Dreisbach and Robertson 1987; Haddad and Winchester 1990; Proctor et al. 1988). Contradictions exist in the literature regarding the efficacy or desirability of administering emetics (Bronstein and Currance 1988; Ellenhorn and Barceloux 1988; Haddad and Winchester 1990). Additional studies clarifying this issue would be helpful. Also, studies directed at finding a more efficient way to remove barium from the body would be useful. It is unclear whether mechanisms other than hypokalemia contribute to the toxic effects produced in acute high-level exposure situations. Additional information on the mechanisms responsible for the toxic effects of barium could aid in the development of effective treatments. Magnesium has been reported to antagonize the neuromuscular effects (Dreisbach and Robertson 1987). Additional studies examining the efficacy of administering soluble magnesium salts to antagonize the effects of barium would also be helpful. No information was located on treatment strategies for long-term low-level exposures. Research on procedures for mitigating such chronic exposure situations would be helpful.

2.9.3 On-going Studies

A 2-year lifetime study of barium chloride in drinking water was conducted in rats and mice by the National Toxicology Program. The study was completed in the 1987 fiscal year, however, the histopathological section is still in progress (NTP 1990).

One on-going study regarding health effects of barium was reported in the FEDRIP (1989) database. An epidemiological study is presently being conducted by L. Frohman. The relationship between barium in drinking water and the cardiovascular risk effects to humans is being assessed. No other information was obtained.

3. CHEMICAL AND PHYSICAL INFORMATION

3.1 CHEMICAL IDENTITY

Barium is an alkaline earth metal of atomic number 56 in Group IIA of the periodic table of elements. It reacts with several other elements to form commercially-important salts. The chemical formula, structure, synonyms, and identification numbers for barium and its compounds are listed in Table 3-l.

3.2 PHYSICAL AND CHEMICAL PROPERTIES

Important physical and chemical properties of barium and its compounds are listed in Table 3-2.

TABLE 3-1. Chemical Identity of Barium and Compounds[a]

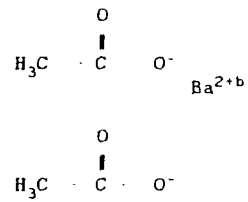
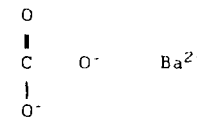
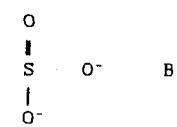
Characteristic	Barium	Barium acetate[b]	Barium carbonate
Synonyms	Elemental barium; barium ion; barium, alloys, non-pyrophoric; barium, alloys, pyrophoric; barium, metal, non-pyrophoric[c]	Acetic acid, barium salt; barium diacetate; barium acetate monohydrate[d,e]	Carbonic acid, barium salt; witherite[e,f]
Trade names	No data	No data	C.I. Pigment White 10; C.I. 77099[g]
Chemical formula	Ba; Ba^{2+}	$Ba(C_2H_3O_2)_2$; $Ba(CH_3CO_2)_2$; $Ba(CH_3CO_2)_2$[b,h,i]	$BaCO_3$
Chemical structure	Ba		
Identification numbers:			
CAS registry	7440-39-3	543-80-6[j]	513-77-9
NIOSH RTECS	CQ8370000	AF4550000[l]	CQ8600000[l]
EPA hazardous waste	D005[m]	No data	No data
OHM/TADS	7216597	No data	7216598
DOT/UN/NA/IMCO shipping	1339, 1400, 1854	No data	1564[c]
HSDB	4481	No data	950
NCI	No data	No data	No data

TABLE 3-1 (Continued)

Characteristic	Barium chloride	Barium cyanide	Barium hydroxide
Synonyms	Barium dichloride; barium chloride dihydrate[e,n]	Barium dicyanide	Barium dihydroxide; barium hydrate; barium hydroxide lime; barium hyroxide monohydrate; barium hydroxide octahydrate[b,n]
Trade names	SBA-0108E[l]	No data	Caustic baryta
Chemical formula	$BaCl_2$; $BaCl_2.2H_2O$[o]	BaC_2N_2; $Ba(CN)_2$[c]	$Ba(OH)_2$; $Ba(OH)_2.H_2O$; $Ba(OH)_2.8H_2O$[b,d]
Chemical structure	Ba^{2+} Cl^- Cl^-	Ba2+ C N[-b] C - N[-]	Ba^{2+} -OH[b] -OH
Identification numbers:			
CAS registry	10361-37-2	542-62-1	17194-00-2
NIOSH RTECS	CQ8750000	CQ8785000	No data
EPA hazardous waste	No data	P013	No data
OHM/TADS	7217223	7216599	7216600[p]
DOT/UN/NA/IMCO shipping	No data	1565	No data
HSDB	2633	403	1605
NCI	C61074[l]	No data	No data

TABLE 3-1 (Continued)

Characteristic	Barium oxide[b]	Barium sulfate	Barium sulfide[b]
Synonyms	Barium monoxide; barium protoxide[b,k]	Artificial heavy spar; artificial barite; barytes; blanc fixe; precipitated barium sulfate; sulfuric acid, barium salt[f,q]	No data
Trade names	No data	Baridol; CI 77120; CI Pigment White 21; Citobaryum; Enamel White; E-Z-Paque; Solbar; Steripaque	No data
Chemical formula	BaO[o]	$BaSO_4$	BaS[b]
Chemical structure	Ba ·· O[b]		Ba S[b]
Identification numbers:			
CAS registry	1304-28-5[j]	7727-43-7	21109-95-5[e]
NIOSH RTECS	CQ9800000[k]	CR0600000[l]	No data
EPA hazardous waste	No data	No data	No data
OHM/TADS	No data	No data	No data
DOT/UN/NA/IMCO shipping	No data	No data	No data
HSDB	No data	5041	No data
NCI	No data	No data	No data

[a]All information obtained from HSDB 1990 except where noted
[b]Windholz 1983
[c]DOT 1986
[d]Hawley 1981
[e]Sax and Lewis 1989
[f]EPA 1985c
[g]Hayes 1982
[h]Weast 1989
[i]Perry and Chilton 1973
[j]Sax and Lewis 1987
[k]Sax and Feiner 1984
[l]RTECS 1989
[m]EPA 1980a
[n]Kirkpatrick 1985
[o]Parmeggiani 1983
[p]OHM/TADS 1989
[q]Kunesh 1985

CAS = Chemical Abstracts Services; DOT/UN/NA/IMCO = Department of Transportation/United Nations/North America/International Maritime Dangerous Goods Code; EPA = Environmental Protection Agency; HSDB = Hazardous Substances Data Bank; NCI = National Cancer Institute; NIOSH = National Institute for Occupational Safety and Health; OHM/TADS = Oil and Hazardous Materials/ Technical Assistance Data System; RTECS = Registry of Toxic Effects of Chemical Substances

TABLE 3-2. Physical and Chemical Properties of Barium and Compounds[a]

Property	Barium	Barium acetate	Barium carbonate
Molecular weight	137.3	255.45	197.37
Color	Silver-white	White	White
Physical state	Malleable metal[e]	Crystals	Heavy powder or crystals[c]
Melting point	710°C[c]; 725°C	41°C (monohydrous)[b]	1740°C (α form, at 90 atm)
Boiling point	1600°C[c]; 1640°C	No data	Decomposes at 1300°C
Density	3.51 g/cm^3 (at 20°C)	2.468 g/cm^3 (anhydrous); 2.19 (monohydrous)[b]	4.25 g/cm^3[h]
Specific gravity	3.5 (at 20°C)[f]	2.02 (below 24.7°C)[h]	4.43
Odor	No data	No data	Odorless[i]
Odor threshold:	No data	No data	No data
Solubility:			
Water	Decomposes (temperature unspecified)[g]	588 g/L (at 0°C)[h]; 750 g/L (at 100°C, monohydrous)[b]	0.025 g/L (temperature unspecified)[c]; 0.022 g/L (at 18°C)[j]; 20 mg/L (at 20°C); 0.0065 pph and 60 mg/L (at 100°C)
Organic solvents			
Alcohol		1 g/700 mL[c]	Insoluble
Benzene	Soluble	No data	No data
Partition coefficients	Insoluble No data	No data	No data
Vapor pressure	10 mmHg (at 1049°C)[g]	No data	Essentially zero[k]
Henry's law constants	No data	No data	No data
Autoignition temperature	No data	No data	No data
Flashpoint	No data	No data	No data
Flammability limits	Explosion hazard if exposed to moist air[f]	No data	Nonflammable[i]
Conversion factors	No data	No data	No data
Explosive limits	No data	No data	No data

TABLE 3-2 (Continued)

Property	Barium chloride	Barium cyanide	Barium hydroxide
Molecular weight	208.27 (anhydrous); 244.31 (dihydrous)[b]	189.40	171.38[c]; 315.48 (octahydrous)[d]
Color	Colorless	White	White[c]
Physical state	Flat crystals[c]	Crystalline powder[c]	Powder[c]
Melting point	Transition at 925°C to cubic crystals (anhydrous)[l]; 960°C (anhydrous)[m]; 1130°C (dihydrous)[d]	No data	408°C (anhydrous)[e]; 78°C (octahydrous)[d]
Boiling point	1560°C (at 760 mmHg)	No data	780°C[d]; 550°C (octahydrous)[b]
Density	3.86 g/cm^3 (at 24°C)	No data	3.743 g/cm^3[c]
Specific gravity	3.1[h]	No data	2.18 (at 16°C)[f]; 4.495 (anhydrous)[b]
Odor	Odorless[k]	No data	No data
Odor threshold:	No data	No data	No data
Solubility:			
Water	375 g/L (at 26°C)[f]	800 g/L (at 14°C)	16.7 g/L (at 0°C)
Organic solvents			
Alcohol	Soluble in methanol	18 g/100 cm^3	Soluble
Partition coefficients	No data	No data	No data
Vapor pressure	Essentially zero[k]	No data	No data
Henry's law constants	No data	No data	No data
Autoignition temperature	No data	Nonflammable	No data
Flashpoint	No data	Nonflammable	No data
Flammability limits	No data	Nonflammable	No data
Conversion factors	No data	No data	No data
Explosive limits	No data	No data	Explosive > 216°C[n]

TABLE 3-2 (Continued)

Property	Barium oxide	Barium sulfate	Barium sulfide
Molecular weight	153.36	233.4	169.4
Color	White to yellowish-white[c]	White or yellowish	Grayish-white or pale yellow
Physical state	Powder or crystals	Crystals	Powder
Melting point	1920°C[c]; Decomposes at 400°C	1580°C (decomposes)[b]	1200°C; >2000°C
Boiling point	2000°C[k]	1149°C (monoclinical transitition point)[d]	Decomposes
Density	2.7 g/cm^3; 5/7 g/cm^3[c]	4.50 g/cm^3	4.25 g/cm^3
Specific gravity	5.72 (cubic)[h]	No data	No data
Odor	Odorless[k]	Odorless[c]	Sulfurous
Odor threshold	No data	No data	No data
Solubility:			
Water	1500 g/L (at 0°C)[b]; 908 g/L (at 80°C)[b]	0.00115 g/L (at 0°C)[m]; 0.00413 (at 100°C)	Decomposes (at 0°C)
Organic solvents			
Alcohol	Soluble[c]	Insoluble[d]	Insoluble
Partition coefficients	No data	No data	No data
Vapor pressure	Essentially zero[k]	No data	No data
Henry's law constants	No data	No data	No data
Autoignition temperature	No data	No data	No data
Flashpoint	No data	No data	No data
Flammability limits	Produces heat on contact with water or steam[k]	No data	Flammable by spontaneous chemical reactions[l]
Conversion factors	No data	No data	No data
Explosive limits	Contact with CO_2 or H_2S may cause explosion[l]	Heating with aluminum may cause violent explosions.	Air, moisture, or acid fumes may cause it to ignite[l]

[a]All references are to Weast 1989 unless otherwise specified.
[b]Perry and Chilton 1973
[c]Windholz 1983
[d]Parmeggiani 1983
[e]Hawley 1981
[f]Stokinger 1981
[g]EPA 1984
[h]Kirkpatrick 1985
[i]DOT 1986
[j]Meister 1989
[k]NIOSH/OSHA 1978
[l]Sax and Lewis 1989
[m]EPA 1987d
[n]HSDB 1989

4. PRODUCTION, IMPORT, USE, AND DISPOSAL

4.1 PRODUCTION

Barium is a dense alkaline earth metal which occurs naturally in ore deposits and makes up 0.05% of the earth's crust (Kojola et al. 1978). Barium and its compounds may be found in nature or produced industrially for various uses. The largest natural source of barium is barite ore which is composed largely of barium sulfate and found in beds or masses in limestone, dolomite, shales and other sedimentary formations (Miner 1969b). Crude barite is then turned into crushed barite which not only has its own industrial uses but which also serves, in turn, as the source for the production of other barium compounds. Crushed barite is first converted to barium sulfide by hightemperature, solid-phase reduction with a carbonaceous reducing agent. Barium sulfide is the starting point for the chemical manufacture of most other barium compounds (Kirkpatrick 1985). One such useful compound is lithophone consisting of 28% zinc sulfide (ZnS) and 72% barium sulfate ($BaSO_4$). Barium sulfate is produced from high-grade (75%-98%) ore in association with granite and shale, is then crushed, and then beneficiated by froth flotation ,or by jigging, and dried (Stokinger 1981). Barium carbonate, also used to be mined from the earth as witherite (Hayes 1982), however, it is no longer mined commercially (Bodek et al. 1988).

Barite occurs in abundance in Alaska, Arkansas, California, Georgia, Missouri, Nevada, and Tennessee as well as in Canada and Mexico. This substance was produced at 38 mines in seven U.S. states in 1973. Total U.S. production for 1973 was 1,104,000 tons, a figure which represented 23% of world production. Nevada supplied 50% of this total with Missouri ranking second in domestic production of barite ore. Domestic production levels for 1969 were much lower at 603,000 tons (Davis 1972). A list of barium production and processing facilities in the United States along with the production or processing volume for each are provided in Table 4-1.

4.2 IMPORT/EXPORT

For the year 1969, U.S. imports of barite ore totaled 344,000 tons, and the export volumes were at 10,000 tons (Davis 1972). Import levels for 1973 were 716,000 tons while exports of barium sulfate and carbonate reached about 68,000 tons (Stokinger 1981). Import and export levels both increased significantly from 1969 to 1973.

4.3 USE

Barium and its compounds are used in oil and gas drilling muds, automotive paints, stabilizers for plastics, case hardening steels, bricks, tiles, lubricating oils, and jet fuel as well as in various types of pesticides (Bodek et al. 1988; EPA 1982; Venugopal and Luckey 1978). The

TABLE 4-1

Facilities That Manufacture or Process Barium and Compounds[a]

State[b]	No. of facilities	Range of maximum amounts on site in thousands of pounds[c]	Activities and uses[d]
AL	9	1-999	2, 3, 7, 8, 9, 13
AR	2	1-99	9
AZ	3	10-9,999	6, 11, 12
CA	34 (2)[e]	0-999	1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 12, 13
CO	4	1-999	2, 8, 9, 13
CT	10	0.1-999	1, 2, 3, 4, 7, 8, 9, 10, 11, 13
DE	1	10-99	1, 4, 7
FL	3 (1)[e]	1-99	7, 8, 9
GA	12 (2)[e]	0-49,999	1, 2, 3, 4, 7, 8, 9, 12
IA	11	0.1-99	8, 9, 13
ID	2	10-9,999	1, 5, 8, 12
IL	29 (1)[e]	0.1-49,999	1, 2, 3, 7, 8, 9, 10, 12
IN	16	0-999	1, 3, 4, 7, 8, 9, 11
KS	3	1-99	8
KY	16 (1)[e]	0-999	2, 7, 8, 9
LA	10 (1)[e]	0-499,999	1, 2, 4, 7, 8, 9, 10
MA	7	10-99	1, 3, 4, 8, 9, 10, 12
MD	8	1-999	1, 3, 4, 7, 8, 9, 11
MI	38 (5)[e]	0.1-999	1, 2, 3, 4, 7, 8, 9, 11, 12, 13
MN	4	1-99	6, 8, 12
MO	16	1-499,999	4, 5, 7, 8, 9, 10, 11
MS	4 (1)[e]	0-99	2, 8, 9, 12

TABLE 4-1 (Continued)

State[b]	No. of facilities	Range of maximum amounts on site in thousands of pounds[c]	Activities and uses[d]
NC	15	0.1-999	2, 7, 8, 9, 11, 12
ND	2 (1)[e]	10-99	9
NE	4	1-999	2, 7, 8, 9, 13
NJ	32 (4)[e]	0.1-9,999	1, 2, 3, 4, 7, 8, 9, 10, 11, 12
NM	1	10-99	12
NV	1	10-99	4, 10
NY	28 (1)[e]	1-99,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12
OH	76 (4)[e]	0.1-999	1, 2, 3, 4, 6, 7, 8, 9, 10, 12, 13
OK	10	0-999	2, 3, 7, 8, 9, 11, 12
OR	2	10-99	2, 9, 11, 13
PA	39 (2)[e]	0-9,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13
PR	1	10-99	1, 4, 7
RI	2 (1)[e]	10-99	3, 7, 8
SC	6 (1)[e]	1-999	1, 5, 8, 9, 12, 13
TN	10 (1)[e]	1-9,999	1, 3, 5, 7, 8, 9, 11, 13
TX	34 (5)[e]	1-99,999	2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12
UT	6 (1)[e]	10-99,999	1, 2, 5, 8, 9, 10, 12, 13
VA	9	0-999	7, 8, 9
VT	2	1-99	12

TABLE 4-1 (Continued)

State[b]	No. of facilities	Range of maximum amounts on site in thousands of pounds[c]	Activities and uses[d]
WA	3	1-999	2, 8, 9, 12
WI	10	1-999	1, 3, 4, 7, 8, 9, 11, 12
WV	4	1-999	8, 11, 12

[a]TRI 1989
[b]Post office state abbreviations
[c]Data in TRI are maximum amounts on site at each facility.
[d]Activities/Uses:

1. produce
2. import
3. for on-site use/processing
4. for sale/distribution
5. as a byproduct
6. as an impurity
7. as a reactant
8. as a formulation component
9. as an article component
10. for repackaging only
11. as a chemical processing aid
12. as a manufacturing aid
13. ancillary or other use

[e]Number of facilities reporting "no data" regarding maximum amount of the substance on site.

largest use of mined barite, which accounts for 85%-95% of the total output is oil and gas well drilling (Bodek et al. 1988; Stokinger 1981). The rest of barite ore (or crude barium sulfate) is utilized frequently in the paint, glass, and rubber industries as well as in the production of other barium compounds. Such barium compounds as the carbonate, chloride, and hydroxide are important in the brick, ceramic, photographic, and chemical manufacturing industries (Bodek et al. 1988).

Industrial uses of barium and its compounds are wide and varied. Barium metal and its alloys, for example, are often used as "getters" to remove gases from vacuum tubes due to their ability to absorb gases (Stokinger 1981). One of barium carbonate's major uses is as a rodenticide (Meister 1989; Worthing 1987), however, it also plays an important role in the brick, tile, ceramics, oil drilling, and chemical manufacturing industries (IL0 1983; Kirkpatrick 1985). Barium sulfate, in the chemically treated, blanc fixe form, is used in high-quality paints as well as in glass- and papermaking (IL0 1983). The chloride is used for chlorine and sodium hydroxide manufacture, as a flux for aluminum alloys, and in pigment and textile dye manufacture. Barium oxide is used to dry gases and solvents, and the hydroxide compound plays a role in glass manufacturing, synthetic rubber vulcanization, sugar refining, and animal and vegetable oil refining. Finally, the main function of barium sulfide is to act as a starting point for the production of a number of other barium compounds (IL0 1983; Kirkpatrick 1985).

Barium and its compounds have several important medical uses as well. Barium chloride was formerly used in treating complete heart block, because periods of marked bradycardia and asystole were prevented through its use. This use was abandoned, however, mainly due to barium chloride's toxicity (Hayes 1982). Characterized by extreme insolubility, chemically pure barium sulfate is non-toxic to humans. It is frequently utilized as a benign, radiopaque aid to x-ray diagnosis, because it is normally not absorbed by the body after oral intake (Doull et al 1980; IL0 1983; Rae 1977). In addition to the extensive use of barium sulfate in studying gastrointestinal motility and diagnosis of gastrointestinal disease, barium sulfate may be chosen as the opaque medium for the x-ray examination of respiratory and urinary systems as well (IL0 1983; Sacchetti 1972). Moreover, the literature suggests that radioactive isotopes of barium, such as ^{135m}Ba, ^{131}Ba, and ^{140}Ba, may prove very useful in studying skeletal metabolism as bone-scanning agents (Hayes 1982; Spencer et al. 1971).

4.4 DISPOSAL

In case of a spill, it is suggested that persons not wearing protective equipment be restricted from the area. Furthermore, ventilation should be provided in the room and the spilled material collected in as safe a manner as possible. Barium compounds (particularly soluble ones) should be placed in sealed containers and reclaimed or disposed of in a secured sanitary landfill (Joseph 1985; NIOSH/OSHA 1978). It is also suggested that all federal, state,

and local regulations concerning barium disposal should be followed (HSDB 1989). No other guidelines or regulations concerning disposal of barium and its compounds were found.

5. POTENTIAL FOR HUMAN EXPOSURE

5.1 OVERVIEW

Barium is a naturally occurring component of minerals that are found in small but widely distributed amounts in the earth's crust, especially in igneous rocks, sandstone, shale, and coal (Kunesh 1978; Miner 1969a). Barium enters the environment naturally through the weathering of rocks and minerals. Anthropogenic releases are primarily associated with industrial processes. Barium is present in the atmosphere, urban and rural surface water, soils, and many foods.

Under natural conditions, barium is stable in the +2 valence state and is found primarily in the form of inorganic complexes. Conditions such as pH, Eh (oxidation-reduction potential), cation exchange capacity, and the presence of sulfate, carbonate, and metal oxides will affect the partitioning of barium and its compounds in the environment, The major features of the biogeochemical cycle of barium include wet and dry deposition to land and surface water, leaching from geological formations to groundwater, adsorption to soil and sediment particulates, and biomagnification in terrestrial and aquatic food chains.

The general population is exposed to barium through consumption of drinking water and foods, usually at low levels. Workers in barium mining or processing industries and individuals who reside near such industries might be exposed to relatively high levels, primarily through the inhalation of fugitive dust containing barium compounds. The most recent occupational exposure estimates indicate that about 10,000 people were potentially exposed to barium and about 474,000 to barium compounds in workplace environments in the United States in 1980.

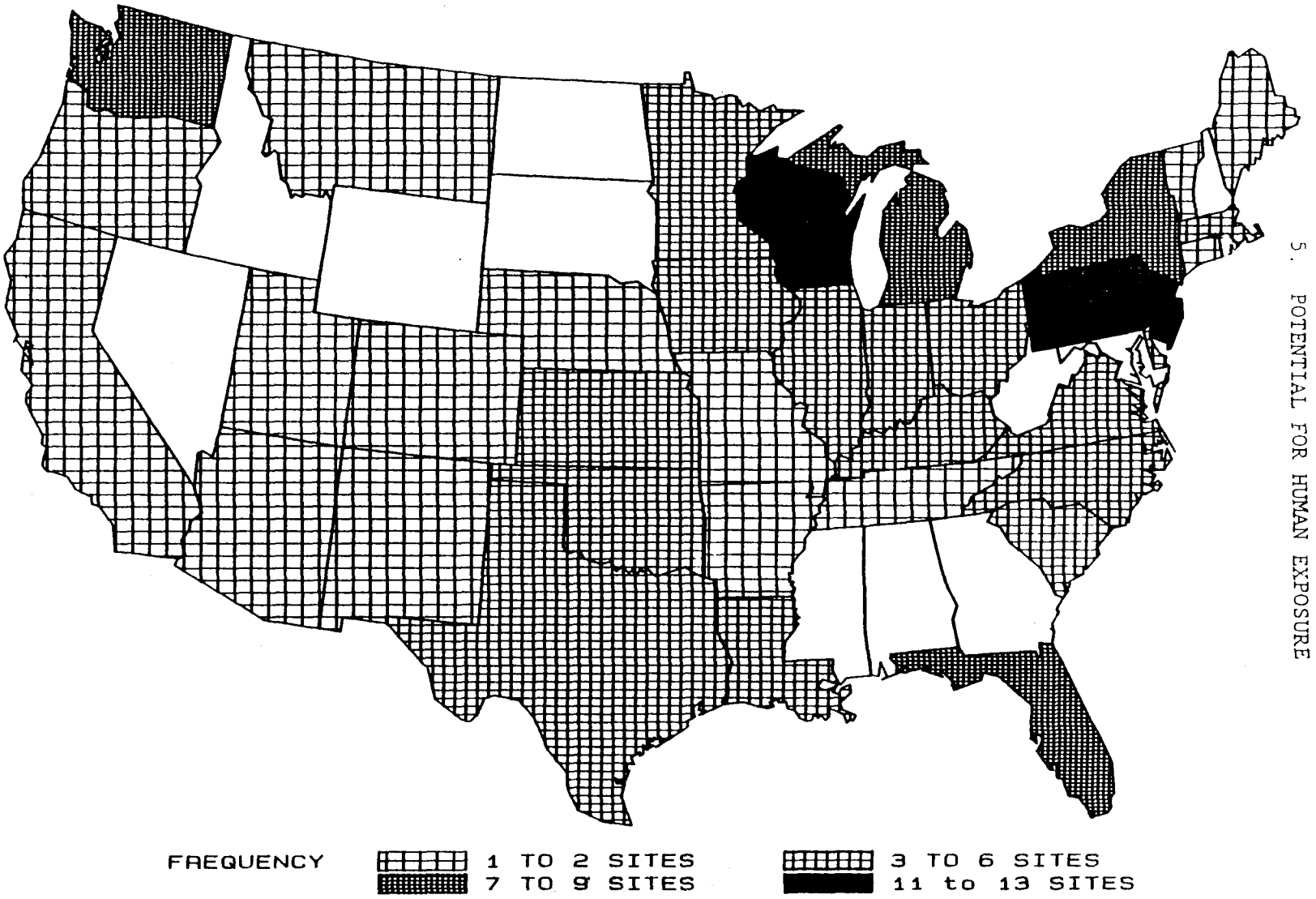
EPA has identified 1,177 NPL sites. Barium has been found at 154 of the total number of sites evaluated for barium. Barium cyanide and barium carbonate have also been found at 1 and 8 sites, respectively (View 1989). However, we do not know how many of the 1,177 sites have been evaluated for barium, barium cyanide, or barium carbonate. As more sites are evaluated by EPA, these numbers may change. The frequency of these sites within the United States can be seen in Figure 5-l.

5.2 RELEASES TO THE ENVIRONMENT

Barium is a highly reactive metal that occurs naturally only in a combined state. The element is released to environmental media by both natural processes and anthropogenic sources.

According to the SARA Section 313 Toxics Release Inventory (TRI), an estimated total of 16.3 million pounds of barium and barium compounds were released to the environment from manufacturing and processing facilities in

FIGURE 5-1. FREQUENCY OF NPL SITES WITH BARIUM CONTAMINATION *



* Derived from View 1989

the United States in 1987 (TRI 1989) (see Table 5-l). Most of these barium releases were to land, The quality of the TRI data must be viewed with caution since the 1987 data represent first-time, incomplete reporting of estimated releases by these facilities. Only certain types of facilities were required to report. This is not an exhaustive list.

5.2.1. Air

Barium is released primarily to the atmosphere as a result of industrial emissions during the mining, refining, and production of barium and barium chemicals, fossil fuel combustion (Miner 1969a), and entrainment of soil and rock dust into the air (Schroeder 1970). In addition, coal ash, containing widely variable amounts of barium, is also a source of airborne barium particulates (Miner 1969a; Schroeder 1970). In 1969, an estimated 18% of the total U.S. barium emissions to the atmosphere resulted from the processing of barite ore, and more than 28% of the total was estimated to be from the production of barium chemicals. The manufacture of various end products (e.g., drilling well muds, and glass, paint, and rubber products) and the combustion of coal were estimated to account for an additional 23% and 26% of the total barium emissions for 1969, respectively (Davis 1972).

According to TRI, an estimated total of 0.6 million pounds of barium and barium compounds were released to the atmosphere from manufacturing and processing facilities in the United States in 1987 (TRI 1989).

Estimates of barium releases from individual industrial processes are available for particulate emissions from the drying and calcining of barium compounds and for fugitive dust emissions during the processing of barite ore. Soluble barium compounds (unspecified) are emitted as particulates from barium chemical dryers and calciners to the atmosphere during the processing of barium carbonate, barium chloride, and barium hydroxide (Reznik and Toy 1978). Uncontrolled particulate emissions of soluble barium compounds from chemical dryers and calciners during barium processing operations may range from 0.04 to 10 g/kg of final product. Controlled particulate emissions are less than 0.25 g/kg of final product. Based on an uncontrolled emission factor of 5 g/kg and a controlled emission factor of 0.25 g/kg, total particulate emissions from the drying and calcining of barium carbonate, barium chloride, and barium hydroxide are estimated to be 160 metric tons (352,800 pounds) per year (Reznik and Toy 1978).

Fugitive dust emissions occur during processing (grinding and mixing) of barite ore and may also occur during the loading of bulk product of various barium compounds into railroad hopper cars (Reznik and Toy 1978). Based on an emission factor of 1 g/kg, total emissions of fugitive dust from the domestic barium chemicals industry during the grinding of barite ore have been estimated to be approximately 90 metric tons (198,450 pounds) per year (Reznik and Toy 1978). Other particulate emissions from the industrial production of barium compounds include an estimated 820 metric tons (1.8 million pounds) per

TABLE 5-1. Releases to the Environment from Facilities That Manufacture or Process Barium and Compounds[a]

State[c]	No. of facilities	Range of reported amounts released in thousands of pounds[b]						
		Air	Underground injection	Water	Land	Total Environment[d]	POTW[e] transfer	Off-site waste
AL	9	0-2.3	0-0	0-0.3	0-9.3	0-9.6	0-0.1	0-16
AR	2	0.3-0.3	0-0	0-0	0-0	0.3-0.3	0-0	0-2.5
AZ	3	0-0.3	0-0	0-0	0-5,300	0-5,300	0-0	0-0
CA	34	0-7.9	0-2.4	0-5.5	0-16.2	0-24.5	0-0.3	0-73.7
CO	4	0-0.6	0-0	0-0.1	0-0	0-0.8	0-0	0-346
CT	10	0-0.5	0-0	0-0.3	0-0	0-0.8	0-0.3	0-78.5
DE	1	0.5-0.5	0-0	0-0	0-0	0.5-0.5	0.6-0.6	0-0
FL	3	0-0.3	0-0	0-0	0-0	0-0.3	0-0	0-59.2
GA	12	0-9.5	0-0	0-17	0-0.1	0-26.5	0-1.2	0-4,300
IA	11	0-0.3	0-0	0-0.1	0-5	0-5	0-0.1	0-4.3
ID	2	0-0.5	0-0	0-1	0-180.3	0-181.8	0-0.3	0-0.3
IL	29	0-1.8	0-0	0-0.3	0-1,161	0-1,163	0-0.8	0-1,639
IN	16	0-4.7	0-0.3	0-0.1	0-0.3	0-4.7	0-5.4	0-56.6
KS	3	0-0.3	0-0	0-0	0-0.5	0-0.5	0-0.3	0-0.5
KY	16	0-2.2	0-0	0-0.5	0-207.3	0-207.3	0-6.8	0-91.2
LA	10	0-36.6	0-0	0-0.3	0-0	0-36.6	0-0.3	0-34.3
MA	7	0-2.3	0-0	0-0	0-0	0-2.3	0-0.3	0-37
MD	8	0-6.1	0-0	0-2.2	0-0	0-6.1	0-0.3	0.3-60
MI	38	0-16	0-0	0-2	0-1.9	0-16	0-46	0-1,800
MN	4	0.3-18	0-0	0-1	0-4.2	0.3-18	0.3-0.3	0-1.4
MO	16	0-14.7	0-0	0-0.3	0-0.1	0-14.7	0-120	0-66
MS	4	0-1.1	0-0	0-0	0-0.3	0-1.1	0-0	0-1.2
NC	15	0-6.1	0-0	0-0	0-100.3	0-100.3	0-2.1	0-252.3
ND	2	0.3-0.3	No Data	0-0	0-0.3	0.5-0.5	0-0	0-0
NE	4	0-0.3	0-0	0-0	0-0	0-0.3	0-0	0-84.2
NJ	32	0-6.2	0-0	0-0.3	0-144.5	0-144.7	0-42.1	0-93.5
NM	1	0-0	0-0	0-0	0-0	0-0	0-0	0-0
NV	1	8.5-8.5	0-0	0-0	0-0	8.5-8.5	0-0	0-0
NY	28	0-14.8	0-0	0-16	0-88	0-93.7	0-130	0-385.2
OH	76	0-58.8	0-0	0-180	0-10.5	0-180	0-24.6	0-45.4
OK	10	0-0.4	0-0	0-0.3	0-0.3	0.1-0.5	0-0.1	0-1.4
OR	2	0.5-0.5	0-0	0-0.8	0-0	0.5-1.3	0-0	1.2-108
PA	39	0-1.1	0-0	0-1.6	0-154.7	0-155.2	0-10.9	0-93.7
PR	1	0-0	0-0	0-0	0-0	0-0	44-44	0-0

TABLE 5-1 (Continued)

State[c]	No. of facilities	Range of reported amounts released in thousands of pounds[b]						
		Air	Underground injection	Water	Land	Total Environment[d]	POTW[e] transfer	Off-site waste
RI	2	0-1.9	0-0	0-0	0-0	0-1.9	0-0	0-0
SC	6	0-9.8	0-0	0-0	0-67.9	0-67.9	0-12.5	0-67.9
TN	10	0-2.8	0-0	0-0.3	0-18	0-18	0-93.9	0-619.4
TX	34	0-262	0-0	0-4	0-109	0-262	0-0.5	0-100
UT	6	0-9.2	0-0	0-0.3	0-6,900	0-6,909	0-0	0-8.4
VA	9	0-21.5	0-0	0-0.3	0-0.5	0-21.5	0-0.3	0-32
VT	2	0.1-0.3	0-0	0-0	0-0	0.1-0.3	0-0	3.6-37.8
WA	3	0-86	0-0	0-0	0-1.6	0-87.6	0-0	0-1.3
WI	10	0-4.3	0-0.3	0-1.1	0-0	0.1-4.3	0-4.6	0-78.9
WV	4	0-0.8	0-0	0-0.9	0-0	0-0.9	0-0.3	0-18

[a]TRI 1989
[b]Data in TRI are maximum amounts released by each facility. Quantities reported here have been rounded to the nearest hundred pounds, except those quantities > 1 million pounds which have been rounded to the nearest thousand pounds.
[c]Post office state abbreviation
[d]The sum of all releases of the chemical to air, land, water, and underground injection wells by a given facility.
[e]Publicly owned treatment works

year from uncontrolled kilns during the processing of barite ore and 8 metric tons (17,640 pounds) per year from black ash (i.e., barium sulfide) rotary kilns during the production of barium hydroxide (Reznik and Toy 1978).

The use of barium in the form of organometallic compounds as a smoke suppressant in diesel fuels results in the release of solids to the atmosphere (Miner 1969a; Ng and Patterson 1982; Schroeder 1970). The maximum concentration of soluble barium in exhaust gases containing barium-based smoke suppressants released from test diesel engines and operating diesel vehicles is estimated to be 12,000 mg/m^3, when the barium concentration in the diesel fuel is 0.075% by weight and 25% of the exhausted barium (at a sampling point 10 ft from the engine and upstream from the muffler) is soluble (Golothan 1967). Thus, 1 L of this exhaust gas contains an estimated 12 mg soluble barium or 48 mg total barium (Schroeder 1970).

5.2.2 Water

The primary source of naturally occurring barium in drinking water results from the leaching and eroding of sedimentary rocks into groundwater (Kojola et al. 1978). Although barium occurs naturally in most surface water bodies (i.e., approximately 99% of those examined) (Kopp and Kroner 1967), releases of barium to surface waters from natural sources are much lower than those to groundwater (Kojola et al. 1978).

About 80% of the barium produced is used as barite to make high-density oil and gas well drilling muds, and during offshore drilling operations there are periodic discharges of drilling wastes in the form of cuttings and muds into the ocean (Ng and Patterson 1982). For example, in the Santa Barbara Channel region, about 10% of the muds used are lost into the ocean (Ng and Patterson 1982). The use of barium in offshore drilling operations may increase barium pollution, especially in coastal sediments (Ng and Patterson 1982).

Barium has been detected with a positive geometric mean concentration of 101.6 mg/L in groundwater samples from approximately 58% of the 2,783 hazardous waste sites that have had samples analyzed by the Contract Laboratory Program (CLP) (CLPSD 1989). Barium has also been detected with a positive geometric mean of 62.6 mg/L in surface water samples from 27% of the sites in the CLP statistical database (CLPSD 1989). Note that these data from the CLP Statistical Database (CLPSD) represent frequency of occurrence and concentration information for NPL sites only.

According to TRI, an estimated total of 312,000 pounds of barium and barium compounds were released to surface waters from manufacturing and processing facilities in the United States in 1987 (TRI 1989).

5.2.3 Soil

The process of drilling for crude oil and natural gas generates waste drilling fluids or muds, which are often disposed of by land farming. Most of these fluids are water based and contain barite and other metal salts. Thus barium may be introduced into soils as the result of land farming these slurried reserve pit wastes (Bates 1988).

The use of barium fluorosilicate and carbonate as insecticides (Beliles 1979; Meister 1989) might also contribute to the presence of barium in agricultural soils.

According to TRI, an estimated total of 14.9 million pounds of barium and barium compounds were released to soils from manufacturing and processing facilities in the United States in 1987 (TRI 1989).

Barium has been detected with a positive geometric mean concentration of 100.5 ppm in soil samples from approximately 52% of the hazardous waste sites that have had samples analyzed by the CLP (CLPSD 1989). Note that these data from the CLPSD represent frequency of occurrence and concentration data for NPL sites only.

5.3 ENVIRONMENTAL FATE

5.3.1 Transport and Partitioning

Most barium released to the environment from industrial sources is in forms that do not become widely dispersed (Ng and Patterson 1982). In the atmosphere, barium is likely to be present in particulate form (EPA 1984). Although chemical reactions may cause changes in speciation of barium in air, the main mechanisms for the removal of barium compounds from the atmosphere are likely to be wet and dry deposition (EPA 1984).

In aquatic media, barium is likely to precipitate out of solution as an insoluble salt (i.e., as $BaS0_4$ or $BaC0_3$). Waterborne barium may also adsorb to suspended particulate matter (Bodek et al. 1988; EPA 1984; Lagas et al. 1984). Precipitation of barium sulfate salts is accelerated when rivers enter the ocean because of the high sulfate content in the ocean (Bowen 1966). Sedimentation of suspended solids removes a large portion of the barium content from surface waters (Benes et al. 1983). Barium in sediments is found largely in the form of barium sulfate (barite). Coarse silt sediment in a turbulent environment will often grind and cleave the barium sulfate from the sediment particles leaving a buildup of dense barites (Merefield 1987). Estimated soil: water distribution coefficients (Kd) (i.e., the ratio of the quantity of barium sorbed per gram of sorbent to the concentration of barium remaining in solution at equilibrium) range from 200 to 2,800 for sediments and sandy loam soils (Baes et al. 1984; Rai et al. 1984).

The uptake of barium by fish and marine organisms is also an important removal mechanism (Bowen 1966; Schroeder 1970). Barium levels in sea water range from 2 to 63 mg/L with a mean concentration of about 13 μg/L (Bowen 1979). Barium was found to bioconcentrate in marine plants by a factor of 1,000 times the level present in the water. Bioconcentration factors in marine animals, plankton, and in brown algae of 100, 120, and 260, respectively, have been reported (Bowen 1966; Schroeder 1970).

Barium added to soils (e.g., from the land farming of waste drilling muds) may either be taken up by vegetation or transported through soil with precipitation (Bates 1988). Relative to the amount of barium found in soils, little is bioconcentrated by plants (Schroeder 1970). However, this transport pathway has not been comprehensively studied.

Barium is not very mobile in most soil systems. The rate of transportation of barium in soil is dependent on the characteristics of the soil material. Soil properties that influence the transportation of barium to groundwater are cation exchange capacity and calcium carbonate ($CaCO_3$) content. In soil with a high cation exchange capacity (e.g., fine textured mineral soils or soils with high organic matter content), barium mobility will be limited by adsorption (Bates 1988; Kabata-Pendias and Pendias 1984). High $CaC0_3$ content limits mobility by precipitation of the element as $BaC0_3$ (Lagas et al. 1984). Barium will also precipitate as barium sulfate in the presence of sulfate ions (Bodek et al. 1988; Lagas et al. 1984). Barium is more mobile and is more likely to be leached from soils in the presence of chloride due to the increased solubility of barium chloride as compared to other chemical forms of barium (Bates 1988; Lagas et al. 1984). Barium complexes with fatty acids (e.g., in acidic landfill leachate) will be much more mobile in the soil due to the lower charge of these complexes and subsequent reduction in adsorption capacity (Lagas et al. 1984).

Barium mobility in soil is reduced by the precipitation of barium carbonate and sulfate. Humic and fulvic acid have not been found to increase the mobility of barium (EPA 1984).

5.3.2 Transformation and Degradation

5.3.2.1 Air

Elemental barium is oxidized readily in moist air (EPA 1983a, 1987a; Kunesh 1978). The residence time of barium in the atmosphere may be several days, depending on the size of the particulate formed, the chemical nature of the particulate, and environmental factors such as rainfall (EPA 1984).

5.3.2.2 Water

Under natural conditions barium will form compounds in the +2 oxidation state. Barium does not hydrolyze appreciably except in highly alkaline environments (i.e., at pH levels greater than or equal to 10) (Bodek et al. 1988).

Appreciable levels of barium sulfate occur because natural water often contains high sulfate concentrations. Since the solubility of barium sulfate is low, only trace amounts of barium dissolve in surface water (Bodek et al. 1988; NAS 1977). At pH levels of 9.3 or below, barium sulfate may limit barium concentrations in natural waters (Bodek et al. 1988). The solubility of barium sulfate increases considerably in the presence of chloride (Cl^-) and other anions (e.g., $N0_3$- and CO_3^{-2}), and at pH levels of 9.3 or below, the barium ion (Ba^{+2}) is the dominant species (Bodek et al. 1988; NAS 1977). The Ba^{+2} ion is stable under the pH-Eh range of natural systems. However, natural and treated waters usually contain sufficient sulfate so that a barium ion concentration of more than 1,000-1,500 mg/L cannot be maintained in solution (EPA 1983a; Hem 1959; Lagas et al. 1984; McCabe et al. 1970).

As pH levels increase above 9.3 and in the presence of carbonate, barium carbonate becomes the dominant species (Bodek et al. 1988; Singer 1974). Barium carbonate also exhibits fast precipitation kinetics and very low solubility and in alkaline environments limits the soluble barium concentration (Faust and Aly 1981; Hem 1959; Rai et al. 1984; Singer 1974). Barium forms salts of low solubility with arsenate, chromate, fluoride, oxalate, and phosphate ions (Bodek et al. 1988; EPA 1983a; Kunesh 1978). The chloride, hydroxide, and nitrate of barium are water-soluble (Bodek et al. 1988; EPA 1983a; Kirkpatrick 1978) and are frequently detected in aqueous environments (Rai et al. 1984).

Barium also forms complexes with natural organics in water (e.g., fatty acids in acidic landfill leachates) to a limited extent (Lagas et al. 1984; Morel 1983; Rai et al. 1984).

5.3.2.3 Soil

Barium reacts with metal oxides and hydroxides in soil and is subsequently adsorbed onto soil particulates (Hem 1959; Rai et al. 1984). Adsorption onto metal oxides in soils and sediments probably acts as a control over the concentration of barium in natural waters (Bodek et al. 1988). Under typical environmental conditions, barium displaces other adsorbed alkaline earth metals from MnO_2 SiO_2, and TiO_2, (Rai et al. 1984). However, barium is displaced from $A1_20_3$ by other alkaline earth metals (Rai et al. 1984). The ionic radius of the barium ion in its typical valence state (Ba^{+2}) makes isomorphous substitution possible only with strontium and generally not with the other members of the alkaline earth elements (Kirkpatrick 1978). Among

the other elements that occur with barium in nature, substitution is common only with potassium but not with the smaller ions of sodium, iron, manganese, aluminum, and silicon (Kirkpatrick 1978).

Barium is also adsorbed onto soil and subsoil through electrostatic interactions (Bodek et al. 1988; Singer 1974). The cation exchange capacity of the sorbent largely controls the retention of barium in soils (Bodek et al. 1988). Barium is strongly adsorbed by clay minerals (Kabata-Pendias and Pendias 1984; Lagas et al. 1984).

Barium can also form salts with acetate, nitrate, chloride, and hydroxide ions in soil. The mobility of barium in soils increases upon formation of these water soluble salts (Bodek et al. 1988). In general, the solubility of barium compounds increases with decreasing pH.

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

5.4.1 Air

Urban and suburban air concentrations have been found to range from less than 0.005 to 1.5 mg/m^3 (Tabor and Warren 1958). No distinct pattern related to industrialization appeared in the results reported on 754 samples from 18 cities and four suburban areas in the United States. For example, in Houston, Texas and its suburbs, 76% of the samples contained barium at levels ranging from 0.005 to 1.5 mg/m^3, whereas in Fort Worth, Texas, 66% of the samples had values below 0.005 mg/m^3 (Tabor and Warren 1958).

A more recent compilation of atmospheric data shows barium concentrations in urban atmospheres of North America ranging from $2x10^{-4}$ to $2.8x10^{-2}$ μg/m^3 with a mean concentration of $1.2x10^{-2}$ μg/m^3 (Bowen 1979). In contrast, barium levels in samples from the South Pole and northern Norway were $1.6x10^{-5}$ and $7.3x19^{-4}$ μg/m^3, respectively (Bowen 1979).

Maximum ground-level barium concentrations (as soluble compounds) associated with uncontrolled atmospheric particulate emissions from chemical dryers and calciners at barium-processing plants have been estimated (using dispersion modeling) to range from 1.3 to 330 mg/m^3 over a 24-hour averaging time at locations along facility boundaries (i.e., away from the source of emission) (Reznik and Toy 1978).

5.4.2 Water

Barium has been found in almost all raw surface waters and public drinking water supplies sampled (i.e., approximately 99%) (Kopp 1969) at concentrations ranging from about 2 to 380 mg/L with mean concentrations generally on the order of 10 to 60 mg/L (Barnett et al. 1969; Bowen 1979; Durfor and Becker 1964; Durum and Haffty 1961; Kopp 1969; Kopp and Kroner 1967; McCabe et al. 1970; Tuovinen et al. 1980).

Barium concentrations in groundwater supplies have been known to exceed EPA's maximum contaminant level (MCL) of 1.0 mg/L (1,000 mg/L); this may be due to leaching and erosion of barium from sedimentary rocks (Calabrese 1977; Kojola et al. 1978). For example, community water supplies from deep rock and drift wells in northeastern Illinois have been found to have barium concentrations ranging from 1,100 to 10,000 mg/L (Calabrese 1977).

Barium has also been found in sea water at concentrations ranging from 2 to 63 mg/L with a mean concentration of 13 μg/L (Bowen 1979).

5.4.3 Soil

Barium is relatively abundant in the earth's crust and is found in most soils at concentrations ranging from about 15 to 3,000 ppm (Bowen 1979; Schroeder 1970; Shacklette and Boerngen 1984). The barium content in cultivated and uncultivated soil samples collected during a number of field studies ranged from 15 to 1,000 ppm (mean concentration of 300 ppm) for B horizon soils (subsurface soils) in the eastern United States and from 70 to 5,000 ppm (mean concentration of 560 ppm) for B horizon soils in the western United States. Barium content ranged from 150 to 1,500 ppm for surface horizon soils collected in Colorado (mean concentration of 550 ppm) (Connor and Shacklette 1975).

5.4.4 Other Environmental Media

Barium occurs in many foods at low levels. Brazil nuts have notably high concentrations of barium (3,000-4,000 ppm) (Beliles 1979). Some plants bioconcentrate barium from the soil (Beliles 1979; Reeves 1979; Schroeder 1970). The barium content in corn samples from Georgia, Missouri, and Wisconsin collected during a number of field studies ranged from 5 to 150 ppm with mean concentrations ranging from 15 to 54 ppm (Connor and Shacklette 1975). The barium content in other cultivated plants (e.g., lima beans, cabbage, soybeans, and tomatoes) from Georgia, Missouri, and Wisconsin ranged from 7 to 1,500 ppm (mean concentration range: 38-450 ppm) with the highest levels occurring in cabbage from Georgia and soybeans from Missouri and the lowest levels occurring in Georgia tomatoes (Connor and Shacklette 1975).

Barium is also found in anaerobic sewage sludge at concentrations ranging from 100 to 9,000 ppm (mean concentration: 800 ppm) and in aerobic sewage sludge at concentrations ranging from 100 to 300 ppm (mean concentration: 200 ppm) (Sommers 1977).

5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

The primary routes of exposure of humans to barium are consumption of food and water and inhalation of ambient air (ICRP 1974; Reeves 1979). Based on compliance monitoring data from the Federal Reporting Data System (FRDS), of the approximately 214 million people in the United States who are connected to a public water supply, it is estimated that about 150,000 people are exposed to barium concentrations greater than EPA's MCL of 1.0 mg/L (1,000 mg/L) (EPA 1987c). However, since 94% of all samples collected from public water supplies of the 100 largest cities in the United States had barium concentrations of less than 100 mg/L (Durfor and Becker 1964), it is likely that most of the people connected to a public water supply receive drinking water with barium concentrations below the MCL. Assuming an average adult drinking water consumption rate of 1.4 L/day (EPA 1989b) and that barium is pre.sent at concentrations of less than 100 mg/L, the average adult daily intake of barium through the consumption of drinking water would be less than 140 mg/day (2 mg/kg/day for a 70-kg adult). Based on an average barium drinking water concentration of 40 mg/L, Hadjimarkos (1967) calculated the average barium intake from drinking water to be about 80 mg/day (1 mg/kg/day for a 70-kg adult). This estimated intake level is consistent with the above estimate of less than 140 mg/day.

The International Commission on Radiological Protection (ICRP 1974) has estimated that intake of barium through inhalation ranges from 0.09 to 26 mg/day. Based on reported urban air concentrations for barium (<0.005-1.5 mg/m^3) (Tabor and Warren 1958) and assuming an average adult ventilation rate of 20 m^3/day (EPA 1989b), the calculated daily respiratory intake of barium ranges from less than 0.1 to 30 mg, which is comparable to the ICRP estimated intake range above. Based on the 8-hour time-weighted average threshold limit value (TLV) in workplace air of 500 $\mu g/m^3$ (ACGIH 1988), and assuming an 8-hour inhalation of 10 m^3 of air, a daily barium workplace intake of 5,000 μg can be calculated. NAS (1977) estimated that 75% of inhaled barium could be absorbed into the bloodstream if soluble barium salts were involved.

Since average ground level concentrations of an emission vary with the distance from the emission point, the population around a source site will be exposed to differing emission levels. Using an average population density of 27 persons/km^2 (based on actual population data from areas surrounding barium production and processing plants), it has been estimated that approximately O-886 persons within an area of up to 32.8 km^2 around a source site could be exposed to soluble barium compound concentrations of greater than 1.67 mg/m^3 in ambient air (Reznik and Toy 1978). Assuming that the average adult daily ventilation rate is 20 m^3 (EPA 1989b), breathing these ambient air barium concentrations would result in daily respiratory intakes of greater than 32 mg. No other correlations have been established between barium concentrations in air and geographical areas or land-use types.

5. POTENTIAL FOR HUMAN EXPOSURE

Based on consumption of food and beverages in long-term balance studies of four individuals, daily barium intake was estimated to range from 650 to 1,770 mg/day (Tipton et al. 1966, 1969). If an average barium intake of 80 mg/day from drinking water in the United States is assumed (Hadjimarkos 1967), the barium intake from the consumption of non-drinking water dietary sources alone would range from 570 to 1,690 mg/day. Thus, food is typically the primary source of barium exposure for the general population. Gastrointestinal absorption of barium from food is reported to be approximately 6% (ranging from 1% to 15%) (ICRP 1974).

Mean daily balances (excluding loss via hair and sweat) determined from long-term balance studies of four adult subjects ranged from a negative balance of 800 μg to a positive balance of 890 μg (Tipton et al. 1966, 1969). Based on data from these studies, Schroeder (1970) estimated that human daily intake from food (1,160 kg), water (80 μg), and air (10 μg) would be approximately 1,250 μg, and that loss from urine (180 μg), feces (1,010 ,μg) and other sources (e.g., sweat and hair) (85 μg) would be 1,275 μg. Using these latter estimates of barium intake and loss, a negative barium balance of 25 μg would occur. According to ICRP, the average daily intake of barium from food and fluids (750 μg) and ambient air (0.09-26 μg) ranges from 750 to 776 μg. In addition, ICRP (1974) estimated that approximately 825 pg of barium is lost daily through the urine (50 μg), feces (690 μg), sweat (10 μg), and hair (75 μg). These intake and loss estimates indicate a negative daily balance of up to 75 μg. The day-to-day intake of barium is likely to vary with the quantity and types of food ingested since the barium content in foods varies widely (Schroeder 1970).

In a study of the barium content of the major human organs and tissues, the total body content of barium for a 70-kg adult male was estimated to be about 22,000 μg (ICRP 1974; Schroeder et al. 1972). Ninety-three percent of this barium was found in bone and connective tissue. Large amounts of the remaining 7% existed in fat, skin, and lungs (ICRP 1974; Schroeder et al. 1972).

Occupational exposure to barium primarily occurs in workers and miners who inhale barium sulfate (or the ore, barite) and barium carbonate dust during the mining of barite and the manufacturing and processing (e.g., mixing, grinding, and loading) of barium compounds (Beliles 1979; Reznik and Toy 1978; Schroeder 1970).

Preliminary data from a workplace survey, the National Occupational Exposure Survey (NOES), conducted by NIOSH from 1980 to 1983, estimated the number of workers potentially exposed to various chemicals in the workplace in 1980 (NIOSH 1989), including a separate tally of female workers. The data for barium and barium compounds included in the survey are summarized below:

Chemical	Number of plants	Total workers (female workers)
Barium	815	10,308 (3,598)
Barium carbonate	4,494	61,019 (6,889)
Barium chloride	4,293	57,767 (15,249)
Barium hydroxide	1,423	35,351 (12,208)
Barium oxide (BaO_2)	46	511 (325)
Barium nitrate	353	9,625 (2,699)
Barium sulfate	20,089	305,887 (83,800)
Barium sulfide	7	7 (0)
Chromic acid (H_2CrO_4), barium salt (1:1)	20	3,546 (1,984)

The NOES database does not contain information on the frequency, concentration, or duration of exposure of workers to any of the chemicals listed therein. This is a survey that provides only estimates of the number of workers potentially exposed to chemicals in the workplace.

5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

The general population is commonly exposed to barium primarily through ingestion of drinking water and consumption of food and beverages. However, certain populations face greater than average exposures to this element due to environmental sources, such as drinking water (EPA 1987c). High levels of barium have been reported in groundwater from deep rock and drift wells in several communities in northeastern Illinois (Brenniman et al. 1981; Calabrese 1977) where barium is a naturally occurring geochemical pollutant found almost exclusively in the Cambrian-Ordovician Aquifer (Gilkeson et al. 1978). Other populations that might receive increased exposure to barium are consumers of crops grown on soils that have been used for the land farming of waste oil-well drilling muds (Bates 1988). Individuals who work at or live near barium mining, manufacturing, or processing plants might inhale higher ambient air concentrations or increased amounts of fugitive dust containing barium particulates. Populations living in the vicinity of the 154 NPL sites known to be contaminated with barium may also be exposed to higher than background levels of the compound through contact with contaminated waste site media. No information was found regarding the sizes of these populations or their intake levels of barium.

5.7 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA as amended directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of barium is available. Where adequate information is not available, ATSDR, in conjunction with the NTP, is required to assure the initiation of a program of research designed to determine the health effects

(and techniques for developing methods to determine such,health effects) of barium.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that, if met, would reduce or eliminate the uncertainties of human health assessment. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

5.7.1 Data Needs

Physical and Chemical Properties. The physical and chemical properties of metallic barium and its inorganic compounds have been well characterized (DOT 1986; EPA 1980a, 1984. 1985c, 1987d; Hawley 1981; Hayes 1982; HSDB 1989; Kirkpatrick 1985; Kunesh 1985; Meister 1989; NIOSH/OSHA 1978; OHM/TADS 1989; Parmeggiani 1983; Perry and Chilton 1973; RTECS 1989; Sax and Lewis 1987, 1989; Sax et al. 1984; Stokinger 1981; Weast 1989; Windholz 1983). Physical and chemical properties of organic compounds of barium have not been comprehensively examined probably due to the limited extent of formation of these compounds. However, further study of the properties of these compounds would help in understanding their role in the environmental fate and transport of barium, particularly at hazardous waste sites where high levels of organic contaminants might be present.

Production, Import/Export, Use, and Disposal. Because barium compounds occur naturally and are widely used in oil well drilling muds, in steel, rubber and plastic products, glass and ceramics, chemical, and pyrotechnics industries, in insecticides, and as a smoke suppressant in diesel fuels (Bodek et al. 1988; EPA 1982; IL0 1983; Kirkpatrick 1985; Meister 1989; Stokinger 1981; Venugopal and Luckey 1978; Worthing 1987), the potential for human exposure to these compounds, such as through ingestion of food and water or inhalation of ambient air, is substantial. However, recent data on production volumes and import and export were not available. In addition, only limited information on disposal of barium compounds was available (HSDB 1989; Joseph 1985; NIOSH/OSHA 1978). Additional information on production, import, export, and disposal would be useful in assessing the potential for the release of, and exposure to, barium compounds.

According to the Emergency Planning and Community Right-to-Know Act of 1986, 42 U.S.C. Section 11023, industries are required to submit chemical release and off-site transfer information to the EPA. The Toxic Release Inventory (TRI), which contains this information for 1987, became available in May of 1989. This database will be updated yearly and should provide a list of industrial production facilities and emissions.

5. POTENTIAL FOR HUMAN EXPOSURE

Environmental Fate. The partitioning of barium in environmental media is influenced by the specific form of the compound and such site-specific conditions as pH and cation exchange capacity (Bates 1988; Bodek et al. 1988; Bowen 1966; Kabata-Pendias and Pendias 1984; Lagas et al. 1984). Upon release to the environment, barium is most likely to partition to soils and sediments (Baes et al. 1984; Rai et al. 1984). Barium is transported in the atmosphere, surface waters, soil runoff, and groundwater. In surface waters and soils, barium may ionize and form various salts depending on the pH and the availability of anions (Bates 1988; Bodek et al. 1988; Bowen 1966; Kabata-Pendias and Pendias 1984; Lagas et al. 1984). Additional information on the transport and transformation of barium in the atmosphere would be useful in developing a more complete understanding of the environmental fate of barium compounds.

Bioavailability from Environmental Media. Barium is absorbed following ingestion (Chou and Chin 1943; Cuddihy and Griffith 1972; McCauley and Washington 1983; Taylor et al. 1962) and inhalation (Cuddihy and Ozog 1973b). The bioavailability of barium from air, water, and food has been examined rather extensively in animals (Chou and Chin 1943; Cuddihy and Griffith 1972; McCauley and Washington 1983; Taylor et al. 1962) and humans (Tipton et al. 1969). However, bioavailability from soil has not been studied. Since soil is an important repository for barium, information on barium absorption from ingested soil would be useful in developing an understanding of the potential for exposure following ingestion of contaminated soils, particularly at hazardous waste sites.

Food Chain Bioaccumulation. There is information that barium bioconcentrates in certain plants and aquatic organisms (Bowen 1966; Schroeder 1970). However, the extent to which plants bioconcentrate barium from soil or to which uptake occurs in terrestrial animals is not well characterized. Further studies on the bioconcentration of barium by plants and terrestrial animals and on the biomagnification of barium in terrestrial and aquatic food chains would be useful to better characterize the environmental fate of barium and define the importance of food chain accumulation as a source of human exposure.

Exposure Levels in Environmental Media. Barium has been detected in the atmosphere (Bowen 1979), surface water (Barnett et al. 1969; Bowen 1979; Durfor and Becker 1964; Durum and Haffty 1961; Kopp 1969; Kopp and Kroner 1967; McCabe et al. 1970; Tuovinen et al. 1980), groundwater (Calabrese 1977; Kojola et al. 1970), soils (Bowen 1979; Schroeder 1970; Shacklette and Boerngen 1984), and foodstuffs (Beliles 1979; Connor and Shacklette 1975; Schroeder 1970). There are reliable data to characterize the potential for human exposure via intake of drinking water (Durfor and Becker 1964; Hadjimarkos 1967), and foods (Tipton et al. 1966, 1969); however, the data are not current. Recent data on barium levels in plants and ambient air, soils, and groundwater, particularly from hazardous waste sites, would be useful in

helping to develop a more complete understanding of the potential for human exposure.

Exposure Levels in Humans. Barium can be detected in blood, urine, feces, and biological tissues (Mauras and Allain 1979; Schramel 1988; Shiraishi et al. 1987). However, there are no data correlating barium levels in tissues and fluids with exposure levels. Additional data are needed on levels of barium in human tissues and fluids following occupational and general population exposure, particularly at hazardous waste sites. This information may be useful in establishing exposure indices for these populations.

Exposure Registries. No exposure registries for barium were located. This compound is not currently one of the compounds for which a subregistry has been established in the National Exposure Registry. The compound will be considered in the future when chemical selection is made for subregistries to be established. The information that is amassed in the National Exposure Registry facilitates the epidemiological research needed to assess adverse health outcomes that may be related to the exposure to this compound.

5.7.2 On-going Studies

Remedial investigations and feasibility studies conducted at the 154 NPL sites known to be contaminated with barium will add to the available database . on exposure levels in environmental media, exposure levels in humans, and exposure registries and will increase the current knowledge regarding the transport and transformation of barium in the environment. No other long-term research studies pertaining to the environmental fate of barium or to occupational or general population exposures to barium were identified.

6. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting and/or measuring and monitoring barium in environmental media and in biological samples. The intent is not to provide an exhaustive list of analytical methods that could be used to detect and quantify barium. Rather, the intention is to identify well-established methods that are used as the standard methods of analysis. Many of the analytical methods used to detect barium in environmental samples are the methods approved by federal agencies such as EPA and the National Institute for Occupational Safety and Health (NIOSH). Other methods presented in this chapter are those that are approved by groups such as the Association of Official Analytical Chemists (AOAC) and the American Public Health Association (APHA). Additionally, analytical methods are included that refine previously used methods to obtain lower detection limits, and/or to improve accuracy and precision.

6.1 BIOLOGICAL MATERIALS

Inductively coupled plasma-atomic emission spectrometry (ICP-AES) has been used for measuring low levels of barium in the blood, urine, and bones of humans and animals (Mauras and Allain 1979; Schramel 1988; Shiraishi et al. 1987) (see Table 6-l). In general, biological samples are nebulized and the resulting aerosol is transported to the plasma torch. Atomic-line emission spectra are produced by the inductively coupled plasma for specific element and the intensities of the lines (bands) are monitored by a photomultiplier tube. A line emission at 455.50 nm was observed for barium (Mauras and Allain 1979; Oppenheimer et al. 1984). Detection limits of 0.25 μg barium/L of urine, 0.6 μg barium/L of blood, and 0.0005 μg of barium per gram of bone were achieved (Mauras and Allain 1979; Shiraishi et al. 1987). Advantages of ICP-AES technique include moderate costs, fairly rapid analysis time, and high sensitivity (Mauras and Allain 1979; Oppenheimer et al. 1984). The presence of spectral interferences is a disadvantage of ICP-AES technique. These interferences are caused when a sample contains elements or compounds that have analytical emission lines (bands) that overlap the line chosen for the analyte. Boric acid or sodium borate (at a concentration of greater than 100 mg boron/L of sample) was reported to interfere with the line emission spectra of barium at 455.50 nm (Mauras and Allain 1979).

Neutron activation analysis (NAA) technique has also been used for determining low levels of barium in human blood (Olehy et al. 1966). This technique is based on the interaction of the nuclei of individual barium atoms with neutron irradiation, resulting in the emission of x-rays (photons). Detection limits of 7 μg barium/L of erythrocyte and 66 μg barium/L of plasma were obtained (Olehy et al. 1966). The advantages of the NAA technique are its nondestructive nature of sample and minimum sample manipulation. Disadvantages of this technique include its high costs and a nuclear reactor may not be readily available to many laboratories.

TABLE 6-1. Analytical Methods for Determining Barium in Biological Materials

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Urine and blood	Dilute sample with demineralized water, introduce into the plasma and analyze	ICP-AES	0.25 µg/L (urine) 0.6 µg/L (blood)	3%-7% coefficient of variation	Mauras and Allain 1979
Plasma and erythrocyte	Ash sample, digest with acid and irradiate	NAA	7 µg/L (erythrocyte) 66 µg/L (plasma)	28.5% RSD (erythrocyte) 7.6% RSD (plasma)	Olehy et al. 1966
Biological tissues	Digest sample in acid; precipitate as the sulfate and analyze	Gravimetry	No data	No data	Borchardt et al. 1961
Visceral materials (intestine, stomach, liver, spleen, and kidney	Ash sample and analyze	Spectrography	No data	No data	Baisane et al. 1978
Fetus bones	Ash sample and digest with acid	ICP-AES	0.0005 µg/g	0.5% RSD	Shiraishi et al. 1987

ICP-AES = inductively coupled plasma-atomic emission spectrometry; NAA = neutron activation analysis; RSD = relative standard deviation.

6.2 ENVIRONMENTAL SAMPLES

Atomic absorption spectroscopy (AAS) is the most prevalent analytical technique for measuring low levels of barium and its compounds (i.e., barium carbonate, barium sulfate, and barium chloride) in air, water, waste water, geological materials (calcium carbonate), unused lubricating oil, and diagnostic meals containing barium sulfate (see Table 6-2).

Samples may be prepared for AAS in a variety of ways (Hui-Ming and Yao-Han 1984; Johnson et al. 1983; Murata and Noguchi 1974; Pierce and Brown 1977; Renshaw 1973; Sharp and Knevel 1971; Sugiyama et al. 1984). Acid digestion with nitric acid is the most common method of preparation. Sample dilution with nitric acid or other agents to solubilize barium from the matrix can also be employed. If the concentration of barium in the dissolved sample is very low, preconcentration techniques such as chelation or extraction may be employed.

Flame atomic absorption spectroscopy (FAAS) (Methods 208.1 and 7080) and graphite furnace atomic absorption spectroscopy (GFAAS) (Methods 208.2 and 7081) are the techniques recommended by the Office of Solid Waste and Emergency Response of EPA for determining ppb (μg/L) levels of barium in water and waste water (EPA 1979a, 1979b, 1986c). Parts-per-trillion (sub μg/L) levels of barium in sea and freshwater have been detected by GFAAS (Epstein and Zander 1979; Roe and Froelich 1984). The advantages that GFAAS and FAAS techniques offer are that they are sensitive techniques, use relatively simple and inexpensive instrumentation, and have high accuracy and precision. In addition, GFAAS technique requires a small amount of sample and is more sensitive than FAAS methodology for determining barium in aqueous media (Edelbeck and West 1970; Oppenheimer et al. 1984).

FAAS (Method 7056) is the technique recommended by NIOSH for detecting soluble barium compounds in air (NIOSH 1987b). Atomic absorption spectroscopy has also been employed for detecting barium in air at 20 ppb (Miner 1969a).

Other analytical techniques that have been employed for measuring barium and its compounds in environmental media include x-ray fluorescence spectroscopy (XFS), neutron activation analysis (NAA), scintillation spectroscopy, and spectrography (Boothe and James 1985; Landis and Coons 1954; Larsen 1973; Murata and Noguchi 1974; Oppenheimer et al. 1984). XFS and NAA methods are less sensitive than other available analytical methods for measuring barium or its compounds in environmental media. Scintillation spectroscopy and spectrography are less commonly used to measure barium in the environment relative to other analytical methods.

TABLE 6-2. Analytical Methods for Determining Barium in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air	Collect sample on cellulose and extract with hot acid; evaporate extract to dryness and dissolve residue in acid	FAAS	No data	No data	NIOSH 1987b (Method 7056)
Water	Acidify sample and pass through ion-exchange resin	FAAS	3 µg/L	11.6% RSD	Pierce and Brown 1977
	Pass sample through ion-exchange resin	FAES	µg/L levels	No data	Johnson et al. 1983
	Extract sample with buffered HFA solution	FAAS	5 µg/L	No data	Edelbeck and West 1970
	No data	GFAAS	7 µg/L	No data	Fagioli et al. 1984
	Inject sample directly into graphite furnace	GFAAS	0.6 µg/L (seawater) 0.2 µg/L (freshwater)	13% RSD	Roe and Froelich 1984
Water and wastewater	Digest sample and evaporate to dryness; dissolve residue in acid	FAAS, GFAAS	100 µg/L (FAAS) 2 µg/L (GFAAS)	94%-113% (FAAS) 96%-102% (GFAAS)	EPA 1979a, 1979b, and 1986c (Methods 208.1, 208.2, 7080 and 7081)
Industrial wastewater	Digest sample; mix with cation-exchange resin, dry, and analyze	XFS	290 µg/L (on a 500 ml samples)	5.1% RSD	Murata and Noguchi 1974
Unused lubricating oil	Dissolve sample in 2-methylpropan-2-ol: toluene (3:2); add potassium naphthenate solution	FAAS	No data	No data	Holding and Rowson 1975
Rocks and minerals (calcium carbonate)	Precipitate barium from sample; dissolve in ammoniacal solution of EDTA	FAAS	Low µg/g levels	118%	Bano 1973

TABLE 6-2 (Continued)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Diagnostic meals containing barium sulfate	Add sample to EDTA solution and warm	FAAS	No data	98.6%-102.5%	Sharp and Knevel 1971
Compound formulation ($Ba^{14}CO_3$)	Prepare solution of sample in EDTA and count	Scintillation spectrometry	No data	No data	Larsen 1973

$Ba^{14}CO_3$ = radiolabeled barium carbonate; EDTA = ethylenediamine tetraacetic acid; FAAS = flame atomic absorption spectroscopy; FAES = flame atomic emission spectroscopy; GFAAS = graphite furnace atomic absorption spectroscopy; HFA = hexafluoroacetylacetone; RSD = relative standard deviation; XFS = x-ray fluorescence spectroscopy

6.3 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA as amended directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of barium is available. Where adequate information is not available, ATSDR, in conjunction with the NTP, is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of barium.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR. NTP, and EPA. They are defined as substance-specific informational needs that, if met, would reduce or eliminate the uncertainties of human health assessment. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

6.3.1 Data Needs

Methods for Determining Biomarkers of Exposure and Effect. Several methods are a available for measuring biomarkers of exposure. ICP-AES is the analytical method used for measuring barium in blood, urine and bone of humans and animals at ppt (sub μg/L) levels (Mauras and Allain 1979; Schramel 1988; Shiraishi et al. 1987). NAA technique has also been employed for measuring barium in blood of humans and animals at ppb (μg/L) levels (Olehy et al. 1966). These techniques are sensitive for measuring background levels of barium in the population. However, it is not known whether data collected using these techniques have been used to correlate the levels of barium in biological tissues and fluids to exposure levels.

At present, no biomarkers of effect are available for barium. There are no data to indicate whether a biomarker, if available, would be preferred over chemical analysis for monitoring effects from long-term and short-term exposure to barium.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. GFAAS and FAAS are the most widely used analytical techniques for measuring barium and its compounds in air (NIOSH 1987b), water (Edelbeck and West 1970; Fagioli et al. 1988; Johnson et al. 1983; Pierce and Brown 1977; Roe and Froelich 1984), waste water (EPA 1979a, 1979b, 1986c; Murata and Noguchi 1974), rocks and minerals (Bano 1973), unused lubricating oil (Holding and Rowson 1975), and diagnostic meals (Sharp and Knevel 1971). The media of most concern for potential human exposure to barium is water. GFAAS and FAAS techniques are sensitive for measuring background levels of barium in aqueous media (Epstein and Zander 1979; Roe and Froelich 1984).

However, it is not known whether these techniques are sensitive for measuring levels of barium at which health effects might begin to occur. FAAS and GFAAS are the methods (Methods 208.1, 208.2, 7080, and 7081) recommended by EPA for detecting ppb levels of barium in water and waste water (EPA 1979a, 1979b, 1986c). GFAAS has also been employed to detect ppt levels of barium in aqueous media (Epstein and Zander 1979; Roe and Froelich 1984). No additional methods for detecting barium and its compounds in environmental media appear to be useful at this time.

6.3.2 On-going Studies

No on-going studies regarding techniques for measuring and determining barium in biological and environmental samples were located.

7. REGULATIONS AND ADVISORIES

Barium is on the list of chemicals appearing in "Toxic Chemicals Subject to Section 313 of the Emergency Planning and Right-to-Know Act of 1986" (EPA 1987b).

No international regulations pertaining to barium and its compounds were found. The national and state regulations and guidelines regarding barium in air, water, and other media are summarized in Table 7-1.

7. REGULATIONS AND ADVISORIES

TABLE 7-1. Regulations and Guidelines Applicable to Barium

Agency	Description	Information	References
NATIONAL			
Regulations:			
a. Air:			
OSHA	PEL TWA (8-hr, final rule)		OSHA 1989
	Barium (soluble compounds)	0.5 mg/m^3	
	Barium sulfate		
	(total dust)	10 mg/m^3	
	(respirable fraction)	5 mg/m^3	
b. Water:			
EPA ODW	MCL (proposed) for barium in drinking water	5 mg/L	EPA 1989a
	MCL (present) for barium in drinking water	1 mg/L	EPA 1975b (40 CFR 141.11)
	AADI[a]	1.8 mg/L	EPA 1985b
FDA	Bottled water; quality standard	1.0 mg/L	FDA 1977 (21 CFR 103.35)
d. Other:			
EPA OERR	CERCLA reportable quantity		EPA 1986a (40 CFR 117.3)
	Barium cyanide	10 lb (4.54 kg)	
EPA OSW	Designation of hazardous substances		EPA 1978 (40 CFR 116.4)
	Barium cyanide	Yes	
	Listings as toxic waste: Maximum concentration of contaminants for characteristic of EP toxicity (barium)	100.0 mg/L	EPA 1980a (40 CFR 261.24)
	Listing as acute hazardous waste: Discarded commercial chemical products off-specifications species container residues, and spill residues thereof		EPA 1980b (40 CFR 261.33)
	Barium cyanide	Yes	
	Listing as hazardous waste constituents		EPA 1988b (40 CFR 261, Appendix VIII)
	Barium and compounds; barium cyanide	Yes	
	Groundwater monitoring list (total barium)	Yes	EPA 1987a (40 CFR 264, Appendix IX)
	Maximum concentration for groundwater protection (barium)	1.0 mg/L	EPA 1982 (40 CFR 264.94)
EPA OTS	Toxic chemical release reporting; community right-to-know (proposed)		EPA 1987b
	Barium	Yes	
OSHA	Meets the criteria for the proposed OSHA medical records rule	Yes	OSHA 1982
Guidelines:			
a. Air:			
ACGIH	TLV TWA		ACGIH 1986
	Barium	0.5 mg/m^3	
	Barium sulfate (total dust)	10 mg/m^3	
	Short-term excursions to 3x above TLV for no more than 30 min during an 8-hr workday		ACGIH 1988
EPA	Inhalation AIC for barium	0.01 mg/day	EPA 1984
	Inhalation AIS for barium	0.098 mg/day	EPA 1984
NIOSH	IDLH	250 mg/m^3	NIOSH 1985
b. Water:			
EPA ODW	BAT for IOC (barium)	Ion exchange; lime softening; reverse osmosis	EPA 1989a

7. REGULATIONS AND ADVISORIES

TABLE 7-1 (Continued)

Agency	Description	Information	References
NATIONAL (cont.)			
EPA ODW	MCLG (proposed) for barium	5 mg/L	EPA 1989a
	Health advisories:		EPA 1987d
	1-Day (modified DWEL for 10-kg child)	0.51 mg/L	
	10-Day (modified DWEL for 10-kg child)	0.51 mg/L	
	Longer-term		
	Modified DWEL for 10-kg child	0.51 mg/L	
	Modified DWEL for 70-kg adult	1.8 mg/L	
	Lifetime	1.5 mg/L	
NAS	SNARL		NAS 1982
	24-Hour	6.0 mg/L	
	Chronic	4.7 mg/L	
c. Other:			
EPA	RfD (oral)		
	Barium	$7x10^{-2}$ mg/kg/day	IRIS 1991
STATE			
Regulations and Guidelines:			
a. Air:	Acceptable ambient air concentrations		NATICH 1988
Connecticut	(8-hr)	10.0000 $\mu g/m^3$	
Florida (Tampa)	(8-hr)	0.0050 mg/m^3	
Nevada	(8-hr)	0.0120 mg/m^3	
New York	(1-yr)	0.6700 $\mu g/m^3$	
North Dakota	(8-hr)	0.0050 mg/m^3	
Virginia	(24-hr)	8.0000 $\mu g/m^3$	
b. Water:	Drinking water quality standards and guidelines in drinking waters		FSTRAC 1988
Massachusetts		100 µg/L	
Maine		1000 µg/L	
Minnesota		1500 µg/L	
	Maximum contaminant levels (MCLs) for barium		CELDS 1989
Alabama	Limits:		
	Drinking water standards	1.0 mg/L	
	Maximum concentration for EP toxicity	100 mg/l	
	Groundwater	1 mg/L	
Alaska	Public water supply	1.0 mg/L	
Arizona	Limits:		
	Community water systems	1.0 mg/L	
	Non-community water systems	2.0 mg/L	
	Protected use of surface water	1.0 mg/L	
California	Community water systems	1.0 mg/L	
Colorado	Limits:		
	Community water systems	1.0 mg/L	
	Groundwater	1.0 mg/L	
Connecticut	Drinking water	1.0 mg/L	
Delaware	Drinking water	1.0 mg/L	
District of Columbia	Surface and groundwater for public water supply	1.0 mg/L	

7. REGULATIONS AND ADVISORIES

TABLE 7-1 (Continued)

Agency	Description	Information	References
STATE (cont.)			
Florida	Surface and potable waters	1.0 mg/L	
Florida	Maximum contaminant level for community and non-community water systems	1.0 mg/L	
Georgia	Community water systems	1.0 mg/L	
Hawaii	Drinking water from surface sources	1.0 mg/L	
Idaho	Limits:		
	Drinking water	1.0 mg/L	
	Domestic water supplies	1.0 mg/L	
Illinois	Public and food processing use from underground water supply	1.0 mg/L	
Illinois	General water quality secondary contact and indigenous aquatic life	5.0 mg/L	
Illinois	Effluent (sewer and treatment)	2.0 mg/L	
Illinois	Finished water	1.0 mg/L	
Indiana	Limits:		
	Lake Michigan and contiguous harbors	1000 µg/L	
	Drinking water	1.0 mg/L	
	All state waters	1.0 mg/L	
Indiana	Hazardous and solid waste facilities groundwater protection	1.0 mg/L	
Iowa	Surface waters, class B and C water wildlife, aquatic and potable	1.0 mg/L	
Iowa	Public water systems	1.0 mg/L	
Kansas	Drinking water	1.0 mg/L	
Kentucky	Limits:		
	Community water systems	1.0 mg/L	
	Surface water	1.0 mg/L	
Kentucky	Hazardous and solid waste facilities groundwater protection	1.0 mg/L	
Maine	Drinking water	1.0 mg/L	
Maryland	Drinking water supply	1.0 mg/L	
Massachusetts	Groundwater (class I and II)	1.0 mg/L	
	Groundwater discharge/effluent	1.0 mg/L	
Minnesota	Drinking water (class A, B, and D)	1.0 mg/L	
Minnesota	Community water systems	1.0 mg/L	
Mississippi	Drinking water	1.0 mg/L	
Missouri	Drinking water supply	1.0 mg/L	
Missouri	Effluent limitations for subsurface water	1.0 mg/L	
Missouri	Aquifer recharge that has an effect on aquatic life	1000 µg/L	
Montana	Public water supply	1.0 mg/L	
Nebraska	Community water systems	1.0 mg/L	
Nebraska	Groundwater	1.0 mg/L	
Nebraska	Maximum concentration of EP toxicity at hazardous waste sites	100 mg/L	
Nebraska	Public drinking water	1.0 mg/L	

7. REGULATIONS AND ADVISORIES

TABLE 7-1 (Continued)

Agency	Description	Information	References
STATE (cont.)			
Nevada	Limits:		
	Aquatic life	<5.0 mg/L	
	Recreation, wildlife	<1.0 mg/L	
New Hampshire	Public water systems	1.0 mg/L	
New Jersey	Surface waters	1.0 mg/L	
New Mexico	Community water systems	1.0 mg/L	
New Mexico	Groundwater - human	1.0 mg/L	
New York	Groundwater (class GA for drinking) allowable level	1.0 mg/L	
New York	Community water supplies	1.0 mg/L	
New York	Effluent	2.0 mg/L	
North Carolina	Drinking and food processing class WS-I and WS-II	1.0 mg/L	
North Carolina	Community water systems	1.0 mg/L	
North Carolina	Drinking water (class GA)	1.0 mg/L	
	Potable mineral water (class GSA)	1.0 mg/L	
North Carolina	Maximum concentration for EP toxicity	100 mg/L	
	Maximum concentration for groundwater protection	1.0 mg/L	
North Dakota	Class i, ii, and iii waters	1.0 mg/L	
North Dakota	Drinking water	1.0 mg/L	
Ohio	Lake Erie, public, agricultural, industrial, and bathing water supplies	1.0 mg/L	
Ohio	Ohio River, water quality standards (permissible concentration)	1.0 mg/L	
Ohio	Drinking water	1.0 mg/L	
Ohio	Ohio River Valley for domestic and industrial uses	1.0 mg/L	
Ohio	Surface waters	1.0 mg/L	
Oklahoma	Raw water	1.0 mg/L	
Oklahoma	Public water supply	1.0 mg/L	
Oklahoma	Effluent concentrations	5.0 mg/L	
Oregon	Maximum contaminant level	1.0 mg/L	
Puerto Rico	Limits:		
	Coastal waters	1000 µg/L	
	Surface waters	1000 µg/L	
	Potable water	1.0 mg/L	
Rhode Island	Drinking water	1.0 mg/L	
South Dakota	Community water systems (MCL)	1.0 mg/l	
South Dakota	Domestic water supply	1.0 mg/L	
Tennessee	Community water systems; maximum containment level	1.0 mg/L	
Tennessee	Effluent, municipal and domestic wastewater treatment	5.0 mg/L	
Tennessee	Maximum concentration For EP toxicity at hazardous waste sites	100 mg/L	
	Maximum groundwater concentration	1.0 mg/L	

TABLE 7-1 (Continued)

Agency	Description	Information	References
STATE (cont.)			
Texas	Community water systems	1.0 mg/L	
Texas	Discharge to inland and tidal waters	avg=1.0 mg/L composite= 2.0 mg/l	
Utah	Raw water for domestic water system	1.0 mg/L	
Utah	Drinking water	1.0 mg/L	
Vermont	Drinking water	1.0 mg/L	
Virginia	Limits:		
	Drinking or domestic use	1.0 mg/L	
	Groundwater	1.0 mg/L	
	Surfacewater	1.0 mg/L	
Washington	Public water supply	1.0 mg/L	
West Virginia	Public water supply	1.0 mg/L	
Wisconsin	Effluent discharge from potassium iodide plant	ave: 0.003 lbs/1000lbs max: 0.009 lbs/1000lbs	
Wisconsin	Community water systems	1.0 mg/L	
Wyoming	Groundwater	1.0 mg/L	
	Fish and aquatic life	5.0 mg/L	

[a]Assumes consumption of 2 liters of water per day

AADI = Acceptable Average Daily Intake; ACGIH = American Conference of Governmental Industrial Hygienists; AIC = Acceptable Intake Chronic; AIS = Acceptable Intake Subchronic; BAT = Best Available Technology; CERCLA = Comprehensive Environmental Response, Compensation, and Liability Act; DWEL = Drinking Water Equivalent Level; EP = Extraction Procedure; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; IDLH = Immediately Dangerous to Life or Health Level; IOC = Inorganic Chemical; IRIS = Integrated Risk Information System; MCL = Maximum Contaminant Level; MCLG = Maximum Contaminant Level Goal; NAS = National Academy of Sciences; NIOSH = National Institute for Occupational Safety and Health; ODW = Office of Drinking Water; OERR = Office of Emergency and Remedial Response; OSHA = Occupational Safety and Health Administration; OSW = Office of Solid Wastes; OTS = Office of Toxic Substances; PEL = Permissible Exposure Limit; RfD = Reference dose; SNARL = Suggested No-Adverse-Response Level; TLV = Threshold Limit Value; TWA = Time-Weighted Average

8. REFERENCES

ACGIH. 1982. TLVs Threshold Limit Values for chemical substances and .physical agents in the work environment. American Conference of Governmental Industrial Hygienists, Cincinnati, OH.

*ACGIH. 1986. Documentation of the Threshold Limit Values and biological exposure indices. 5th ed. American Conference of Governmental Industrial Hygienists, Cincinnati, OH, 47-48.

*ACGIH. 1988. Documentation of the Threshold Limit Values and biological exposure indices. American Conference of Governmental Industrial Hygienists, Cincinnati, OH.

Akinfieva TA, Gerasimova IL. 1984. [Comparative toxicity of some barium compounds.] Gig Tr Prof Zabol 6:45-46. (Russian)

*Alcalde AI, Ilundain A. 1988. The effect of BaCl, on intestinal sugar transport in the rat In vitro. Rev Esp Fisiol 44:147-150.

*Antonio A, Rocha e Silva M, Yashuda Y. 1973. The tachyphylactic effect of barium on intestinal smooth muscle. Arch Int Pharmacodyn Ther 204:260-267.

*Ault B, Evans RH, Francis AA, et al. 1980. Selective depression of excitatory amino-acid induced depolarizations by magnesium ions in isolated spinal cord preparations. J Physiol 307:413-428.

*Ayre JE. 1966. Human cell-dysplasia following barium. Ind Med Surg 35:393-399.

*Baes CF, III, Sharp RD, Sjoreen AL, et al. 1984. A review and analysis of parameters for assessing transport of environmentally released radionucleotides through agriculture. Report to US Department of Energy by Oak Ridge National Laboratory, Oak Ridge, Tennessee. ORNL-5786.

Baisane SO, Chincholkar VS, Mattoo BN. 1979. Spectrographic determination of barium in biological material. Forensic Sci Int 12:127-129.

Bano FJ. 1973. The determination of trace amounts of barium in calcium carbonate by atomic-absorption spectrophotometry. Analyst 98:655-658.

Barnes CD, Utherington LG. 1973. Drug dosages laboratory animals handbook. 2nd ed. 53.

---

*Cited in text

8. REFERENCES

*Barnes D, Bellin J. DeRosa C. et al. 1988. Reference dose (RfD): Description and use in health risk assessments. Vol. I, Appendix A: Integrated risk information system supportive documentation. U.S. Environmental Protection Agency, Office of Health and Environmental Assessment. EPA 600/8-86-032a.

*Barnett PR, Skougstad MW, Miller KJ. 1969. Chemical characterization of a public water supply. .J Am Water Works Assoc 61:61-67.

*Bates MH. 1988. Land farming of reserve pit fluids and sludges: Fates of selected contaminants. Water Res 22:793-797.

*Bauer GCH, Carlsson A, Lindquist B. 1956. A comparative study on the metabolism of 140Ba and 45Ca in rats. Biochem J 631535-542.

*Bauer GCH, Carlsson A, Lindquist B. 1957. Metabolism of 140Ba in man. Acta Orthop Stand 26:241-254.

*Beliles RP. 1979. The lesser metals. In: Oehme FW, ed. Hazardous and toxic substances. Vol. 2. Toxicity of heavy metals in the environment. Parts 1 and 2, New York, NY: Marcel Dekker, Inc, 547-615.

*Benes P, Sebesta F, Sedlacek J, et al. 1983. Particulate forms of radium and barium in uranium mine waste waters and receiving river waters. Water Res 17:619-624.

Bentley A, Piper K. 1987. X-ray contrast media. Part 1. Barium sulfate preparations. Pharm J 238:138-139.

*Berggren PO, Andersson T, Hellman B. 1983. The interaction between barium and calcium in β-cell-rich pancreatic islets. Biomed Res 4:129-137.

Berman CZ, Jacobs MG, Bernstein A. 1965. Hazards of the barium enema examination as studied by electrocardiographic telemetry: Preliminary report. J Amer Geri Sot 13:672-686.

BIF. 1970. Chemicals used on treatment of water and waste water engineering data [brochure]. Unit of General Signal Corp, Providence, RI.

*Bligh PH, Taylor DM. 1963. Comparative studies of the metabolism of strontium and barium in the rat. Biochem J 87:612-618.

*Bodek I, Lyman WJ, Reehl WF, et al, eds. 1988. Environmental inorganic chemistry: Properties, processes, and estimation methods. New York, NY: Permagon Press, 7.3.1-7.3-4; B.2-B.7; B.11-B.13; B.17-B.18.

8. REFERENCES

*Boothe PN. James WD. 1985. Neutron activation analysis of barium in marine sediments from the north central Gulf of Mexico. J Trace Microprobe Tech 3:377-399.

Borchardt P, Dindial W, Mettenleiter M. 1961. A rapid semimicromethod for the determination of phosphorus and barium in biologic preparations. Clin Chem 7:264-267.

*Borzelleca JF, Condie LW Jr, Egle JL Jr. 1988. Short-term toxicity (one-and ten-day gavage) of barium chloride in male and female rats. J Am Co11 Toxicol 7:675-685.

*Boullin DJ. 1965. Effect of divalent ions on release of ^{3}H-noradrenaline by sympathetic nerve stimulation. J Physiol 183:76P-77P.

*Boullin DJ. 1967. The action of extracellular cations on the release of the sympathetic transmitter from peripheral'nerves. J Physiol 189:85-99.

*Bowen HJM. 1966. Trace elements in biochemistry. New York, NY: Academic Press, Inc.

*Bowen HJM. 1979. Environmental chemistry of the elements. New York, NY: Academic Press, Inc.

Bowen HJM, Cawse PA. 1963. The determination of inorganic elements in biological tissue by activation analysis. Isotope Research Division (AERE). Wantage, England: United Kingdom Atomic Energy Authority. AERE-R-4309.

*Boyd EM, Abel M. 1966. The acute toxicity of barium sulfate administered intragastrically. Can Med Assoc J 94:849-853.

*Brenniman CR, Levy PS. 1985. Epidemiological study of barium in Illinois drinking water supplies. In: Calabrese EJ, Tuthill RW, Condie L, eds. Inorganics in water and cardiovascular disease. Princeton, NJ: Princeton Scientific Publishing Co, 231-240.

*Brenniman GR, Kojola WH, Levy PS, et al. 1979a. Health effects of human exposure to barium in drinking water. Cincinnati, Ohio: US Environmental Protection Agency, Office of Research and Development, Health Effects Research Laboratory. EPA/600/1-79/003.

*Brenniman GR, Namekata T, Kojola WH, et al. 1979b. Cardiovascular disease death rates in communities with elevated levels of barium in drinking water. Environ Res 20:318-324.

*Brenniman GR, Kojola WH, Levy PS, et al. 1981. High barium levels in public drinking water and its association with elevated blood pressure. Arch Environ Health 36:28-32.

8. REFERENCES

*Breuing EP, Kaminskas R, Kobashi YL, et al. 1987. Effects of sodium and calcium concentrations on the barium chloride-induced electrical and contractile responses of the guinea-pig vas deferens. Braz J Med Biol Res 20:231-242.

*Bronstein AC, Currance PL, eds. 1988. Emergency care for hazardous materials exposure. St. Louis, MO: CV Mosby Company, 66, 127-128.

Brown JR, Mastromatteo E, Horwood J. 1963. Zirconium lactate and barium zirconate. Am Ind Hyg Assoc J 34:131-136.

Browning E. .1969. Toxicity of industrial metals. 2nd ed. New York, NY: Appleton-Century Crofts, 64.

*Calabrese EJ. 1977. Excessive barium and radium-226 in Illinois drinking water. J Environ Health 39:366-369.

Calabrese EJ. 1978. Pollutants and high-risk groups: The biological basis of increased human susceptibility to environmental and occupational pollutants. New York, NY: John Wiley and Sons.

Calvery HO. 1942. Trace elements in foods. Food Res 7:313-329.

*CAS. 1989. Chemical Abstracts Service (database). Chemical Abstracts.
Casarett LJ, Doull J. 1975. The basic science of poisons. New York, NY: MacMillan Publishing Co, 466.

*CELDS. 1989. Computer-aided Environmental Legislative Data Systems (database). University of Illinois, Urbana, Illinois.

Cember H, Watson JA. 1958. Bronchogenic carcinoma from radioactive barium sulfate. AMA Arch Ind Health 17:230-235.

*Cember.H, Watson JA, Novak ME. 1961. The influence of radioactivity and lung burden on the pulmonary clearance rate of barium sulfate. Am Ind Hyg Assoc J 22:27-32.

Chandra S. 1981. Interaction of barium chloride and barium carbonate at elevated temperatures. J Am Ceram Sot 64:ClOl-C102.

*Chou C, Chin YC. 1943. The absorption, fate and concentration in serum of barium in acute experimental poisoning. Chinese Med J 61:313-322.

Chow TJ, Earl JL, Reed JH, et al. 1978. Barium content of marine sediments near drilling sites: A potential pollutant indicator. Mar Pollut Bull 9:97-99.

8. REFERENCES

Clary JJ, Tardiff RG. 1974a. The absorption distribution and excretion of orally administered $^{133}BaCl_2$ in weanling male rats. Cincinnati, Ohio: National Institute for Occupational Safety and Health and US Environmental Protection Agency.

Clary JJ, Tardiff RG. 1974b. The absorption distribution and excretion of orally administered $^{133}BaC1_2$ in weanling male rats [abstract]. Toxicol Appl Pharmacol 29:139.

*Clement JG. 1981. $BaCl_2$-induced contractions in the guinea pig ileum longitudinal muscle: Role of presynaptic release of neurotransmitters and Ca^{2+} translocation in the postsynaptic membrane. Can J Physiol Pharmacol 59:541-547.

*CLPSD. 1989. Contract Laboratory Program Statistical Database. US Environmental Protection Agency. July 12, 1989.

*Connor JJ, Shacklette HT. 1975. Background geochemistry of some rocks, soils, plants, and vegetables in the conterminous United States. US Geological Survey Professional Paper. Washington, DC: US Government Printing Office. 574-F.

Copson RL. 1956. Production of chromium chemicals. In: Udy MJ, ed. Chromium. Vol. 1, New York, NY: Reinhold, 262-282.

*Cove JKJ, Snyder RN. 1974. Fatal barium intravasation during barium enema. Radiology 112:9-10.

Creason JP, Svendsgaard DJ, Bumgarner JE, et al. 1978. Maternal-fetal tissue levels of sixteen trace elements in eight communities. Research Triangle Park, NC: US Environmental Protection Agency. EPA/600/1-78/033.

*Cuddihy RG, Griffith WC. 1972. A biological model describing tissue distribution and whole-body retention of barium and lanthanum in beagle dogs after inhalation and gavage. Health Phys 23:621-633.

Cuddihy RG, Ozog JA. 1973a. Nasal absprption of CsCl, $SrC1_2$, $BaC1_2$, and $CeCl_3$ in Syrian hamsters [abstract]. Health Phys 25:315.

*Cuddihy RG, Ozog JA. 1973b. Nasal absorption of CsCl, $SrC1_2$, $BaCl_2$ and $CeCl_3$ in Syrian hamsters. Health Physics 25:219-224.

*Cuddihy RG, Hall RP, Griffith WC. 1974. Inhalation exposures to barium aerosols: Physical, chemical, and mathematical analysis. Health Phys 26:405-416.

8. REFERENCES

Dangel R.A. 1975. h study of corrosion products in Seattle Water Department Tolt distribution system. Environmental Protection Technology Series. Cincinnati, Ohio: US Environmental Protection Agency, Office of Research and Development, National Environmental Research Center. EPA-670/2-75-036.

Dare PRM, Hewitt PJ, Hicks R, et al. 1984. Barium in welding fume. Ann OCCUP Hyg 281445-448.

*Das NC, Singh V. 1970. Unusual type of cardiac arrest: Case report. Armed Forces Med J India 26:344-352.

*Davis WE. 1972. National inventory of sources and emissions. Barium, boron, copper, selenium, and zinc 1969. Barium section. Prepared by W. E. Davis and Associates, Leawood, Kansas. Washington, DC: US Environmental Protection Series, Office of Air Programs. Contract #68-02-0100.

*Delfino G, Amerini S, Mugelli A. 1988. Barium cardiotoxicity: Relationship between ultrastructural damage and mechanical effects. Toxicol in vitro 2:49-55.

*de No RL, Feng TP. 1946, Analysis of the effect of barium upon nerve with particular reference to rhythmic activity. J Cell Comp Physiol 28:397-464.

*Dencker L, Nilsson A, Ronnback C, et al. 1976. Uptake and retention of ^{133}Ba and ^{133}Ba-^{140}La in mouse tissues. Acta Radiol 15:273-87.

*Diengott D, Rozsa 0, Levy N, et al. 1964. Hypokalemia in barium poisoning. Lancet 2:343-344.

Diwan JJ. 1985. Ba^{2+} uptake and the inhibition by Ba^{2+} of K^{+} flux into rat liver mitochondria. J Membr Biol 84:165-171.

*Doig AT. 1976. Baritosis: A benign pneumoconiosis. Thorax 31:30-39.

*Domanski T, Trojanowska B. 1980. Studies on metabolic kinetics of lead and alkaline earth elements (Ca, Ba). Acta Physiol Pol 31:439-447.

*Domanski T, Liniecki J, Witkowska D. 1969. Kinetics of calcium, strontium, barium, and radium in rats. In: Mays CW, Jee WSS, Lloyd RD, et al, eds. Delayed effects of bone-seeking radionuclides. Salt Lake City, UT: University of Utah Press, 79-94.

*DOT. 1986. CHRIS (Chemical Hazards Response Information System) hazardous chemical data, commandant instruction. Department of Transportation, U.S. Coast Guard. Washington, DC: U.S. Government Printing Office. M.16465.12A

Douglas WW. 1968. Stimulus-secretion coupling: The concept and clues from chromaffin and other cells. Brit J Pharmacol 34:451-474.

8. REFERENCES

Douglas WW, Rubin RP. 1963. The mechanism of catecholamine release from the adrenal medulla and the role of calcium in stimulus-secretion coupling. J Physiol 167:288-310.

*Douglas WW, Rubin RP. 1964a. The effects of alkaline earths and other divalent cations on adrenal medullary secretion. J Physiol 175:231-241.

Douglas WW, Rubin RP. 1964b. Stimulant action of barium on the adrenal medulla. Nature 203:305-307.

*Doull J, Klaassen CD, Amdur MD, eds. 1980. Casarett and Doull's toxicology. 2nd ed. New York, NY: MacMillan Publishing Co, 438; 466.

Doull J, Klaassen CD, Amdur MD, eds. 1986. Casarett and Doull's toxicology: The basic science of poisons. 3rd ed. New York, NY: Macmillan Publishing Co, 344; 389; 567; 623-624; 675; 694.

*2Dreisbach RH, Robertson WO, eds. 1987. Handbook of poisoning: Prevention, diagnosis & treatment. 12th ed. Norwalk, CT: Appleton & Lange, 119-120.

*Durfor CN, Becker E. 1964. Public water supplies of the 100 largest cities in the United States, 1962. US Department of the Interior, US Geological Survey. Washington, DC: US Government Printing Office. Water-Supply 1812.

*Durum WH, Haffty J. 1961. Occurrence of minor elements in water. Washington, DC: US Department of the Interior, US Geological Survey. Circular 445.

Eastwood GL. 1972. ECG abnormalities associated with the barium enema. J Am Med Assoc 219:719-721.

*Ebeigbe AB, Aloamaka CP. 1987. Mechanism of contractile action of barium ion on rat aortic smooth muscle. Can J Physiol Pharmacol 65:2454-2458.

*Edelbeck L, West PW. 1970. Determination of trace concentrations of barium extracted from aqueous systems. Anal Chim Acta 52:447-453.

*Ehara T, Inazawa M. 1980. Calcium-dependent slow action potentials in potassium-depolarized guinea-pig ventricular myocardium enhanced by barium ion. Naunyn-Schmiedebergs Arch Pharmacol 315:47-54.

Einbroot HJ, Wobker F, Klippel HG. 1972. [Experimental studies on the accumulation and distribution of barium sulfate in the rat following inhalation]. Int Arch Arbeitsmed 30:237-244. (German)

*Ellenhorn MJ, Barceloux G, eds. 1988. Medical toxicology: Diagnosis and treatment of human poisoning. New York, NY: Elsevier, 1017.

8. REFERENCES

*Ellsasser JC, Farnham JE, Marshall JH. 1969. Comparative kinetics and autoradiography of ^{45}Ca and ^{133}Ba in ten-year-old beagle dogs. J Bone Joint Surg 518:1397-1412.

*Elwood PC, Abernethy M, Morton M. 1974. Mortality in adults and trace elements in water. Lancet 1470-1472.

EPA. 1975a. Region V joint federal/state survey of organics and inorganics in selected drink water supplies. Draft report. Chicago, IL: US Environmental Protection Agency.

EPA. 1975b. US Environmental Protection Agency. Code of Federal Regulations. 40 CFR 141.11.

EPA. 1977. National interim primary drinking water regulations. Washington, DC: US Environmental Protection Agency. EPA 570/g-76-003.

*EPA. 1978. US Environmental Protection Agency. Code of Federal Regulations. 40 CFR 116.4.

*EPA. 1979a. Method 208.1. Atomic absorption, direct aspiration. Methods for chemical analysis of water and wastes. Washington, DC: US Environmental Protection Agency. EPA-600/4-79-020, 76-77.

*EPA. 1979b. Method 208.2. Atomic absorption, furnace technique. Methods for chemical analysis of water and wastes. Washington, DC: US Environmental Protection Agency. EPA-600/4-79-020, 78-79.

*EPA. 1980a. US Environmental Protection Agency. Code of Federal Regulations. 40 CFR 261.24.

*EPA. 1980b. US Environmental Protection Agency. Code of Federal Regulations. 40 CE'R 261.33.

*EPA. 1982. US Environmental Protection Agency, Code of Federal Regulations. 40 CFR 264.94.

*EPA. 1983a. Reportable quantity for barium. Prepared by the Environmental Criteria and Assessment Office, Cincinnati, OH. Washington, DC: US Environmental Protection Agency, Office of Solid Waste and Emergency Response.

EPA. 1983b. Barium occurrence in drinking water, food, and air. US Environmental Protection Agency, Office of Drinking Water.

8. REFERENCES

*EPA. 1984. Health effects assessment for barium. Prepared by Environmental Criteria and Assessment Office, Cincinnati, OH. Washington. DC: US Environmental Protection Agency, Office of Solid Waste and Emergency Response. EPA/540/1-86/021.

EPA. 1985a. Draft, health effects criteria document for barium. Washington, DC: US Environmental Protection Agency, Office of Drinking Water.

*EPA. 1985b. US Environmental Protection Agency. Federal Register 50:46936.

*EPA. 1985c. Drinking water criteria document for barium (final draft). Washington, DC: US Environmental Protection Agency, Office of Drinking Water, Criteria and Standards Division. TR-540-60F.

*EPA. 1986a. US Environmental Protection Agency. Code of Federal Regulations. 40 CFR 117.3.

EPA. 1986b. Review of 37 office of drinking water health advisories. US Environmental Protection Agency. SAB-EHC-87-004-006.

*EPA. 1986c. Test methods for evaluating solid wastes. Vol. IB: Laboratory manual physical/chemical methods. 3rd ed. Washington, DC: US Environmental Protection Agency, Office of Solid Waste and Emergency Response. Methods 7080 and 7081; SW-846.

*EPA. 1987a. US Environmental Protection Agency. Code of Federal Regulations. 40 CFR 264, Appendix IX.

*EPA. 1987b. US Environmental Protection Agency. Federal Register 52:21152.

*EPA. 1987c. Drinking water health criteria document on barium (final draft). Washington, DC: US Environmental Protection Agency, Office of Drinking Water, Criteria and Standards Division. TR-832-892.

*EPA. 1987d. Health advisories for 'Legionella' and seven inorganics (including barium, cadmium, chromium, cyanide, mercury, nickel and nitrate/nitrite). Washington, DC: US Environmental Protection Agency, Office of Drinking Water.

EPA. 1988a. Review of the barium health criteria document. Metals Subcommittee of the Science Advisory Board's Environmental Health Committee. Washington, DC: US Environmental Protection Agency.

*EPA. 1988b. US Environmental Protection Agency. Code of Federal Regulations. 40 CFR 261, Appendix VIII.

*EPA. 1989a. US Environmental Protection Agency. Federal Register 54:22062.

8. REFERENCES

*EPA . 1989b. Exposure factors handbook. Washington, DC: US Environmental Protection Agency, Office of Health and Environmental Assessment. EPA 600/S-89-043.

*EPA. 1989c. Interim methods for development of inhalation reference doses, Washington, DC: US Environmental Protection Agency, Office of Health and Environmental Assessment. EPA 600/8-88/066F.

*Epstein MS, Zander AT. 1979. Direct determination of barium in sea and estuarine water by graphite furnace atomic spectrometry. Anal Chem 51:915-918.

Erre N, Manta F, Parodo A. 1980. The short-term retention of barium in man Health Phys 38:225-227.

*Essing H-G, Buhlmeyer G, Valentin H, et al. 1976. [Exclusion of disturbances to health from long years of exposure to barium carbonate in the production of steatite ceramics]. Arbeitsmedizin Sozialmedizin Praventivmedizin 11:299-302. (German)

*Fagioli F, Locatelli C, Lanciotti E, et al. 1988. Determination of barium in bottled drinking water by graphite furnace atomic absorption spectrometry. Anal Lett 21:2107-2116.

*Faust SD, Aly OM. 1981. Chemistry of natural waters. Ann Arbor, Michigan: Ann Arbor Science Publishers. 400 pp.

Fazekas IG, Felkai B, Melegh B. 1953. [Central nervous system effects of $BaCl_2$ poisoning]. Virohows Archiv, Bd S 3248:110-115. (German)

*FDA. 1977. Food and Drug Administration. Code of Federal Regulations. 21 CFR 103.35

Feczko PJ, Simms SM, Bakirci N. 1989. Fatal hypersensitivity reaction during a barium enema. Am J Roentgen01 153:275-276.

*FEDRIP. 1989. Federal Research in Progress (database). National Technical Information Service.

*Foster PR, Elharrar V, Zipes DP. 1977. Accelerated ventricular escapes induced in the intact dog by barium, strontium and calcium. J Pharmacol Exp Ther 200:373-383.

Franks WR. 1955. Differential susceptibility of animals to dust. A critical review. AMA Arch Ind Health 288-296.

8. REFERENCES

*FSTRhC. 1988. Federal-State Toxicology and Regulatory Alliance Committee, Chemical Communication Subcommittee (database). Summary of state and federal drinking water standards and guidelines. March 1988.

Garner RJ, Jones HG, Sansom BF. 1960. Fission products and the dairy cow: 2. Some aspects of the metabolism of the alkaline-earth elements calcium, strontium and barium. Biochem J 76:572-579.

Gerritse RE, Vriesema R, Dalenberg JW, et al. 1982. Effect of sewage sludge on trace element mobility in soils. J Environ Qua1 11:359-364.

Gibbs G, Lueker RD, Baxley WA, et al. 1972. Cardiac arrhythmia associated with barium enema. Rocky Mt Med J 69:63-66.

*Gilkeson RH, Specht SA, Cartwright K, et al. 1978. Geologic studies to identify the source for high level of radium and barium in Illinois ground-water supplies: A preliminary report. Illinois State Geological Survey and Illinois State Water Survey. Urbana, Illinois: University of Illinois, Water Resources Center. UILU-WRC-78-0135.

Gogte ST. 1970. Ethylenediaminetetraacetic acid tetracycline and toxicity of barium chloride and sodium fluoride [letter to editor]. Indian J Physiol Pharmacol 14:61-62.

*Golothan DW. 1967. Diesel engine exhaust smoke: The influence of fuel properties and the effects of using barium-containing fuel additive. Society of Automotive Engineers. S.A.E.-670092, 616-640.

*Gore DJ, Patrick G. 1982. A quantitative study of the penetration of insoluble particles into the tissue of the conducting airways. Ann Occup Hyg 26:149-161.

Gosselin RE, Hodge NC, Smith RP, et al. 1976. Clinical toxicology of commercial products. 4th ed. Baltimore, MD: Williams and Wilkins Co.

Gosselin RE, Smith RP, Hodge HC. 1984. Barium. Clinical toxicology of commercial products. 5th ed. Baltimore, MD: Williams & Wilkins Co, II12; II112-II113; II126; II274; II161-II163.

Gotsev T. 1944. [Blood pressure and heart activity: III. Action of barium on the circulation]. Arch Exp Pathol Pharmakol 203:564-577. (German)

*Gould DB, Sorrel1 MR, Lupariello AD. 1973. Barium sulfide poisoning: Some factors contributing to survival. Arch Intern Med 132:891-894.

Graham CF. 1934. Barium chloride poisoning [abstract]. J Am Med Assoc 102:1471.

8. REFERENCES

*Greengard P, Straub RW. 1959. Restoration by barium 0.f action potentials in sodium-deprived mammalian B and C fibers. J Physiol 145:562-569.

Gutwein EE, Landolt RR, Brenchley DL. 1974. Barium retention in rats exposed to combustion products from diesel fuel containing a barium-based antismoke additive. J Air Pollut Contr Ass 24:40-43.

*Haddad LM, Winchester JF, eds. 1990. Clinical management of poisoning and drug overdose. 2nd ed. Philadelphia, PA: WB Saunders Company, 1129.

*Hadjimarkos DM. 1967. Effect of trace elements in drinking water on dental caries. J Pediatr 70:967-969.

*Hampel CA, Hawley GG, eds. 1973. The encyclopedia of chemistry. 3rd ed. New York, NY: Van Nostrand Reinhold Company, 125-127,

*Hardcastle J, Hardcastle PT, Noble JM. 1983a. The secretory action of $BaCl_2$ in rat small intestine In vitro. J Physiol 338:5OP-51P.

*Hardcastle J, Hardcastle PT, Noble JM. 1983b. The effect of barium chloride on intestinal secretion in the rat. J Physiol 344:69-80.

*Hardcastle J, Hardcastle PT, Noble JM. 1985. The secretory action of barium chloride in rat colon. J Physiol 361:19-33.

*Harrison GE, Carr TEF, Sutton A. 1967. Distribution of radioactive calcium, strontium, barium and radium following intravenous injection into a healthy man. Int J Radiat Biol 131235-247.

Hartford WH. 1979. Chromium compounds. In: Kirk RE, Othmer DF, Grayson M, et al., eds. Encyclopedia of chemical technology. Vol. 6, 3rd ed. New York, NY: John Wiley & Sons, 82-86; 97-98; 101; 105-110; 113; 115.

*Hawley GG. 1977. The condensed chemical dictionary. 9th ed. New York, NY: Van Nostrand Reinhold Co, 105-110.

*Hawley GG, ed. 1981. The condensed chemical dictionary. 10th ed. New York, NY: Van Nostrand Reinhold Company, 105-110.

*Hayes WJ Jr. 1982. Pesticides studied in man. Baltimore, MD: Williams and Wilkins Co.

Healy WB, Ludwig TG. 1968. Barium content of teeth, bone and kidney of twin sheep raised on pastures of differing barium content. Arch Oral Biol 13:559-563.

8. REFERENCES

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

*Hicks R, Caldas LQA, Dare PRM, et al. 1986. Cardiotoxic and bronchoconstrictor e.ffects of industrial metal fumes containing barium. Archives of Toxicology, Suppl 9. Toxic interfaces of neurones, smoke and genes. Secaucus, NJ: Springer-Verlag New York, Inc.

*Hiraoka M, Ikeda K, Sano T. 1980. The mechanism of barium-induced automaticity in ventricular muscle fibers. Adv Myocardiol 1:255-266.

*Holding ST, Rowson JJ. 1975. The determination of barium in unused lubricating oils by means of atomic-absorption spectrophotometry. Analyst 100:465-470.

Holusa R, Wobker F, Einbroot HJ. 1973. [Histological changes in the lung following short-term inhalation or barium sulfate (animal experiments)]. Beitr Silikoseforsch Pneumokoniose 25:1-14. (German)

*HSDB. 1989. Hazardous Substances Data Bank. National Library of Medicine, National Toxicology Information Program, Bethesda, MD.

*Hui-Ming H, Yao-Han L. 1984. Determination of trace Na, K, Ba, and Li by graphite furnace atomic emission spectrometry. Spectrochim Acta 39B:493-499.

*Huston J Jr, Wallach DP, Cunningham GJ. 1952. Pulmonary reaction to barium sulfate in rats. AMA Archives of Pathology 54:430-438.

Hutcheson DP, Gray DH, Venugopal B, et al. 1975. Studies of nutritional safety of some heavy metals in mice. J Nutr 105:670-675.

Hwang H, Dasgupta PK. 1985. Spectrophotometric determination of trace aqueous sulfate using barium-beryllon II. Mikrochim Acta 1:313-324.

ICRP. 1972. Alkaline earth metabolism in adult man. A report by a task group of Committee 2 of the International Commission on Radiological Protection. New York, NY: Pergamon Press. ICRP Publication 20

*ICRP. 1973. International Commission on Radiological Protection. Alkaline earth metabolism in adult man. Health Phys 24:125-221.

*ICRP. 1974. International Commission on Radiological Protection. Report of the task group on reference man. New York, NY: Pergamon Press.

*ILO. 1983. International Labour Office encyclopedia of occupational health and safety. Volume I and II. Geneva, Switzerland: International Labour Office, 242-244.

8. REFERENCES

*IRIS. 1991. Integrated Risk Information System (database). US Environmental Protection Agency, Environmental Criteria and Assessment Office, Cincinnati, OH.

+Jaklinski A, Maj J, Przegalinski E. 1967. Experimental studies on barium poisoning. J Forensic Med 14:13-15.

*Johnson KE, Yerhoff FW, Robinson J, et al. 1983. Determination of barium at ng ml^{-1} levels by flame emission spectrometry after ion-exchange separation from 1000-fold amounts of calcium. Anal Chim Acta 149:129-135.

*Joseph EZ. 1985. Chemical safety data guide. Washington, DC: Bureau of National Affairs. Inc.

*Kabata-Pendias A, Pendias H. 1984. Trace elements in soils and plants. Boca Raton, Florida: CRC Press, Inc.

*Karaki H, Ikeda M, Urakawa N. 1967. Effects of external calcium and some metabolic inhibitors on barium-induced tension changes in guinea pig taenia coli. Jpn J Pharmacol 17:603-612.

*Katzung BC, Morgenstern J. 1976. The effects of potassium and barium on ventricular automaticity and the pacemaker current. Proc West Pharmacol Sot 19:299-302.

*Kay S. 1954. Tissue reaction to barium sulfate contrast medium. AMA Arch Pathol 57:279-284.

*Kirkpatrick T. 1978. Barium compounds. In: Grayson M, Eckroth D, eds. Kirk-Othmer encyclopedia of chemical technology. Vol. 3, 3rd ed. New York, NY: John Wiley and Sons, 463-479.

*Kirkpatrick T. 1985. Barium compounds. In: Grayson M, Eckroth D, eds. Kirk-Othmer concise encyclopedia of chemical technology. New York, NY: John Wiley and Sons, 147-148.

Kirpekar SM, Misu, Y. 1967. Release of noradrenaline by splenic nerve stimulation and its dependence on calcium. J Physiol 188:219-234.

*Kojola WH, Brenniman GR, Carnow BW. 1978. A review of environmental characteristics and health effects of barium in public water supplies. Rev Environ Health 3:79-95.

Kolacinski Z. 1987. [Suicidal poisoning with barium nitrate]. Pol Tyg Lek 42:339-341. (Polish)

8. REFERENCES

Kolpakov W. 1971. [Effect of barium chloride on production of humoral factors stimulating leukopoiesis]. Patol Fiziol Eksp Ter 14:64-66. (Russian)

*Kopp JF. 1969. The occurrence of trace elements in water. In: Hemphill DD, ed. Proceedings of the third annual conference on trace substances in environmental health. Columbia, Missouri: University of Missouri, 59-73.

*Kopp JF, Kroner RC. 1967. Trace metals in waters of the United States. A five-year summary of trace metals in rivers and lakes of the United States (Ott 1, 1962-Sept 30, 1967). Cincinnati, OH: US Department of Interior, Federal Water Pollution Control Administration, Division of Pollution Surveillance.

*Kopp SJ, Perry HM Jr, Feliksik JM, et al. 1985. Cardiovascular dysfunction and hypersensitivity *to* sodium pentobarbital induced by chronic barium chloride ingestion. Toxicol Appl Pharmacol 77:303-314.

*Korman EF, Ward JF, Myers LS Jr. 1978. Toxic effects of metals on DNA synthesis. In: Mahlum DD, ed. Developmental toxicology of energy related pollutants, proceedings of the 17th annual Hanford biology symposium, Washington, DC, October 17-19, 1977. Sponsored by Division of Biomedical and Environmental Research, Department of Energy, and Pacific Northwest Laboratories, Battelle Memorial Institute, 384-395.

*Kramer HJ, Gonick HC, Lu E. 1986. In vitro inhibition of Na-K-ATPase by trace metals: Relation to renal and cardiovascular damage. Nephron 44:329-336.

*Kunesh CJ. 1978. Barium. In: Grayson M, Eckroth D, eds. Kirk-Othmer encyclopedia of chemical technology. Vol. 3, 3rd ed. New York, NY: John Wiley and Sons, 457-463.

*Kunesh CJ. 1985. Barium. In: Grayson M, Eckroth D, eds. Kirk-Othmer concise encyclopedia of chemical technology, New York, NY: John Wiley and Sons, 146-147.

*Lagas P, Loch JPG, Born CM, et al. 1984. The behavior of barium in a landfill and the underlying soil. Water, Air, Soil Pollut 22:121-129.

Lai JCK, Chan AWK, Minski MJ, et al. 1985. Application of inStrumenta neutron activation analysis to the study of trace metals in brain and metal toxicity. In: Gabay S, Harris J, Ho BT, eds. Neurology and neurobiology. Vol. 15. Metal ions in neurology and psychiatry. New York, NY: Alan R. Liss, Inc, 323-344.

*Landis FP, Coons MC. 1954. A rapid spectrographic method for the determination of beryllium in air dust. Appl Spectroscopy 8:71-75. .

8. REFERENCES

*Larsen PO. 1973. A convenient method for liquid scintillation counting of barium carbonate-^{14}C. Int J Appl Radiat Isot 24:612-613.

*Lengemann FW. 1959. The site of action of lactose in the enhancement of calcium utilization. J Nutr 69:23-27.

*Lewi Z, Bar-Khayim Y. 1964. Food-poisoning from barium carbonate. Lancet 342-343.

Li C. 1982. [Experimental studies on the pathogenesis of barium chloride-induced myocardial necrosis in conditions of potassium deficiency]. Yingyang Xuebao 4:341-347. (Chinese)

*Liniecki J. 1971. Kinetics of calcium, strontium, barium and radium in rabbits. Health Phys 21:367-376.

London JE. 1988. Preliminary toxicological study of yttrium barium copper oxide. Carried out by Los Alamos National Laboratory, University of California. Washington, DC: US Department of Energy, Office of Health and Energy Research. LA-11437-MS

*Losee FL, Cutress TW, Brown R. 1974. Natural elements of the periodic table in human dental enamel. Caries Res 8:123-134.

Luckey TD. 1975. Introduction to heavy metal toxicity, safety and hormology. Environ Qua1 Saf l:l-3.

Macdonald AMG, Sirichanya P. 1969. The determination of metals in organic compounds by oxygen-flask combustion or wet combustion. Microchem J 14:199-206.

*Mascher D. 1973. Electrical and mechanical responses in ventricular muscle fibers during barium perfusion. Pflugers Arch 342:325-346.

*Mattila MJ, Anyos K, Puisto EL. 1986. Cardiotoxic actions of doxepin and barium chloride in conscious rabbits, Arch Toxicol, Suppl, Toxic Interfaces Neurones, Smoke Genes 9:205-208.

*Mauras Y, Allain P. 1979. [Determination of barium in water and biological fluids by emission spectrometry with an indirectively-coupled plasma]. Anal Chim Acta 110:271-277. (French)

*McCabe LJ, Symons JM, Lee RD, et al. 1970. Survey of community water supply systems. J Am Water Works Assoc 62:670-687.

*McCauley PT, Washington IS. 1983. Barium bioavailability as the chloride, sulfate or carbonate salt in the rat. Drug Chem Toxicol 6:209-217.

8. REFERENCES

*McCauley PT, Douglas BH, Laurie RD, et al. 1985. Investigations into the effect of drinking water barium on rats. Adv Mod Environ Toxicol, Inorg Drinking Water Cardiovasc Dis 9:197-210.

*McNally WD. 1925. Two deaths from the administration of barium salts. J Am Med Assoc 84:1805-1807.

MEDLARS II. 1989. Medical Literature Analysis and Retrieval System II. National Library of Medicine. September 20, 1989.

*Meister RT. ed. 1989. 1989 Farm chemicals handbook. Vol. 75, Willoughby, OH: Meister Publishing Company, C33.

*Merefield JR. 1987. Ten years of barium build-up in the Teign. Mar Pollut Bull 18:220-222.

Miller DL. 1957. Inhalation of barium carbonate [letter the editor]. J Am Med Assoc 165:913.

*Miller RG, Featherstone JDB, Curzon MEJ, et al. 1985. Barium in teeth as indicator of body burden. Performed by Eastman Dental Center, Rochester, NY. Research Triangle Park, NC: Health Effects Research Laboratory, Office of Research and Development. EPA/600/J-85/397.

*Miner S. 1969a. Air pollution aspects of barium and its compounds. Bethesda, MD: Litton Systems, Inc Contract No. Ph-22-68-25, 69.

*Miner S. 1969b. Preliminary air pollution survey of barium and its compounds: A literature review. Raleigh, NC: US Department of Health, Education and Welfare, Public Health Service, Consumer Protection and Environmental Health Service, Consumer Air Pollution and Control Administration. Report No. APTD 69-28.

*Mishra SK, Das PK, Sanyal AK. 1988. Barium-induced contraction of rat vas deferens in calcium-free solution. Arch Int Pharmacodyn Ther 294:85-98.

*Moloukhia MK, Ahmed MW. 1979. Kinetics of barium-140 and radium-223 uptake by human bones. Isot Radiat Res 11:41-49.

*Morel FMM. 1983. Principles of aquatic chemistry. New York, NY: John Wiley and Sons.

*Morrow PE, Gibb FR, Johnson L. 1964. Clearance of insoluble dust from the lower respiratory tract. Health Phys 10:543-555.

*Morton W. 1945. Poisoning by barium carbonate. Lancet 2:738-739.

8. REFERENCES

*Morton MS, Elwood PC, Abernethy M. 1976. Trace elements in water and congenital malformations of the central nervous system in South Wales. Brit J Prev Sot Med 30:36-39.

*Munch DF, Comer HT, Downey JM. 1980. Barium contracture: A model for systole. Am J Physiol 239:H438-H442.

*Murata M, Noguchi M. 1974. An ion exchanger-epoxy resin pelletization method for sample preparation in x-ray fluorescence analysis. Anal Chim Acta 71:295-302.

Myers AG, Snoeyink VL, Snyder DW. 1985. Removing barium and radium through calcium cation exchange. Am Water Works Assoc J 77:60-66.

*Nakazato Y, Onoda Y. 1980. Barium and strontium can substitute for calcium in noradrenaline output induced by excess potassium in the guinea-pig. J Physiol 305:59-71.

*NAS. 1977. Drinking water and health. Vol. 1. National Academy of Sciences. Washington, DC: National Academy Press, 205-305.

*NAS. 1982. Drinking water and health. Vol. 4. National Academy of Sciences. Washington, DC: National Academy Press, 167-170.

*NAS/NRC. 1989. Biologic markers in reproductive toxicology. National Academy of Sciences, National Research Council. Washington, DC: National Academy Press, 15-35.

*NATICH. 1988. National Air Toxics Information Clearinghouse (database). US Environmental Protection Agency, Office of Air Quality Planning and Standards, Research Triangle Park, NC.

*Newton D, Rundo J, Harrison GE. 1977. The retention of alkaline earth elements in man, with special reference to barium. Health Phys 33~45-53.

*NFPA. 1986. Fire protection guide on hazardous materials. 9th ed. Quincy, MA: National Fire Protection Association. NFPA No. SPP-1E.

*Ng A, Patterson CC. 1982. Changes of lead and barium with time in California offshore basin sediments. Geochim Cosmochim Acta 46:2307-2321.

*NIOSH. 1976. National occupational hazard survey (1970) (database). Department of Health and Human Services, National Institute for Occupational Safety and Health.

*NIOSH. 1985. NIOSH pocket guide to chemical health hazards. Washington, DC: US Department of Health and Human Services, National Institute for Occupational Safety and Health. DHHS (NIOSH) Publication No. 85-114.

8. REFERENCES

NIOSH. 1987a. NIOSH manual of analytical methods. In: Eller PM, ed. Vol. 1, 3rd ed. Cincinnati, OH: National Institute for Occupational Safety and Health.

*NIOSH. 1987b. NIOSH manual of analytical methods. Second supplement. National Institute for Occupational Safety and Health. Cincinnati, OH: Publication No. 87-117.

*NIOSH. 1989, National occupational exposure survey (1980-83) (database). Department of Health and Human Services, National Institute for Occupational Safety and Health.

*NIOSH/OSHA. 1978. Occupational health guidelines for chemical hazards: Soluble barium compounds (as barium). National Institute for Occupational Safety and Health; Occupational Safety and Health Administration.

*Nishioka H. 1975. Mutagenic activities of metal compounds in bacteria. Mutat Res 31:185-189.

Nolan DJ, Gourtsoyiannis NC. 1980. Crohn's disease of the small intestine: A review of the radiological appearances in 100 consecutive patients examined by a barium infusion technique. Clin Radio1 31:597-603.

*NTP. 1990. Chemical status report produced from NTP chemtrack system (database). Department of Health and Human Services, National Toxicology Program, Division of Toxicology Research and Testing, Research Triangle Park, NC. January 10, 1990.

*Ogen S, Rosenbluth S, Eisenberg A. 1967. Food poisoning due to barium carbonate in sausage. Isr J Med Sci 3:565-568.

Ohanian EV, Lappenbusch WL. 1983. Problems associated with toxicological evaluations of barium and chromium in drinking water. Tract Subst Environ Health 1:109-120.

*OHM-TADS. 1989. Oil and Hazardous Materials Technical Assistance Data System (database). Chemical Information Systems.

Okawa MT. 1981. Health hazard evaluation determination report No. 78-93-536. Prepared by Mark Stees Corporation, Salt Lake City, UT. Cincinnati, OH: National Institute for Occupational Safety and Health. NIOSH-HE-78-93-536.

*Olehy DA, Schmitt RA, Bethard WF. 1966. Neutron activation analysis of magnesium, calcium, strontium, barium, manganese, cobalt, copper, zinc, sodium, and potassium in human erythrocytes and plasma. J Nucl Med 6:917-927.

8. REFERENCES

*Oppenheimer JA, Eaton AD, Leong LYC, et al. 1984. Multielemental analytical techniques for hazardous waste analysis: The state-of-the-art. Las Vegas, NV: US Environmental Protection Agency, Office of Research and Development, Environmental Monitoring Systems Laboratory. EPA-600/4,84/028.

*OSHA. 1974. Occupational Safety and Health Administration. Code of Federal Regulations. 29 CFR 1910.1000.

*OSHA. 1982. Occupational Safety and Health Administration. Federal Register 47:30420-30434.

*OSHA. 1989. Occupational Safety and Health Administration. Federal Register 54:2920.

*Palder SB, Dalessandri KM. 1988. Barium appendicitis. West J Med 148:462-464.

*Parmeggiani L, ed. 1983. Encyclopedia of occupational health and safety. Prepared under the auspices of the International Labour Organization. Vol. II, 3rd ed. Geneva, Switzerland: International Labour Office.

*Pento JT. 1979. The influence of barium on calcitonin secretion in the pig. Pharmacol Res Conunun 11:221-226.

*Perry RH, Chilton CH, eds. 1973. Chemical engineers' handbook. 5th ed. New York, NY: McGraw-Hill Book Co, 3-8.

*Perry HM Jr, Kopp SJ, Erlanger MW, et al. 1983. Cardiovascular effects of chronic barium ingestion. Trace Subst Environ Health 17:155-164.

*Perry HM Jr, Perry EF, Erlanger MW, et al. 1985. Barium-induced hypertension. Adv Mod Environ Toxicol, Inorg Drinking Water Cardio Vast Dis 9:221-229.

*Perry HM Jr, Kopp SJ, Perry EF, et al. 1989. Hypertension and associated cardiovascular abnormalities induced by chronic barium feeding. J Toxicol Environ Health 28:373-388.

*Peyton JC, Borowitz JL. 1978. Effects of Ba^{2+} and Cd^{2+} on convulsive electroshock sensitivity and ^{45}Ca distribution in brain subcellular fractions in mice. Toxicol Appl Pharmacol 45:95-103.

*Phelan DM, Hagley SR, Guerin MD. 1984. Is hypokalemia the cause of paralysis in barium poisoning. Br Med J 289:882.

Pidgeon LM. 1964. Barium. Kirk-Othmer encyclopedia of chemical technology. Vol. 3, 2nd ed. New York, NY: John Wiley and Sons, 77-80.

8. REFERENCES

*Pierce FD, Brown HR. 1977. A semi-automated technique for the separation and determination of barium and strontium in surface waters by ion exchange chromatography and atomic emission spectrometry. Anal Lett 10:685-699.

Preisman L. 1964. Barium compounds. Kirk-Othmer encyclopedia of chemical technology. Vol. 3, 2nd ed. New York, NY: John Wiley and Sons, 80-98.

*Princenthal RA, Lowman R, Zeman RK, et al. 1983. Ureterosigmoidostomy: The development of tumors, diagnosis, and pitfalls. Am J Roentgen01 141:77-81.

*Proctor NH, Hughes JP, Fischman ML, eds. 1988. Chemical hazards of the workplace. 2nd ed. Philadelphia, PA: JB Lippincott Company, 88-89.

PTS PROMT. 1990. Predicasts Terminal System: PRedicasts Overview of Markets and Technology (database). Predicasts, Cleveland, OH.

*Rae T. 1977. Tolerance of mouse macrophages In vitro to barium sulfate used in orthopedic bone cement. J Biomed Mater Res 11:839-846.

*Rai D, Zachara JM, Schwab AP, et al. 1984. Chemical attenuation rates, coefficients, and constants in leachate migration. Vol. I: A critical review. Prepared by Pacific Northwest Laboratories (Battelle Institute), Richland, Washington. Palo Alto, CA: Electric Power Research Institute. Report EA-3356

Raj GG, Srihari K. 1984. Toxicity of barium carbonate to field rodents, a laboratory and field evaluation. Mysore J Agric Sci 18:131-134.

Rangachari PK. 1975. Ba^{++} as a gastric stimulant: Release of histamine. Am J Physiol 229:627-631.

*Reeves AL. 1979. Barium. In: Friberg L, Nordberg GF, Vouk VB, eds. Handbook on the toxicology of metals. New York, NY: Elsevier/North Holland Biomedical Press, 321-328.

*Reeves AL. 1986. Barium. In: Friberg L, Nordberg GF, Vouk VB, eds. Handbook on the toxicology of metals. 2nd ed. New York, NY: Elsevier Science Publishers BV, 84-94.

*Renshaw GD. 1973. The determination of barium by flameless atomic absorption spectrophotometry using a modified graphite tube atomizer. At Absorpt News1 12:158-160.

*Reznik RB, Toy HD Jr. 1978. Source assessment: Major barium chemicals. Cincinnati, OH: US Environmental Protection Agency. EPA-600/2-78-0046.

8. REFERENCES

*Riley RF. 1987. Barium. In: Parker SP, ed. McGraw-Hill encyclopedia of science and technology. Vol. 2, 6th ed. New York, NY: McGraw-Hill Book Company, 397-399.

*Roe KK, Froelich PN. 1984. Determination of barium in seawater by direct injection graphite furnace atomic absorption spectrometry. Anal Chem 56:2724-2726.

Roeske WR, Higgins C, Karliner JS, et al. 1975. Incidence of arrhythmias and ST-segment changes in elderly patients during barium enema studies. Amer Heart J 90:688-694.

*Roza 0, Berman LB. 1971. The pathophysiology of barium: Hypokalemic and cardiovascular effects. J Pharmacol Exp Ther 177:433-439.

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

Rubin RP. 1970: The role of calcium in the release of neurotransmitter substances and hormones. Pharmacol Rev 22:389-428.

Rumyantsev GI. 1963. [Barium compounds]. [Toxicology of Rare Metals] or Toksikologiia redkikh metallov 118-125. (Russian)

Rundo J. 1967. The retention of barium-133 in man. Int J Radiat Biol 13:301-302.

*Sacchetti G. 1972. Gastric emptying of barium sulfate suspensions in humans: A useful tool for clinical investigations. Farmaco Prat 27180-88.

*Saeki Y, Shibata T, Shiozawa K. 1981. Excitation-contraction coupling in mammalian cardiac muscle during Ba^{2+}-induced contracture. Am J Physiol 240:H216-H221.

*Saito Y, Sakai Y, Urakawa N. 1972. Effect of cholinergic drugs and barium on oxygen consumption in guinea pig taenia coli. Jpn J Pharmacol 22:653-661.

Salomonowitz E, Frick MP, Cragg AH, et al. 1984. The adhesiometer: A simple device to measure adherence of barium sulfate to intestinal mucosa. Am J Roentgenol 142:721-723.

*Sax NI, Feiner B, Fitzgerald JJ, et al. 1984. Dangerous Properties of Industrial Materials. 6th ed. New York, NY: Van Nostrand Reinhold Company.

*Sax NI, Lewis RJ Sr, eds. 1987. Hawley's condensed chemical dictionary. 11th ed. New York, NY: Van Nostrand Reinhold Company, 117-122.

8. REFERENCES

*Sax NI, Lewis RJ Sr. eds. 1989. Dangerous properties of industrial materials. Vol. II, 7th ed. New York, NY: Van Nostrand Reinhold Company.

Schmitt AH. 1987. [Barium-sulfate passage in the intestine of the cat]. Praktische Tierarzt 68:37-38. (German)

*Schott GD, McArdle B. 1974. Barium-induced skeletal muscle paralysis in the rat, and its relation to human familial periodic paralysis. J Neurol Neurosurg Psychiatr 37:32-39.

*Schramel P, 1988, ICP and DCP emission spectrometry for trace element analysis in biomedical and environmental samples: A review. Spectrochim Acta 43:aai-896.

*Schroeder HA. 1970. Barium. Air Quality Monograph. American Petroleum Institute, Washington, DC. Air Quality Monograph No. 70-12.

*Schroeder HA, Kraemer LA. 1974. Cardiovascular mortality, municipal water, and corrosion. Arch Environ Health 28:303-311.

*Schroeder HA, Mitchener M. 1975a. Life-term studies in rats: Effects of aluminum, barium, beryllium, and tungsten. J Nutr 105:421-427.

*Schroeder HA, Mitchener M. 1975b. Life-term effects of mercury, methyl mercury, and nine other trace metals on mice, J Nutr 105:452-453.

*Schroeder HA, Tipton IH, Nason AP. 1972. Trace metals in man: Strontium and barium. J Chronic Dis 25:491-517.

Seaber WM. 1933. Barium as a normal constituent of Brazil nuts. Analyst 58:575-580.

*Seaton A, Ruckley VA, Addison J, et al. 1986. Silicosis in barium miners. Thorax 41:591-595.

*Segreti A, Vocci FJ, Dewey WL. 1979. Antagonism of barium chloride lethality by atropine and naloxone: Analysis by a multivariate logistic model. Toxicol Appl Pharmacol 50:25-30.

*Shacklette HT, Boerngen JG. 1984. Element concentrations in soils and other surficial materials of the conterminous United States. US Geological Survey Professional Paper. Washington, DC: US Government Printing Office. No. 1270.

Shaffer HA, Eckard DA, De Lange EE, et al. 1988. Allergy to barium sulfate suspension with angioedema of the stomach and small bowel. Gastrointest Radio1 13:1221-223.

8. REFERENCES

*Shanbaky IO, Borowitz JL. Kessler WV. 1978. Mechanisms of cadmium- and barium-induced adrenal catecholamine release. Toxicol Appl Pharmacol 44:99-105.

*Shanbaky NM, Emran A, Borowitz JL. 1982. Identification of subcellular organelles involved in Ba^{2+} - and Cd^{2+}-induced adrenomedullary secretion. Toxicol Appl Pharmacol 62:167-171.

*Shankle R, Keane JR. 1988. Acute paralysis from inhaled barium carbonate. Arch Neurol 45:579-580.

Shapiro MA, Hill WH, Rosenberg FA, et al.. 1960. Report on research project at University of Pittsburgh. In: Faber HA, Bryson LJ, eds. Proceedings, conference on physiological aspects of water quality. Vol. 244, Washington, DC: US Public Health Service, 223-231.

Shapiro MA, Hill WH, Chin PK, et al. 1962. Physiological aspects of water quality. Pittsburgh, PA: University of Pittsburgh. RG5309.

*Sharp RA, Knevel AM. 1971. Analysis of barium in barium sulfate and diagnostic meals containing barium sulfate using atomic absorption spectroscopy. J Pharm Sci 60:458-460.

*Shephard TS, ed. 1989. Catalog of teratogenic agents. 6th ed. Baltimore, MD: The Johns Hopkins University Press, 68.

*Shiraishi K, Kawamura H, Tanaka GI. 1987. Determination of alkaline-earth metals in foetus bones by inductively-coupled plasma atomic-emission spectrometry. Talanta 34:823-827.

*Shvydko NS, Il'in LA, Norets TA, et al. 1971. Comparative behavior of Sr^{89} and Ba^{40}in skin following cutaneous application. Gig Sanit 36:386-390.

Silaev AA. 1974. [Functional state of the cardiovascular system in progeny of rats subjected to the action of barium]. Gig Sanit 8:62-64. (Russian)

Silaev AA, Tarasenko N. 1976. [The effect of barium on the generative function and its hygienic significance]. Gig Tr Prof Zabol 7:33-37. (Russian)

Silinsky EM. 1978. On the role of barium in supporting the asynchronous release of acetylcholine quanta by motor nerve impulses. J Physiol 274:157-171.

*Sill CW, Willis CP. 1966. Determination of radioisotopes of cerium. barium, lanthanum, and neptunium after separation by barium sulfate. Anal Chem 38:97-102.

8. REFERENCES

Simmonds RJ, James AM. 1976. An in vivo investigation of barium meals. Cytobios 16:13-21.

*Singer PC. 1974. Chemical processes for the removal of trace metals from drinking water. In: Sapoznik AR, O'Connor JT, eds. Trace metals in water supplies: Occurrence, significance, and control. Urbana, IL: Engineering Publications Office, University of Illinois.

*Sirover MA, Loeb LA. 1976a. Infidelity of DNA synthesis In vitro: Screening for potential metal mutagens or carcinogens. Science 194:1434-1436.

*Sirover MA, Loeb LA. 1976b. Metal-induced infidelity during DNA synthesis. Proc Nat1 Acad Sci 73:2331-2335.

Sittig M. 1976. Barium. Toxic metals: Pollution control and worker protection. Park Ridge, NJ: Noyes Data Corporation, 35-42.

Sittig M. 1979. Hazardous and toxic effects of industrial chemicals. Park Ridge, NJ: Noyes Data Corporation, 51-52.

*Slavicek J. 1972. Effect of Ba^{2+} on contractility of the isolated right rat ventricle. Substitution of NaCl for chlorine of hypertonic sucrose. Physiol Bohemoslov 21:189-199.

Snyder DW, Snoeyink VL, Pfeffer JL. 1986. Weak-acid ion exchange for removing barium, radium, and hardness. Am Water Works Assoc J 78:98-104.

Sollman TH, ed. 1948. A manual of pharmacology and its applications to therapeutics and toxicology. Vol. 7, 7th ed. Philadelphia, PA: W.B. Saunders, 478-479.

Sollman TH, ed. 1957. A manual of pharmacology. 8th ed. Philadelphia, PA: W.B. Saunders Co, 665-667.

*Sommers LE. 1977. Chemical composition of sewage sludges and analysis of their potential use as fertilizers. J Environ Qua1 6:225-232.

*Sara S, Carbone MLA, Pacciatini M, et al. 1986. Disomic and diploid meiotic products induced in Saccharomyces cerevisiae by the salts of 27 elements. Mutagenesis 1:21-28.

*Sowden EM. 1958. Trace elements in human tissue: 3. Strontium and barium in non-skeletal tissue. Biochem J 70:712-7X.

*Sowden EM, Pirie A. 1958. Barium and strontium concentrations in eye tissue. Biochem J 70:716-717.

8. REFERENCES

*Sowden EM, Stitch SR. 1957. Trace elements in human tissue: 2. Estimation of the concentrations of stable strontium and barium in human bone. Biochem J 67:104-109.

*Spencer RP, Lange RC. Treves S. 1971. Use of ^{135}Ba and ^{131}Ba as bone scanning agents. J Nucl Med 12:216-221.

*Spritzer AA, Watson JA. 1964. The measurement of ciliary clearance in the lungs of rats. Health Phys 10:1093-1097.

Srivastava AS, Tripathi RS, Pandya RC, et al. 1971. Investigations on the toxicity of barium carbonate and zinc phosphide to field rats. In: Perti SL, Wal YC, Srivastava CP, eds. International symposium on bionomics and control of rodents. Proceedings and recommendations of the symposium. Kanpur. India: Science and Technology Society, 80-83.

*Stewart DW, Hummel RP. 1984. Acute poisoning by a barium chloride burn. J Trauma 24:768-770.

*Stoewsand GS, Anderson JL, Rutzke M, et al. 1988, Deposition of barium in the skeleton of rats fed Brazil nuts. Nutr Rep Int 38:259-262.

*Stokinger HE. 1981. Barium, Ba. In: Clayton GD, Clayton FE, eds. Patty's industrial hygiene and toxicology. Vol. 2A, 3rd ed. New York, NY: John Wiley and Sons, Inc, 1531-1537.

Stokinger HE, Woodward RL. 1958. Toxicologic methods for establishing drinking water standards. J Am Water Works Assoc 50:515-529.

Stremple J, Montgomery C. 1961. Nonspecific electrocardiographic abnormalities: The EKG during the barium enema procedure. Marquette Med Rev 27:20-24.

*Sugiyama M, Fujino O, Matsui M. 1984. Determination of barium in sea water by graphite furnace atomic absorption spectrometry after preconcentration and separation by solvent extraction. Bunseki Kagaku 33:E123-E129.

Sutton A, Shepherd H. 1973. Urinary barium excretion in man and reduction by alginate. Health Phys 25:182-184.

*Sutton A, Humphreys ER, Shepherd H, et al. 1972. Reduction in the retention of radioactive barium in rats following the addition of sodium alginate derivatives to the diet. Int J Radiat Biol 22:297-300.

*Syed IB, Hosain F. 1972. Determination of LD50 of barium chloride and allied agents. Toxicol Appl Pharmacol 22:150-152.

8. REFERENCES

Syed IB, Hosain F, Mann NS. 1981. G.I. tract excretion of barium. Am J Proctol Gastroenterol Colon Rectal Surg 32:16, 18, 20.

*Tabor EC, Warren WV. 1958. Distribution of certain metals in the atmosphere of some American cities. AMA Arch Ind Health 17:145-151.

*Takahashi S, Patrick G. 1987. Long-term retention of ^{133}Ba in the rat trachea following local administration as barium sulfate particles. Radiat Res 110:321-328.

*Talwar KK, Sharma BK. 1979. Myocardial damage due to barium chloride poisoning, Indian Heart J 31:244-245.

Tarasenko NY, Pronin OA. 1974. [Problems of occupational hygiene and industrial toxicology in the production of barium salts]. Gig Sanit 1:27-30. (Russian)

*Tarasenko NY, Pronin OA, Silaev AA. 1977. Barium compounds as industrial poisons (an experimental study). J Hyg Epidemol Microbial Immunol 21:361-373.

*Tardiff RG, Robinson M, Ulmer NS. 1980. Subchronic oral toxicity of $BaCl_2$ in rats. J Environ Pathol Toxicol 4:267-275.

*Taylor DM, Bligh PH, Duggan MH. 1962. The absorption of calcium, strontium, barium and radium from the gastrointestinal tract of the rat. Biochem J 83:25-29.

Thomas RG, Ewing WC, Catron DL, et al. 1973. In vivo solubility of four forms of barium determined by scanning techniques. Amer Ind Hyg Ass J 34:350-359.

Tipton IH, Schroeder HA, Perry HM, et al. 1965. Trace elements in human tissues: Part III. Subjects from Africa, the Near and Far East and Europe. Health Phys 11:403-451.

*Tipton IH, Stewart PL, Martin PG. 1966. Trace elements in diets and excreta. Health Phys 12:1683-1689.

*Tipton IH, Stewart FL, Dickson J. 1969. Patterns of elemental excretion in long term balance studies. Health Phys 16:455-462.

*Toda N. 1970. Barium-induced automaticity in relation to the calcium ions and norepinephrine in the rabbit left atrium. Circ Res 27:45-57.

*TRI. 1989. Toxic Chemical Release Inventory (database). US Environmental Protection Agency, Office of Toxic Substances, Washington, DC.

8. REFERENCES

*Tuovinen OH, Button KS, Vuorinen CL, et al. 1980. Bacterial, chemical, and mineralogical characteristics of tubercles in distribution pipelines. J Am Water Works Assoc 72:626-635.

Underwood EJ. 1971. Trace elements in human and animal nutrition. In: 3rd ed. New York, NY: Academic Press, 375-376.

*Van Duuren BL, Sivak A, Langseth L, et al. 1968. Initiators and promoters in tobacco carcinogenesis. World Conference on smoking and health: Toward a less harmful cigarette. National Cancer Institute Monograph No. 28 173-180.

Venier P, Montaldi A, Gava C, et al. 1985. Effects of nitrilo acetic acid on the induction of gene and mutations and sister-chromatid exchanges by insoluble chromium compounds. Mutat Res 156:219.

*Venugopal B, Luckey TD. 1978. Metal toxicity in mammals. 2nd ed. New York, NY: Plenum Press, 63-67.

*VIEW Database. 1989. Agency for Toxic Substances and Disease Registry (ATSDR), Office of External Affairs, Exposure and Disease Registry Branch, Atlanta, GA. September 25, 1989.

Volf V, Roth Z. 1966a. Retention of strontium 85 in rats: II. Effect of various barium sulfate preparations as influenced by soluble sulfates, carrier strontium, and by the physiologic state of animals. Acta Radio1 Ther Phys Biol 4:113-128.

Volf V, Roth Z. 1966b. Retention of strontium 85 in rats: III. Effect of increasing the doses of sodium and barium sulfates and role of the time factor. Acta Radio1 Ther Phys Biol 4:481-493.

*Volkl H, Greger R, Lang F. 1987. Potassium conductance in straight proximal tubule cells of the mouse, Effect of barium, verapamil and quinidine. Biochim Biophys Acta 900:275-281.

Walker L, Necheles H. 1956. Inhibition by barbiturates of barium-stimulated intestinal motility. Am Ind Hyg Assoc J 185:624-626.

*Walz W, Shargool M, Hertz L. 1984. Barium-induced inhibition of K^+ transport mechanisms in cortical astrocytes- -its possible contribution to the large Ba^{2+} -evoked extracellular K^+ signal in brain. Neuroscience 13:945-949.

*Weast RC, ed. 1974. CRC handbook of chemistry and physics. 53rd ed. Cleveland, OH: Chemical Rubber Co.

*Weast RC, ed. 1989. CRC handbook of chemistry and physics. 70th ed. Boca Raton, Florida: CRC Press, Inc, B.73-B.75.

8. REFERENCES

Weiss G, ed. 1986. Hazardous chemicals data book. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 144; 146.

*Welch SP, Vocci FJ, Dewey WL. 1983. Antinociceptive and lethal effects of intraventricularly administered barium and strontium: Antagonism by atropine sulfate or naloxone hydrochloride. Life Sci 33:359-364.

*Wetherill SF, Guarino MJ, Cox RW. 1981. Acute renal failure associated with barium chloride poisoning. Ann Intern Med 95:187-188.

*Windho M, ed. 1976. The Merck index. 9th ed. Rahway, NJ: Merck & Co, Inc., 127-131.

*Windholz M, ed. 1983. The Merck index. 10th ed. Rahway, NJ: Merck & Co, Inc., 965-993.

*Wanes RG, Stadler BL, Frohman LA. 1990. Lack of effect of drinking water barium on cardiovascular risk factors. Environ Health Perspect 85:355-359.

*Worthing CR, ed. 1987 . The pesticide manual: A world compendium. 8th ed. Thornton Heath, UK: The British Crop Protection Council, 857.

Yagoda H. 1944. The determination of barium in atmospheric dusts. J Ind Hyg Toxicol 26:224-231.

Yamamoto J, Sekiya A, Maekawa H, et al. 1979. Influence of propranolol on the $BaCl^{2}$ toxicity [abstract). Jpn J Pharmacol 29:132P.

*Yamamura M, Nishi M, Furubayashi H, et al. 1985. Barium peritonitis: Report of a case and review of the literature. Dis Colon Rectum 28:347-352.

Young RW, Furr AK, Stoewsand GS, et al. 1978. Lead and other elements in tissues of guinea pigs fed crown vetch grown adjacent to a highway. Cornell Vet 68:521-529.

Zdanowicz JA, Featherstone JDB, Espeland MA, et al. 1987. Inhibitory effect of barium on human caries prevalence. Commun Dent Oral Epidemiol 15:6-g.

9. GLOSSARY

Acute Exposure -- Exposure to a chemical for a duration of lb days or less. as specified in the Toxicological Profiles.

Adsorption Coefficient (K_{oc}) -- The ratio of the amount of a chemical adsorbed per unit weight of organic carbon in the soil or sediment to the concentration of the chemical in solution at equilibrium.

Adsorption Ratio (Kd) -- The amount of a chemical adsorbed by a sediment or soil (i.e., the solid phase) divided by the amount of chemical in the solution phase, which is in equilibrium with the solid phase, at a fixed solid/solution ratio. It is generally expressed in micrograms of chemical sorbed per gram of soil or sediment.

Bioconcentration Factor (BCF) -- The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same period.

Cancer Effect Level (CEL) -- The lowest dose of chemical in a study, or group of studies, that produces significant increases in the incidence of cancer (or tumors) between the exposed population and *its* appropriate control.

Carcinogen -- A chemical capable of inducing cancer.

Ceiling Value -- A concentration of a substance that should not be exceeded, even instantaneously.

Chronic Exposure -- Exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Developmental Toxicity -- The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

Embryotoxicity and Fetotoxicity -- Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the insult occurred. The terms, as used here, include malformations and variations, altered growth, and in utero death.

EPA Health Advisory -- An estimate of acceptable drinking water levels for a chemical substance based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

9. GLOSSARY

Immediately Dangerous to Life or Health (IDLH) -- The maximum environmental concentration of a contaminant from which one could escape within 30 min without any escape-impairing symptoms or irreversible health effects.

Intermediate Exposure -- Exposure to a chemical for a duration of 15-364 days as specified in the Toxicological Profiles.

Immunologic Toxicity -- The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

In vitro -- Isolated from the living organism and artificially maintained, as in a test tube.

In Vivo -- Occurring within the living organism.

Lethal Concentration$_{(LO)}$ (LC$_{LO}$) -- The lowest concentration of a chemical in air which has been reported to have caused death in humans or animals.

Lethal Concentration$_{(50)}$ (LC$_{50}$) -- A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in50% of a defined experimental animal population.

Lethal Dose($_{LO}$) (LD$_{50}$) -- The lowest dose of a chemical introduced by a route other than inhalation that is expected to have caused death in humans or animals.

Lethal Dose($_{50}$) (LD$_{50}$) -- The dose of a chemical which has been calculated to cause death in 50% of a defined experimental animal population.

Lethal Time$_{(50)}$ (LT$_{50}$) -- A calculated period of time within which a specific concentration of a chemical is expected to cause death in 50% of a defined experimental animal population.

Lowest-Observed-Adverse-Effect Level (LOAEL) -- The lowest dose of chemical in a study, or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Malformations -- Permanent structural changes that may adversely affect survival, development, or function.

Minimal Risk Level -- An estimate of daily human exposure to a chemical that is likely to be without an appreciable risk of deleterious effects (noncancerous) over a specified duration of exposure.

9. GLOSSARY

Mutagen -- A substance that causes mutations. A mutation is a change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

Neurotoxicity -- The occurrence of adverse effects on the nervous system following exposure to chemical.

No-Observed-Adverse-Effect Level (NOAEL) -- The dose of chemical at which there were no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

Octanol-Water Partition Coefficient (K_{ow}) -- The equilibrium ratio of the concentrations of a chemical in n-octanol and water, in dilute solution.

Permissible Exposure Limit (PEL) -- An allowable exposure level in workplace air averaged over an 8-hour shift.

q_1* -- The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The q_1* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually pg/L for water, mg/kg/day for food, and $\mu g/m^3$ for air).

Reference Dose (RfD) -- An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RFD is operationally derived from the NOAEL (from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

Reportable Quantity (RQ) -- The quantity of a hazardous substance that is considered reportable under CERCLA. Reportable quantities are (1) 1 lb or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Sect. 311 of the Clean Water Act. Quantities are measured over a 24-hour period.

Reproductive Toxicity -- The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/,or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

9. GLOSSARY

Short-Term Exposure Limit (STEL) -- The maximum concentration to which workers can be exposed for up to 15 min continually, No more than four excursions are allowed per day, and there must be at least 60 min between exposure periods. The daily TLV-TWA may not be exceeded.

Target Organ Toxicity -- This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

Teratogen -- A chemical that causes structural defects that affect the development of an organism.

Threshold Limit Value (TLV) -- A concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a TWA, as a STEL, or as a CL.

Time-Weighted Average (TWA) -- An allowable exposure concentration averaged over a normal a-hour workday or 40-hour workweek.

Toxic Dose (TD_{50}) -- A calculated dose of a chemical, introduced by a route other than inhalation, which is expected to cause a specific toxic effect in 50% of a defined experimental animal population.

Uncertainty Factor (UPI --from experimental data. A factor used in operationally deriving the RfD UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of human, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10.

APPENDIX A

USER'S GUIDE

Chapter 1

Public Health Statement

This chapter of the profile is a health effects summary written in nontechnical language. Its intended audience is the general public especially people living in the vicinity of a hazardous waste site or substance release. If the Public Health Statement were removed from the rest of the document, it would still communicate to the lay public essential information about the substance.

The major headings in the Public Health Statement are useful to find specific topics of concern. The topics are written in a question and answer format. The answer to each question includes a sentence that will direct the reader to chapters in the profile that will provide more information on the given topic.

Chapter 2

Tables and Figures for Levels of Significant Exposure (LSE)

Tables (2-1, 2-2, and 2-3) and figures (2-1 and 2-2) are used to summarize health effects by duration of exposure and endpoint and to illustrate graphically levels of exposure associated with those effects. All entries in these tables and figures represent studies that provide reliable, quantitative estimates of No-Observed-Adverse-Effect Levels (NOAELs), Lowest-Observed- Adverse-Effect Levels (LOAELS) for Less Serious and Serious health effects, or Cancer Effect Levels (CELs). In addition, these tables and figures illustrate differences in response by species, Minimal Risk Levels (MRLs) to humans for noncancer end points, and EPA's estimated range associated with an upper-bound individual lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. The LSE tables and figures can be used for a quick review of the health effects and to locate data for a specific exposure scenario. The LSE tables and figures should always be used in conjunction with the text.

The legends presented below demonstrate the application of these tables and figures. A representative example of LSE Table 2-1 and Figure 2-1 are shown. The numbers in the left column of the legends correspond to the numbers in the example table and figure.

LEGEND

See LSE Table 2-1

(1). Route of Exposure One of the first considerations when reviewing the toxicity of a substance using these tables and figures should be the relevant and appropriate route of exposure. When sufficient data exist,

three LSE tables and two LSE figures are presented in the document. The three LSE tables present data on the three principal routes of exposure, i.e., inhalation, oral, and dermal (LSE Table 2-1, 2-2, and 2-3, respectively). LSE figures are limited to the inhalation (LSE Figure 2-1) and oral (LSE Figure 2-2) routes.

(2). Exposure Duration Three exposure periods: acute (14 days or less); intermediate (15 to 364 days); and chronic (365 days or more) are presented within each route of exposure. In this example, an inhalation study of intermediate duration exposure is reported.

(3). Health Effect The major categories of health effects included in LSE tables and figures are death, systemic, immunological, neurological, developmental, reproductive, and cancer. NOAELs and LOAELs can be reported in the tables and figures for all effects but cancer. Systemic effects are further defined in the "System" column of the LSE table.

(4). Key to Figure Each key number in the LSE table links study information to one or more data points using the same key number in the corresponding LSE figure. In this example, the study represented by key number 18 has been used to define a NOAEL and a Less Serious LOAEL (also see the two "18r" data points in Figure 2-1).

(5). Species The test species, whether animal or human, are identified in this column.

(6). Exposure Freouency/Duration The duration of the study and the weekly and daily exposure regimen are provided in this column. This permits comparison of NOAELs and LOAELs from different studies. In this case (key number 18), rats were exposed to [substance x] via inhalation for 13 weeks, 5 days per week, for 6 hours per day.

(7). System This column further defines the systemic effects. These systems include: respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, and dermal/ocular. "Other" refers to any systemic effect (e.g., a decrease in body weight) not covered in these systems. In the example of key number 18, one systemic effect (respiratory) was investigated in this study.

(8). NOAEL A No-Observed-Adverse-Effect Level (NOAEL) is the highest exposure level at which no harmful effects were seen in the organ system studied. Key number 18 reports a NOAEL of 3 ppm for the respiratory system which was used to derive an intermediate exposure, inhalation MKL of 0.005 ppm (see footnote 'c").

(9). LOAEL A Lowest-Observed-Adverse-Effect Level (LOAEL) is the lowest exposure level used in the study that caused a harmful health effect. LOAELs have been classified into "Less Serious" and "Serious" effects. These distinctions help readers identify the levels of exposure at which adverse health effects first appear and the gradation of effects with ncreasing dose. A brief description of the specific end point used to

quantify the adverse effect accompanies the LOAEL. The “Less Serious" respiratory effect reported in key number 18 (hyperplasia) occurred at a LOAEL of 10 ppm.

(10). Reference The complete reference citation is given in Chapter 8 of the profile.

(11). CEL A Cancer Effect Level (CEL) is the lowest exposure level associated with the onset of carcinogenesis in experimental or epidemiological studies. CELs are always considered serious effects. The LSE tables and figures do not contain NOAELs for cancer, but the text may report doses which did not cause a measurable increase in cancer.

(12). Footnotes Explanations of abbreviations or reference notes for data in the LSE tables are found in the footnotes. Footnote "c" indicates the NOAEL of 3 ppm in key number 18 was used to derive an MRL of 0.005 ppm.

LEGEND

See LSE Figure 2-1

LSE figures graphically illustrate the data presented in the corresponding LSE tables. Figures help the reader quickly compare health effects according to exposure levels for particular exposure duration.

(13). Exposure Duration The same exposure periods appear as in the LSE table. In this example, health effects observed within the intermediate and chronic exposure periods are illustrated.

(14). Health Effect These are the categories of health effects for which reliable quantitative data exist. The same health effects appear in the LSE table.

(15). Levels of Exposure Exposure levels for each health effect in the LSE tables are graphically displayed in the LSE figures. Exposure levels are reported on the log scale "y" axis. Inhalation exposure is reported in mg/m^3 or ppm and oral exposure is reported in mg/kg/day.

(16). NOAEL In this example, 18r NOAEL is the critical end point for which an intermediate inhalation exposure MRL is based. As you can see from the LSE figure key, the open-cir,cle symbol indicates a NOAEL for the test species (rat). The key number 18 corresponds to the entry in the LSE table. The dashed descending arrow indicates the extrapolation from the exposure level of 3 ppm (see entry 18 in the Table) to the MRL of 0.005 ppm (see footnote "b" in the LSE table).

(17). CEL Key number 38r is one of three studies for which Cancer Effect Levels (CELs) were derived. The diamond symbol refers to a CEL for the test species (rat). The number 38 corresponds to the entry in the LSE table.

(18). Estimated Upper-Bound Human Cancer Risk Levels This is the range associated with the upper-bound for lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. These risk levels are derived from EPA's Human Health Assessment Group's upper-bound estimates of the slope of the cancer dose response curve at low dose levels (q_1^*).

(19). Key to LSE Figure The Key explains the abbreviations and symbols used in the figure.

SAMPLE

1 → TABLE 2-1. Levels of Significant Exposure to [Chemical x] - Inhalation

Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect) Less serious (ppm)	LOAEL (effect) Serious (ppm)	Reference
2 → INTERMEDIATE EXPOSURE							
3 → Systemic	5	6	7	8	9		10
4 → 18	Rat	13 wk 5d/wk 6hr/d	Resp	3[b]	10 (hyperplasia)		Nitschke et al. 1981
CHRONIC EXPOSURE							
Cancer						11	
38	Rat	18 mo 5d/wk 7hr/d				20 (CEL, multiple organs)	Wong et al. 1982
39	Rat	89-104 wk 5d/wk 6hr/d				10 (CEL, lung tumors, nasal tumors)	NTP 1982
40	Mouse	79-103 wk 5d/wk 6hr/d				10 (CEL, lung tumors, hemangiosarcomas)	NTP 1982

[a] The number corresponds to entries in Figure 2-1.

12 → [b] Used to derive an intermediate inhalation Minimal Risk Level (MRL) of 5 x 10^{-3} ppm; dose adjusted for intermittent exposure and divided by an uncertainty factor of 100 (10 for extrapolation from animal to humans, 10 for human variability).

CEL = cancer effect level; d = day(s); hr = hour(s); LOAEL = lowest-observed-adverse-effect level; mo = month(s); NOAEL = no-observed-adverse-effect level; Resp = respiratory; wk = week(s)

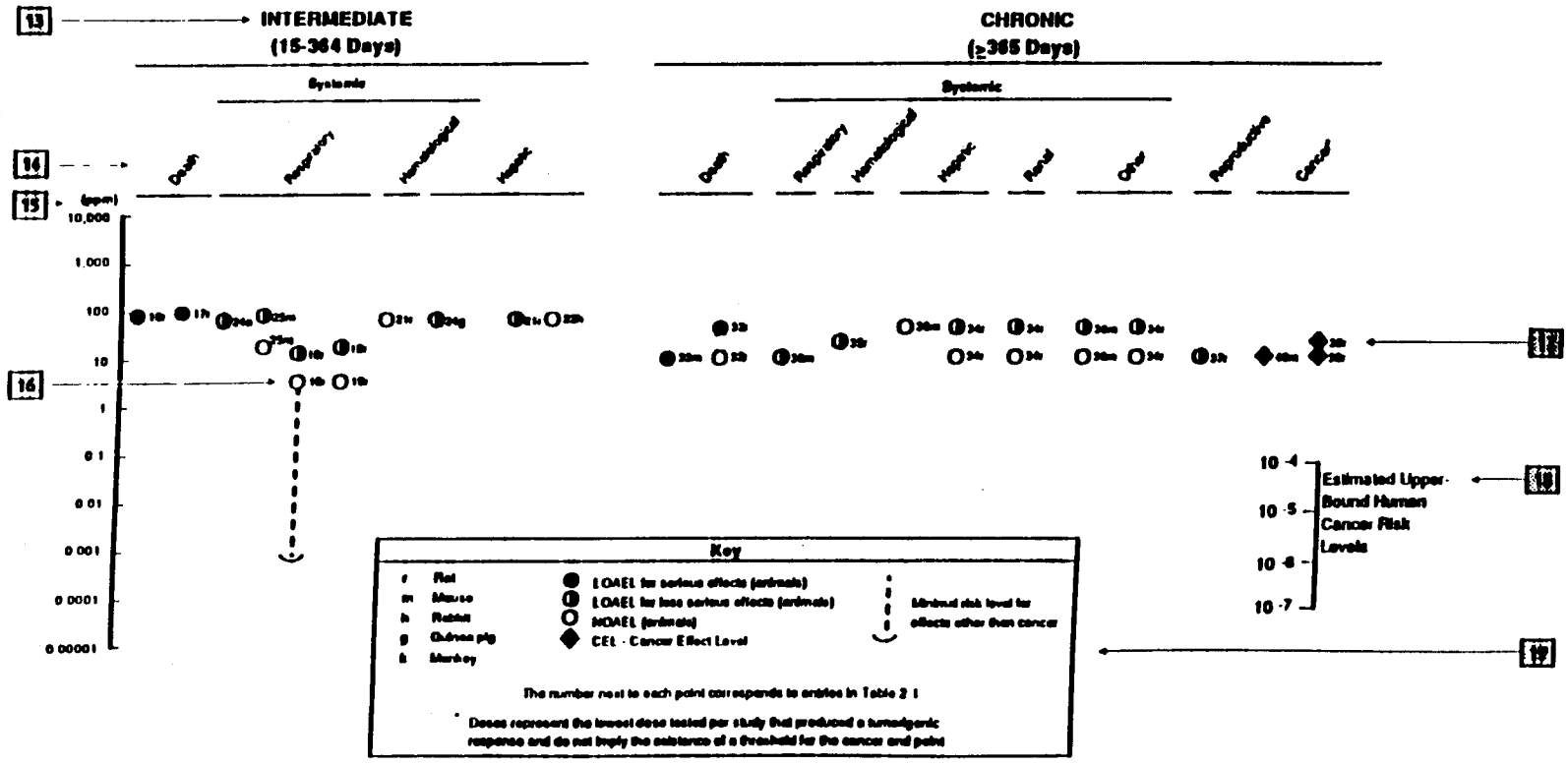


FIGURE 2-1. Levels of Significant Exposure to [Chemical X]-Inhalation

APPENDIX A

Chapter 2 (Section 2.4)

Relevance to Public Health

The Relevance to Public Health section provides a health effects summary based on evaluations of existing toxicological, epidemiological, and toxicokinetic information. This summary is designed to present interpretive, weight-of-evidence discussions for human health end points by addressing the following questions.

1. What effects are known to occur in humans?

2 What effects observed in animals are likely to be of concern to humans?

3. What exposure conditions are likely to be of concern to humans, especially around hazardous waste sites?

The section discusses health effects by end point. Human data are presented first, then animal data. Both are organized by route of exposure (inhalation, oral, and dermal) and by duration (acute, intermediate, and chronic). In vitro data and data from parenteral routes (intramuscular, intravenous, subcutaneous, etc.) are also considered in this section. If data are located in the scientific literature, a table of genotoxicity information is included.

The carcinogenic potential of the profiled substance is qualitatively evaluated, when appropriate, using existingtoxicokinetic, genotoxic, andcarcinogenic data. ATSDR does not currently assess cancer potency or perform cancer risk assessments. MRLs for noncancer end points if derived, and the end points from which they were derived are indicated and discussed in the appropriate section(s).

Limitations to existing scientific literature that prevent a satisfactory evaluation of the relevance to public health are identified in the Identification of Data Needs section.

Interpretation of Minimal Risk Levels

Where sufficient toxicologic information was available, MRLs were derived. MRLs are specific for route (inhalation or oral) and duration (acute, intermediate, or chronic) of exposure. Ideally, MRLs can be derived from all six exposure scenarios (e.g., Inhalation - acute, -intermediate, -chronic; Oral - acute, -intermediate, - chronic). These MRLs are not meant to support regulatory action, but to aquaint health professionals with exposure levels at which adverse health effects are not expected to occur in humans. They should help physicians and public health officials determine the safety of a community living near a substance emission, given the concentration of a contaminant in air or the estimated daily dose received via food or water. MRLs are based largely on toxicological studies in animals and on reports of human occupational exposure.

APPENDIX A

MRL users should be familiar with the toxicological information on which the number is based, Section 2.4, "Relevance to Public Health," contains basic information known about the substance. Other sections such as 2.6, "Interactions with Other Chemicals" and 2.7, "Populations that are Unusually Susceptible" provide important supplemental information.

MRL users should also understand the MRL derivation methodology. MRLs are derived using a modified version of the risk assessment methodology used by the Environmental Protection Agency (EPA) (Barnes and Dourson, 1988; EPA 1989a) to derive reference doses (RfDs) for lifetime exposure.

To derive an MRL, ATSDR generally selects the end point which, in its best judgement, represents the most sensitive human health effect for a given exposure route and duration. ATSDR cannot make this judgement or derive an MRL unless information (quantitative or qualitative) is available for all potential effects (e.g., systemic, neurological, and developmental). In order to compare NOAELs and LOAELs for specific end points, all inhalation exposure levels are adjusted for 24hr exposures and all intermittent exposures for inhalation and oral routes of intermediate and chronic duration are adjusted for continous exposure (i.e., 7 days/week). If the information and reliable quantitative data on the chosen end point are available, ATSDR derives an MRL using the most sensitive species (when information frommultiple species is available) with the highest NOAEL that does not exceed any adverse effect levels. The NOAEL is the most suitable end point for deriving an MRL. When a NOAEL is not available, a Less Serious LOAEL can be used to derive an MRL, and an uncertainty factor (UF) of 10 is employed. MRLs are not derived from Serious LOAELs. Additional uncertainty factors of 10 each are used for human variability to protect sensitive subpopulations (people who are most susceptible to the health effects caused by the substance) and for interspecies variability (extrapolation from animals to humans). In deriving an MRL, these individual uncertainty factors are multiplied together. The product is then divided into the adjusted inhalation concentration or oral dosage selected from the study. Uncertainty factors used in developing a substance-specific MRL are provided in the footnotes of the LSE Tables.

APPENDIX B

ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
ADME	Absorption, Distribution, Metabolism, and Excretion
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
BSC	Board of Scientific Counselors
CDC	Centers for Disease Control
CEL	Cancer Effect Level
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
CLP	Contract Laboratory Program
cm	centimeter
CNS	central nervous system
DHEW	Department of Health, Education, and Welfare
DHHS	Department of Health and Human Services
DOL	Department of Labor
ECG	electrocardiogram
EEG	electroencephalogram
EPA	Environmental Protection Agency
EKG	see ECG
FAO	Food and Agricultural Organization of the United Nations
FEMA	Federal Emergency Management Agency
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
f_1	first generation
fpm	feet per minute
ft	foot
FR	Federal Register
g	gram
GC	gas chromatography
HPLC	high performance liquid chromatography
hr	hour
IDLH	Immediately Dangerous to Life and Health
IARC	International Agency for Research on Cancer
ILO	International Labor Organization
in	inch
Kd	adsorption ratio
kg	kilogram
Koc	octanol-soil partition coefficient
Kow	octanol-water partition coefficient
L	liter
LC	liquid chromatography
LC_{Lo}	lethal concentration low
LC_{50}	lethal concentration 50 percent kill
LD_{Lo}	lethal dose low
LD_{50}	lethal dose 50 percent kill

APPENDIX B

LOAEL	lowest-observed-adverse-effect level
LSE	Levels of Significant Exposure
m	meter
mg	milligram
min	minute
mL	milliliter
mm	millimeters
mmol	millimole
mppcf	millions of particles per cubic foot
MRL	Minimal Risk Level
MS	mass spectroscopy
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute for Occupational Safety and Health
NIOSHTIC	NIOSH's Computerized Information Retrieval System
nm	nanometer
ng	nanogram
NHANES	National Health and Nutrition Examination Survey
nmol	nanomole
NOAEL	no-observed-adverse-effect level
NOES	National Occupational Exposure Survey
NOHS	National Occupational Hazard Survey
NPL	National Priorities List
NRC	National Research Council
NTIS	National Technical Information Service
NTP	National Toxicology Program
OSHA	Occupational Safety and Health Administration
PEL	permissible exposure limit
pg	picogram
pmol	picomole
PHS	Public Health Service
PMR	proportional mortality ratio
ppb	parts per billion
pph	parts per hundred
ppm	parts per million
ppt	parts per trillion
REL	recommended exposure limit
RfD	Reference Dose
RTECS	Registry of Toxic Effects of Chemical Substances
sec	second
SCE	sister chromatid exchange
SIC	Standard Industrial Classification
SMR	standard mortality ratio
STEL	short-term exposure limit
STORET	STORAGE and RETRIEVAL
TLV	threshold limit value
TSCA	Toxic Substances Control Act
TRI	Toxics Release Inventory
TWA	time-weighted average

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U.S.	United States
UF	uncertainty factor
WHO	World Health Organization
>	greater than
≥	greater than or equal to
=	equal to
<	less than
≤	less than or equal to
%	percent
α	alpha
β	beta
δ	delta
γ	gamma
μm	micron
μg	microgram

APPENDIX C

PEER REVIEW

A peer review panel was assembled for barium. The panel consisted df the following members: Dr. Joseph Borowitz, Professor of Pathology, Department of Pharmacology and Toxicology, School of Pharmacy, Purdue University, Lafayette, Indiana; Dr. Joseph Gould, Research Scientist, School of Civil Engineering, Georgia Institute of Technology, Atlanta, Georgia; and Dr. Andrew Reeves, Professor, Occupational and Environmental Health, Wayne State University, Detroit, Michigan. These experts collectively have knowledge of barium's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in the Comprehensive Environmental Response, Compensation, and Liability Act of 1986, Section 104.

A joint panel of scientists from the Agency for Toxic Substances and Disease Registry (ATSDR) and the Environmental Protection Agency has reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply its approval of the profile's final content. The responsibility for the content of this profile lies with the ATSDR.

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