TOXICOLOGICAL PROFILE FOR STRONTIUM

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry

April 2004

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.

UPDATE STATEMENT

A Toxicological Profile for strontium, Draft for Public Comment was released in July 2001. This edition supersedes any previously released draft or final profile.

Toxicological profiles are revised and republished as necessary. For information regarding the update status of previously released profiles, contact ATSDR at:

Agency for Toxic Substances and Disease Registry
Division of Toxicology/Toxicology Information Branch
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FOREWORD

This toxicological profile is prepared in accordance with guidelines* developed by the Agency for Toxic Substances and Disease Registry (ATSDR) and the Environmental Protection Agency (EPA). The original guidelines were published in the *Federal Register* on April 17, 1987. Each profile will be revised and republished as necessary.

The ATSDR toxicological profile succinctly characterizes the toxicologic and adverse health effects information for the hazardous substance described therein. Each peer-reviewed profile identifies and reviews the key literature that describes a hazardous substance's toxicologic properties. Other pertinent literature is also presented, but is 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.

The focus of the profiles is on health and toxicologic information; therefore, each toxicological profile begins with a public health statement that 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 are identified by ATSDR and EPA.

Each profile includes the following:

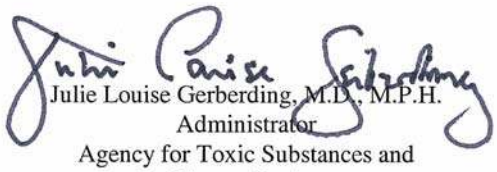
(A) The examination, summary, and interpretation of available toxicologic information and epidemiologic evaluations on a hazardous substance to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects;

(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 that present a significant risk to human health of acute, subacute, and chronic health effects; and

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

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 ATSDR's assessment of all relevant toxicologic testing and information that has been peer-reviewed. Staff of the Centers for Disease Control and Prevention and other Federal scientists have also reviewed the profile. In addition, this profile has been peer-reviewed by a nongovernmental panel and was made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.



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Background Information

The toxicological profiles are developed by ATSDR pursuant to Section 104(i) (3) and (5) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund) for hazardous substances found at Department of Energy (DOE) waste sites. CERCLA directs ATSDR to prepare toxicological profiles for hazardous substances most commonly found at facilities on the CERCLA National Priorities List (NPL) and that pose the most significant potential threat to human health, as determined by ATSDR and the EPA. ATSDR and DOE entered into a Memorandum of Understanding on November 4, 1992 which provided that ATSDR would prepare toxicological profiles for hazardous substances based upon ATSDR's or DOE's identification of need. The current ATSDR priority list of hazardous substances at DOE NPL sites was announced in the Federal Register on July 24, 1996 (61 FR 38451).

QUICK REFERENCE FOR HEALTH CARE PROVIDERS

Toxicological Profiles are a unique compilation of toxicological information on a given hazardous substance. Each profile reflects a comprehensive and extensive evaluation, summary, and interpretation of available toxicologic and epidemiologic information on a substance. Health care providers treating patients potentially exposed to hazardous substances will find the following information helpful for fast answers to often-asked questions.

Primary Chapters/Sections of Interest

Chapter 1: Public Health Statement: The Public Health Statement can be a useful tool for educating patients about possible exposure to a hazardous substance. It explains a substance's relevant toxicologic properties in a nontechnical, question-and-answer format, and it includes a review of the general health effects observed following exposure.

Chapter 2: Relevance to Public Health: The Relevance to Public Health Section evaluates, interprets, and assesses the significance of toxicity data to human health.

Chapter 3: Health Effects: Specific health effects of a given hazardous compound are reported by type of health effect (death, systemic, immunologic, reproductive), by route of exposure, and by length of exposure (acute, intermediate, and chronic). In addition, both human and animal studies are reported in this section.

NOTE: Not all health effects reported in this section are necessarily observed in the clinical setting. Please refer to the Public Health Statement to identify general health effects observed following exposure.

Pediatrics: Four new sections have been added to each Toxicological Profile to address child health issues:

Section 1.6 How Can (Chemical X) Affect Children?
Section 1.7 How Can Families Reduce the Risk of Exposure to (Chemical X)?
Section 3.7 Children's Susceptibility
Section 6.6 Exposures of Children

Other Sections of Interest:

Section 3.9 Biomarkers of Exposure and Effect
Section 3.12 Methods for Reducing Toxic Effects

ATSDR Information Center

Phone: 1-888-42-ATSDR or (404) 498-0110 ***Fax:*** (770) 488-4178
E-mail: atsdric@cdc.gov ***Internet***: http://www.atsdr.cdc.gov

The following additional material can be ordered through the ATSDR Information Center:

Case Studies in Environmental Medicine: Taking an Exposure History—The importance of taking an exposure history and how to conduct one are described, and an example of a thorough exposure history is provided. Other case studies of interest include *Reproductive and Developmental Hazards; Skin Lesions and Environmental Exposures; Cholinesterase-Inhibiting Pesticide Toxicity*; and numerous chemical-specific case studies.

Managing Hazardous Materials Incidents is a three-volume set of recommendations for on-scene (prehospital) and hospital medical management of patients exposed during a hazardous materials incident. Volumes I and II are planning guides to assist first responders and hospital emergency department personnel in planning for incidents that involve hazardous materials. Volume III—*Medical Management Guidelines for Acute Chemical Exposure*s—is a guide for health care professionals treating patients exposed to hazardous materials.

Fact Sheets (ToxFAQs) provide answers to frequently asked questions about toxic substances.

Other Agencies and Organizations

The National Center for Environmental Health (NCEH) focuses on preventing or controlling disease, injury, and disability related to the interactions between people and their environment outside the workplace. Contact: NCEH, Mailstop F-29, 4770 Buford Highway, NE, Atlanta, GA 30341-3724 • Phone: 770-488-7000 • FAX: 770-488-7015.

The National Institute for Occupational Safety and Health (NIOSH) conducts research on occupational diseases and injuries, responds to requests for assistance by investigating problems of health and safety in the workplace, recommends standards to the Occupational Safety and Health Administration (OSHA) and the Mine Safety and Health Administration (MSHA), and trains professionals in occupational safety and health. Contact: NIOSH, 200 Independence Avenue, SW, Washington, DC 20201 • Phone: 800-356-4674 or NIOSH Technical Information Branch, Robert A. Taft Laboratory, Mailstop C-19, 4676 Columbia Parkway, Cincinnati, OH 45226-1998 • Phone: 800-35-NIOSH.

The National Institute of Environmental Health Sciences (NIEHS) is the principal federal agency for biomedical research on the effects of chemical, physical, and biologic environmental agents on human health and well-being. Contact: NIEHS, PO Box 12233, 104 T.W. Alexander Drive, Research Triangle Park, NC 27709 • Phone: 919-541-3212.

Radiation Emergency Assistance Center/Training Site (REAC/TS) provides support to the U.S. Department of Energy, the World Health Organization, and the International Atomic Energy Agency in the medical management of radiation accidents. A 24-hour emergency response program at the Oak Ridge Institute for Science and Education (ORISE), REAC/TS trains, consults, or assists in the response to all kinds of radiation accidents. Contact: Oak Ridge Institute for Science and Education, REAC/TS, PO Box 117, MS 39, Oak Ridge, TN 37831-0117 • Phone 865-576-3131 • FAX 865-576-9522 • 24-Hour Emergency Phone 865-576-1005 (ask for REAC/TS) • e-mail: cooleyp@orau.gov • website (including emergency medical guidance): http://www.orau.gov/reacts/default.htm

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Referrals

The Association of Occupational and Environmental Clinics (AOEC) has developed a network of clinics in the United States to provide expertise in occupational and environmental issues. Contact: AOEC, 1010 Vermont Avenue, NW, #513, Washington, DC 20005 • Phone: 202-347-4976 • FAX: 202-347-4950 • e-mail: AOEC@AOEC.ORG • Web Page: http://www.aoec.org/.

The American College of Occupational and Environmental Medicine (ACOEM) is an association of physicians and other health care providers specializing in the field of occupational and environmental medicine. Contact: ACOEM, 55 West Seegers Road, Arlington Heights, IL 60005 • Phone: 847-818-1800 • FAX: 847-818-9266.

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THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:

1. Health Effects Review. The Health Effects Review Committee examines the health effects chapter of each profile for consistency and accuracy in interpreting health effects and classifying end points.

2. Minimal Risk Level Review. The Minimal Risk Level Workgroup considers issues relevant to substance-specific Minimal Risk Levels (MRLs), reviews the health effects database of each profile, and makes recommendations for derivation of MRLs.

3. Data Needs Review. The Research Implementation Branch reviews data needs sections to assure consistency across profiles and adherence to instructions in the Guidance.

PEER REVIEW

A peer review panel was assembled for strontium. The panel consisted of the following members:

1. Adele L. Boskey, Ph.D., Professor of Biochemistry, Starr Chair in Mineralized Tissues, Hospital for Special Surgery, Weill Medical College of Cornell University, New York, New York,

2. Marvin Goldman, Ph.D., Emeritus Professor of Radiation Biology, Department of Surgical and Radiological Sciences, University of California, Davis, California,

3. Richard Leggett, Ph.D., Life Sciences Division, Oak Ridge National Laboratory, Knoxville, Tennessee, and

4. Bruce Muggenburg, D.V.M., Ph.D., Senior Scientist and Veterinary Physiologist, Toxicology Division, Lovelace Respiratory Research Institute, Albuquerque, New Mexico.

These experts collectively have knowledge of strontium'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 Section 104(I)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended.

Scientists from the Agency for Toxic Substances and Disease Registry (ATSDR) have 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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1. PUBLIC HEALTH STATEMENT

This public health statement tells you about strontium and the effects of exposure.

The Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites make up the National Priorities List (NPL) and are the sites targeted for long-term federal cleanup activities. Strontium and strontium-90 have been found in at least 102 and 12 of the 1,636 current or former NPL sites, respectively. However, the total number of NPL sites evaluated for strontium and strontium-90 are not known. As more sites are evaluated, the sites at which strontium and strontium-90 are found may increase. This information is important because exposure to strontium and strontium-90 may harm you and because these sites may be sources of exposure.

When a substance 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. This release does not always lead to exposure. You are exposed to a substance only when you come in contact with it. You may be exposed by breathing, eating, or drinking the substance, or by skin contact. External exposure to radiation may occur from natural or man-made sources. Naturally occurring sources of radiation are cosmic radiation from space or radioactive materials in soil or building materials. Man-made sources of radioactive materials are found in consumer products, industrial equipment, atom bomb fallout, and to a smaller extent from hospital waste and nuclear reactors.

If you are exposed to strontium, many factors determine whether you'll be harmed. These factors include the dose (how much), the duration (how long), and how you come in contact with it. You must also consider the other chemicals you're exposed to and your age, sex, diet, family traits, lifestyle, and state of health.

1.1 WHAT IS STRONTIUM?

Strontium is a natural and commonly occurring element. Strontium can exist in two oxidation states: 0 and +2. Under normal environmental conditions, only the +2 oxidation state is stable

enough to be important. Pure strontium is a hard, white-colored metal, but this form is not found in the environment. Rather, strontium is usually found in nature in the form of minerals. Strontium can form a variety of compounds. Strontium compounds do not have any particular smell. There are two types of strontium compounds, those that dissolve in water and those that do not. Natural strontium is not radioactive and exists in four stable types (or isotopes), each of which can be written as ^{84}Sr, ^{86}Sr, ^{87}Sr, and ^{88}Sr, and read as strontium eighty-four, strontium eighty-six, etc. All four isotopes behave the same chemically, so any combination of the four would have the same chemical effect on your body.

Rocks, soil, dust, coal, oil, surface and underground water, air, plants, and animals all contain varying amounts of strontium. Typical concentrations in most materials are a few parts per million (ppm). Strontium ore is found in nature as the minerals celestite ($SrSO_4$) and strontianite ($SrCO_3$). After the strontium is extracted from strontium ore, it is concentrated into strontium carbonate or other chemical forms by a series of chemical processes. Strontium compounds, such as strontium carbonate, are used in making ceramics and glass products, pyrotechnics, paint pigments, fluorescent lights, medicines, and other products. For more information, see Chapter 5.

Strontium can also exist as radioactive isotopes (see Chapter 4). ^{90}Sr, or strontium ninety, is the most hazardous of the radioactive isotopes of the chemical element strontium. ^{90}Sr is formed in nuclear reactors or during the explosion of nuclear weapons. Each radioactive element, including strontium, constantly gives off radiation, and this process changes it into an isotope of another element or a different isotope of the same element. This process is called radioactive decay. ^{90}Sr gives off beta particles (sometimes referred to as beta radiation) and turns into yttrium ninety (^{90}Y); ^{90}Y is also radioactive and gives off radiation to form zirconium ninety (^{90}Zr), which is a stable isotope. The radioactive half-life is the time that it takes for half of a radioactive strontium isotope to give off its radiation and change into a different element. ^{90}Sr has a half-life of 29 years.

^{90}Sr has limited use and is considered a waste product. The radioactive isotope ^{89}Sr is used as a cancer therapeutic to alleviate bone pain. ^{85}Sr has also been used in medical applications. For more information about the properties and use of radioactive strontium, see Chapters 4 and 5.

Quantities of radioactive strontium, as well as other radioactive elements, are measured in units of mass (grams) or radioactivity (curies or becquerels). Both the curie (Ci) and the becquerel (Bq) tell us how much a radioactive material decays every second. The becquerel is a new international unit known as the SI unit, and the curie is an older unit; both are used currently. A becquerel is the amount of radioactive material in which 1 atom transforms every second. One curie is the amount of radioactive material in which 37 billion atoms transform every second; this is approximately the radioactivity of 1 gram of radium. For more information on radiation, see Appendix D and the glossary, Chapter 10, at the end of this profile or the *ATSDR Toxicological Profile for Ionizing Radiation.*

1.2 WHAT HAPPENS TO STRONTIUM WHEN IT ENTERS THE ENVIRONMENT?

Stable and radioactive strontium compounds in the air are present as dust. Emissions from burning coal and oil increase stable strontium levels in air. The average amount of strontium that has been measured in air from different parts of the United States is 20 nanograms per cubic meter (a nanogram is a trillion times smaller than a gram). Most of the strontium in air is in the form of stable strontium. Very small dust particles of stable and radioactive strontium in the air fall out of the air onto surface water, plant surfaces, and soil either by themselves or when rain or snow falls. These particles of strontium eventually end up back in the soil or in the bottoms of lakes, rivers, and ponds, where they stay and mix with stable and radioactive strontium that is already there.

In water, most forms of stable and radioactive strontium are dissolved. Stable strontium that is dissolved in water comes from strontium in rocks and soil that water runs over and through. Only a very small part of the strontium found in water is from the settling of strontium dust out of the air. Some strontium is suspended in water. Typically, the amount of strontium that has been measured in drinking water in different parts of the United States by the EPA is less than

1 milligram for every liter of water (1 mg/L). ^{90}Sr in water comes primarily from the settling of ^{90}Sr dust out of the air. Some ^{90}Sr is suspended in water. In general, the amount of ^{90}Sr that has been measured in drinking water in different parts of the United States by EPA is less than one-tenth of a picocurie for every liter of water (0.1 pCi/L or 0.004 Bq/L).

Strontium is found naturally in soil in amounts that vary over a wide range, but the typical concentration is 0.2 milligrams per kilogram (kg) of soil (or 0.2 mg/kg). The disposal of coal ash, incinerator ash, and industrial wastes may increase the concentration of strontium in soil. Generally, the amount of ^{90}Sr in soil is very small and is only a fraction of the total concentration of strontium in soil. Higher concentrations of ^{90}Sr in soil may be found near hazardous waste sites, radioactive waste sites, and Department of Energy facilities located around the United States. A major portion of stable and radioactive strontium in soil dissolves in water, so it is likely to move deeper into the ground and enter groundwater. However, strontium compounds may stay in the soil for years without moving downward into groundwater. In the environment, chemical reactions can change the water-soluble stable and radioactive strontium compounds into insoluble forms. In some cases, water-insoluble strontium compounds can change to soluble forms. For more information about the transport properties of stable and radioactive strontium in the environment, see Chapter 6.

1.3 HOW MIGHT I BE EXPOSED TO STRONTIUM?

Strontium is found nearly everywhere in small amounts, and you can be exposed to low levels of strontium by breathing air, eating food, drinking water, or accidentally eating soil or dust that contains strontium. Food and drinking water are the largest sources of exposure to strontium. Because of the nature of strontium, some of it gets into fish, vegetables, and livestock. Grain, leafy vegetables, and dairy products contribute the greatest percentage of dietary strontium to humans. The concentration of strontium in leafy vegetables, such as cabbage, grown in the United States is less than 64 mg in a kg of the fresh vegetables (i.e., 64 ppm). For most people, the intake of strontium will be moderate. More information about strontium exposure can be found in Chapter 6.

^{90}Sr is found nearly everywhere in small amounts from past nuclear accidents and fallout from nuclear explosions. You can be exposed to low levels of ^{90}Sr by eating food, drinking water, or accidentally eating soil or dust that contains ^{90}Sr. Food and drinking water are the largest sources of exposure to ^{90}Sr. Because of the nature of ^{90}Sr, some of it gets into fish, vegetables, and livestock. Grain, leafy vegetables, and dairy products contribute the greatest percentage of dietary ^{90}Sr to humans. The concentration of ^{90}Sr in fresh vegetables grown in the United States is less than 9 pCi (or 0.3 Bq) in 1 kg of dried vegetables (in a hot oven). The intake of radioactive strontium for most people will be small. You can take in more ^{90}Sr if you eat food that was grown on a radioactive strontium-contaminated hazardous waste site. More information about radioactive strontium exposure can be found in Chapter 6.

1.4 HOW CAN STRONTIUM ENTER AND LEAVE MY BODY?

Both stable strontium and radioactive strontium enter and leave the body in the same way.

If a person breathes in vapors or dust containing a chemical form of strontium that is soluble in water, then the chemical will dissolve in the moist surface inside the lungs and strontium will enter the bloodstream relatively quickly. If the chemical form of strontium does not dissolve in water easily, then particles may remain in the lung for a time. When you eat food or drink water that contains strontium, only a small portion leaves the intestines and enters the bloodstream. Studies in animals suggest that infants may absorb more strontium from the intestines than adults. If a fluid mixture of a strontium salt is placed on the skin, the strontium will pass through the skin very slowly and then enter the bloodstream. If the skin has scratches or cuts, strontium will pass through the skin much more quickly.

Once strontium enters the bloodstream, it is distributed throughout the body, where it can enter and leave cells quite easily. In the body, strontium behaves very much like calcium. A large portion of the strontium will accumulate in bone. In adults, strontium mostly attaches to the surfaces of bones. In children, whose bones are still growing, strontium may be used by the body to create the hard bone mineral itself. As a result the strontium will be stored in the bone for a long time (years). Because of the way bone grows, strontium will be locally dissolved from

bone and recirculate through the bloodstream, where it may be reused by growing bone, or be eliminated. This process accounts for the slow removal of strontium from the body.

Strontium is eliminated from the body through urine, feces, and sweat. Elimination through urine may occur over long periods, when small amounts of strontium are released from bone and do not get recaptured by bone. When strontium is taken in by mouth, the portion that does not pass through the intestinal wall to enter the bloodstream is eliminated through feces during the first day or so after exposure.

See Chapter 3 for further information.

1.5 HOW CAN STRONTIUM AFFECT MY HEALTH?

To protect the public from the harmful effects of toxic chemicals and to find ways to treat people who have been harmed, scientists use many tests.

One way to see if a chemical will hurt people is to learn how the chemical is absorbed, used, and released by the body. In the case of a radioactive chemical, it is also important to gather information concerning the radiation dose and dose rate to the body. For some chemicals, animal testing may be necessary. Animal testing may also be used to identify health effects such as cancer or birth defects. Without laboratory animals, scientists would lose a basic method to get information needed to make wise decisions to protect public health. Scientists have the responsibility to treat research animals with care and compassion. Laws today protect the welfare of research animals, and scientists must comply with strict animal care guidelines.

There are no harmful effects of stable strontium in humans at the levels typically found in the environment. The only chemical form of stable strontium that is very harmful by inhalation is strontium chromate, but this is because of toxic chromium and not strontium itself. Problems with bone growth may occur in children eating or drinking unusually high levels of strontium, especially if the diet is low in calcium and protein. Ordinary strontium salts are not harmful when inhaled or placed on the skin.

Animal studies showed that eating or drinking very large amounts of stable strontium can be lethal, but the public is not likely to encounter such high levels of strontium. In these unusually high amounts, so much strontium was taken into bone instead of calcium that growing bones were weakened. Strontium had more severe effects on bone growth in young animals than in adults.

It is not known whether stable strontium affects reproduction in people. The effect of stable strontium on reproduction in animals is not known. The Department of Health and Human Services has determined that strontium chromate is expected to be a carcinogen, but this is because of chromium. There is no information that any other form of stable strontium causes cancer in humans or animals.

The harmful effects of radioactive strontium are caused by the high energy effects of radiation. Since radioactive strontium is taken up into bone, bone itself and the soft tissues nearby may be damaged by radiation released over time. Because bone marrow is the essential source of blood cells, blood cell counts may be reduced if the dose is too high. This has been seen in humans who received injections of radioactive strontium (^{89}Sr) to destroy cancer tissue that had spread to the bone marrow. Lowered blood cell counts were also seen in animals that breathed or swallowed radioactive strontium. Numerous problems occur when the number of blood cells is too low. A loss of red blood cells, anemia, prevents the body from getting sufficient oxygen, resulting in tiredness. A loss of platelets may prevent the blood from clotting properly, and may result in abnormal bleeding, especially in the intestines. A loss in white blood cells harms the body's ability to fight infectious disease.

Radiation damage may also occur from exposure to the skin. Medically, radioactive strontium probes have been used intentionally to destroy unwanted tissue on the surface of the eye or skin. The eye tissues sometimes become inflamed or abnormally thin after a long time. Thinning of the lower layer of the skin (dermis) has also been reported in animal studies as a delayed effect.

It is not known whether exposure to radioactive strontium would affect human reproduction. Harmful effects on animal reproduction occurred at doses that were more than a million times higher than typical exposure levels for the general population.

Radioactive strontium may cause cancer as a result of damage to the genetic material (DNA) in cells. An increase in leukemia over time was reported in individuals in one foreign population who swallowed relatively large amounts of ^{90}Sr (and other radioactive materials) in river water contaminated by a nuclear weapons plant. Cancers of the bone, nose, and lung (in the case of a breathing exposure), and leukemia were reported in animal studies. In addition, skin and bone cancer were reported in animals that received radiation at high doses to the skin. The International Agency for Research on Cancer (IARC) has determined that radioactive strontium is carcinogenic to humans, because it is deposited inside the body and emits beta radiation. The EPA has determined that radioactive strontium is a human carcinogen.

To learn more about the health effects of exposure to stable or radioactive strontium, see Chapter 3.

1.6 HOW CAN STRONTIUM AFFECT CHILDREN?

This section discusses potential health effects from exposures during the period from conception to maturity at 18 years of age in humans.

Children are exposed to stable strontium in the same manner as adults: usually in small amounts in drinking water and food. Young children who have more hand-to-mouth activity or who eat soil may accidentally eat more strontium. Infants and children with active bone growth absorb more strontium from the gut than adults.

Excess stable strontium causes problems with growing bone. For this reason, children are more susceptible to the effects of stable strontium than adults who have mature bone. Children who eat or drink unusually high levels of stable strontium may have problems with bone growth, but only if the diet is low in calcium and protein. Children who drink milk, especially milk fortified

with vitamin D, are not likely to have bone problems from exposure to excess stable strontium. The amount of stable strontium that is usually taken in from food or water or by breathing is too low to cause bone problems in children. No developmental studies in humans or animals examined the effect on the fetus when the mother takes in excess strontium. However, no problems are expected with fetal bone growth because only small amounts of strontium are transferred from the mother across the placenta to the fetus. Evidence suggests that stable strontium can be transferred from the mother to nursing infants through breast milk, but the presence of calcium and protein in milk protects against bone problems during nursing.

Children take in, use, and get rid of radioactive strontium in the same ways as stable strontium. Children are likely to be more vulnerable than adults to the effects of radioactive strontium because relatively more goes into bone when it is growing. Also, children are potentially more vulnerable than adults to radiation damage because they keep radioactive strontium in bone for a longer time.

Children would be expected to have the same types of effects from exposure to radioactive strontium as exposed adults. Children can be exposed to radioactive strontium at levels higher than background without showing increases in cancer rates. Evidence from one foreign population showed that children who drank water containing unusually high levels of radioactive strontium for 7 years showed an increase in leukemia. High levels of radioactive strontium cause more bone damage and higher bone cancer rates when animals are exposed before birth or as juveniles rather than as adults. In humans and animals, radioactive strontium can be transferred into milk or across the placenta into the fetus.

1.7 HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO STRONTIUM?

If your doctor finds that you have been exposed to significant amounts of strontium, ask whether your children might also be exposed. Your doctor might need to ask your state health department to investigate. Public health officials may publish guidelines for reducing exposure to strontium when necessary.

It is possible that higher-than-normal levels of stable strontium may occur naturally in soil in some places or that higher levels of radioactive strontium may be found in soil near hazardous waste sites. Some children eat a lot of dirt. You should prevent your children from eating dirt. Make sure they wash their hands frequently, and before eating. If you live near a hazardous waste site, discourage your children from putting their hands in their mouths or from engaging in other hand-to-mouth activities.

Since strontium is so common in the environment, and is naturally present in food and water, we cannot avoid being exposed to it. For several reasons, having a balanced diet with sufficient vitamin D, calcium, and protein will be protective by reducing the amount of ingested strontium that is absorbed.

1.8 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO STRONTIUM?

All people have small amounts of stable strontium in their bodies, mostly in bone. It can be measured in the blood, hair, feces, or urine. The amount is usually measured by its mass (grams). Measurements in urine can show whether you have been exposed recently to larger-than-normal amounts of strontium. Measurements in hair can reveal whether you were exposed to high amounts of strontium in the past. Most physicians do not test for strontium in their offices, but can collect samples and send them to a special laboratory. X-rays can show changes in bone that may occur from exposure to high amounts of strontium, but these changes may have other causes (a diet low in vitamin D or a high exposure to some other trace metal).

If a person has been exposed to radioactive strontium, special tests can be used to measure radioactive strontium in blood, feces, or urine. These tests are most useful when done soon after exposure, since radioactive strontium quickly enters into bone and takes many years to be completely removed from bone. Radioactive strontium can be measured by its mass (in grams) or by its radiation emissions. These emissions, which differ for the various isotopes of strontium, are used to tell the amount of radioactive strontium (in curies or bequerels) and the radiation dose that it gives to your body (in sieverts or rem). In a procedure that is similar to

being x-rayed, specialized equipment can measure radioactive strontium that has been incorporated into bone.

For more information, please read Chapters 3 and 7.

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

The federal government develops regulations and recommendations to protect public health. Regulations can be enforced by law. Federal agencies that develop regulations for toxic substances include the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), the Food and Drug Administration (FDA), and the U.S. Nuclear Regulatory Commission (USNRC).

Recommendations provide valuable guidelines to protect public health but cannot be enforced by law. Federal organizations that develop recommendations for toxic substances include the Agency for Toxic Substances and Disease Registry (ATSDR), the National Institute for Occupational Safety and Health (NIOSH), and the FDA.

Regulations and recommendations can be expressed in not-to-exceed levels in air, water, soil, or food that are usually based on levels that affect animals; they are then adjusted to help protect people. Sometimes these not-to-exceed levels differ among federal organizations because of different exposure times (an 8-hour workday or a 24-hour day), the use of different animal studies, or other factors.

Recommendations and regulations are also periodically updated as more information becomes available. For the most current information, check with the federal agency or organization that provides it. Some regulations and recommendations for strontium include the following:

EPA recommends that drinking water levels of stable strontium should not be more than 4 milligrams per liter of water (4 mg/L).

The Department of Energy (DOE) established derived air concentrations (DAC) for workplace exposure to radiation at DOE facilities. The DAC ranges from 0.000000002 microcuries per milliliter (μCi/mL) ($2x10^{-9}$ μCi/mL of air = 70 μBq/mL of air) for radioactive particles remaining in the lung for 100 days to 0.000000008 μCi/mL ($8x10^{-9}$ μCi/mL of air = 300 μBq/mL of air) for radioactive particles remaining in the lung for less than 10 days. The USNRC established an annual intake limit of 20 μCi (7 MBq) for on-the-job exposure to ^{90}Sr in air.

EPA set standards for the concentration of ^{90}Sr in community water supplies. The average annual concentration of ^{90}Sr in water supplies should not exceed 8 pCi/L (0.3 Bq/L). EPA also established maximum contaminant levels (MCLs) in drinking water for radionuclide activities to protect against harmful effects of ^{90}Sr. For beta particles like strontium, the MCL is 4 mrem per year ($4x10^{-5}$ Sv per year). The USNRC set a workplace value of 31 μCi (1.1 MBq) for the amount of ^{90}Sr that can be taken in by mouth in a year without any harmful effects.

More information on regulations and guidelines is available in Chapter 8.

1.10 WHERE CAN I GET MORE INFORMATION?

If you have any more questions or concerns, please contact your community or state health or environmental quality department, your regional Nuclear Regulatory Commission office, or contact ATSDR at the address and phone number below.

ATSDR can also tell you the location of occupational and environmental health clinics. These clinics specialize in recognizing, evaluating, and treating illnesses resulting from exposure to hazardous substances.

Toxicological profiles are also available on-line at www.atsdr.cdc.gov and on CD-ROM. You may request a copy of the ATSDR ToxProfiles CD-ROM by calling the information and technical assistance toll-free number at 1-888-42ATSDR (1-888-422-8737), by email at atsdric@cdc.gov, or by writing to:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road NE
Mailstop F-32
Atlanta, GA 30333
Fax: 1-770-488-4178

For-profit organizations may request a copy of final profiles from the following:

National Technical Information Service (NTIS)
5285 Port Royal Road
Springfield, VA 22161
Phone: 1-800-553-6847 or 1-703-605-6000
Web site: http://www.ntis.gov/

2. RELEVANCE TO PUBLIC HEALTH

2.1 BACKGROUND AND ENVIRONMENTAL EXPOSURES TO STRONTIUM IN THE UNITED STATES

Stable Strontium. Elemental strontium (atomic number 38) occurs naturally in the earth's mantle as a mixture of four stable isotopes, ^{88}Sr, ^{86}Sr, ^{87}Sr, and ^{84}Sr, and is present everywhere in very dilute concentrations. It is very similar to calcium in its environmental and physiological behavior. Strontium is generally found in molecular compounds with other elements. Commercially important strontium minerals include celestite ($SrSO_4$) and strontianite ($SrCO_3$). Strontium is used in the manufacture of ceramics and glass products, primarily in the faceplate glass of televisions and other cathode-ray-tube devices, where it serves to block x-ray emissions.

The general population is exposed to stable strontium primarily by ingestion of food and water, and to a lesser degree, by inhalation. The strontium content in air averages 20 ng/m^3, with higher concentrations resulting from stack emissions from coal-burning plants. Strontium is present in nearly all fresh waters in amounts generally ranging between 0.5 and 1.5 mg/L, with higher levels occurring where there are celestite-rich limestone deposits. The average concentration of stable strontium in soil is approximately 240 mg Sr/kg, but agricultural soils may be treated with phosphate fertilizer or limestone, which contain ~610 mg Sr/kg. Because strontium is chemically similar to calcium, it is taken up from the soil by fruits and vegetables. The average concentration of strontium in fruit produce ranged from 0.0416 to 2.232 µg/L. The total estimated daily exposure to stable strontium is approximately 3.3 mg/day (0.046 mg/kg/day): 400 ng/day from inhalation, 2 mg/day from drinking water, and 1.3 mg/day from the diet (see Chapter 6). Assuming a reference body weight of 70 kg, the typical daily strontium exposure is 46 µg/kg body weight. The strontium content of the human body is approximately 4.6 ppm by weight, 99% of which is localized in bones and teeth. Blood concentrations of strontium are in the range of 20–31 µg/L.

Radioactive Strontium. The radioactive isotopes of strontium do not occur naturally but are produced as a by-product of nuclear fission of ^{235}U, ^{238}U, or ^{239}Pu. The most significant isotopes are ^{90}Sr (half-life of 29 years), ^{89}Sr (half-life of 51 days), and ^{85}Sr (half-life of 65 days), which decay by the emission of beta particles. ^{90}Sr is currently found in spent fuel rods in nuclear reactors and is considered a waste product. Other radioactive strontium isotopes have been employed for medical uses: ^{89}Sr (as Metastron™) as a cancer therapeutic for the relief of bone pain and ^{85}Sr in the radiologic imaging of bone. ^{85}Sr also has

minor commercial applications in thermoelectric power generation, as a beta particle standard source, and in instruments that measure the thickness and density of materials. Disposal and handling of radioactive strontium isotopes are regulated by the U.S. Nuclear Regulatory Commission.

The general population is exposed to very small amounts of radioactive strontium from the ingestion of contaminated water and food; inhalation exposure is negligible. The average concentration of ^{90}Sr in drinking water in 1994 was estimated as 0.1 pCi/L; after 1994, estimates were based on gross beta activity and not reported by individual elements since the amounts were so small. Fresh vegetables contribute more than one third of the yearly dietary intake of ^{90}Sr, followed by grains and dairy products. The current total daily exposure levels to radioactive strontium are estimated to be approximately 5.2 pCi/day (0.16 Bq/day; 0.074 pCi/kg/day): 5 pCi/day from food and 0.2 pCi/day from drinking water.

See Chapter 6 for more detailed information regarding concentrations of stable and radioactive strontium in environmental media.

2.2 SUMMARY OF HEALTH EFFECTS

Stable Strontium. There is no direct evidence that stable strontium is toxic to humans under normal environmental exposures. The primary toxicological effect of absorbed excess strontium in laboratory animals is abnormal skeletal development (rickets), which occurs only at relatively high oral doses. The inhalation toxicity of pure stable strontium has not been evaluated. At levels normally encountered in the environment, strontium appears to have low toxicity to adults or to juveniles with adequate nutrition. Juveniles, especially those with poor nutrition, are vulnerable because strontium, as an imperfect surrogate for calcium, interferes with bone mineralization in the developing skeleton. The data for adverse health effects of stable strontium in humans are sparse, but indicate a possibility of skeletal effects under special circumstances: an epidemiological study of strontium-related rickets in Turkish children and a few studies of hemodialysis patients who developed osteomalacia because of strontium in dialysis water. Numerous animal studies demonstrated adverse effects on skeletal development in juveniles following ingestion of excess stable strontium (discussed below under Skeletal Effects). No developmental or reproductive studies have been conducted involving exposure to stable strontium during gestation. No studies examined whether stable strontium is carcinogenic to humans or animals. One strontium compound, strontium chromate, is a genotoxic human carcinogen by the inhalation route, but the hazard is caused by hexavalent chromium and not strontium.

Other effects have been observed sporadically and are of unclear physiological significance. Paralysis of the hindlimbs was observed in orally-exposed rats, but it is uncertain whether the cause was neurophysiological or the result of local neuronal damage secondary to deformation of the femora. Minor unspecified changes in hepatic histology and glycogen content were observed in orally-exposed rats. The following section discusses effects in the primary target of stable strontium, the skeleton, in greater detail.

Skeletal Effects. Although strontium, as a molecular surrogate for calcium, can be distributed throughout the body, its main target for deposition is the skeleton. One suggestive epidemiological study found that increased strontium ingestion contributed to an increase in the prevalence of signs of rickets (craniomalacia, rachitic rosary, bulging at the wrist, bony deformities of the leg, and delayed closure of the fontanelles) in children in a region of Turkey. A significantly increased incidence of rickets was associated with a diet restricted to water and cereals grown locally in soils with strontium concentrations in excess of 350 mg/kg. Other contributing factors included probable deficiencies in vitamin D, protein, and calcium after weaning; breast feeding for >2 years appeared to be a protective factor against the development of rickets in this population. The only reports of strontium-related skeletal problems in adults concerned osteomalacia in hemodialysis patients exposed to strontium in dialysis water. Dialysis patients may be unusually susceptible because of their impaired handling of strontium. Stable strontium compounds have been used for the treatment of osteoporosis (see Section 2.3).

Animal studies strongly support the identification of bone as the most sensitive target of strontium toxicity. Relatively high doses of strontium (≥500 mg/kg/day) caused a reduction in bone mineralization (ash weight) and an alteration in the chemical composition of organic bone matrix. In addition, the hypertrophic zones of the epiphyseal growth plates of long bones became abnormally deep and wide, as calcification failed to occur. Severe weakening of the bones resulted from rickets, in which the skeleton could not support the body adequately; deformity of the head of the femur may have contributed to paralysis of the hind limbs in some cases. Young animals were more sensitive to the effect of excess strontium than older animals, possibly because the absorption and retention of strontium were higher in the young. In addition, inadequate calcium and vitamin D in the diet increased the severity of skeletal effects. The chemical form of strontium may influence toxicity by affecting gastrointestinal absorption. One intermediate oral animal study that tested strontium phosphate reported a much higher no-effect level than studies that tested strontium chloride or carbonate. However, cation effects on strontium toxicity have not been studied systematically.

2. RELEVANCE TO PUBLIC HEALTH

Evidence from the few human studies and numerous animal toxicity studies suggest that healthy adults living near hazardous waste sites are unlikely to be exposed to levels of stable strontium sufficiently high to cause adverse skeletal effects. Children living in areas where the soil and drinking water contain relatively high amounts of strontium may be vulnerable to skeletal effects if their nutritional status is poor (deficient in calcium, vitamin D, and/or protein) and if the diet is restricted to foods grown locally. All these conditions are not likely to be common in the United States, since the food supply generally comes from a wide geographic area.

Radioactive Strontium. Exposure to radioactive strontium can result in health consequences that vary depending on the dose, the route of exposure, and the chemical form. Both ^{90}Sr and ^{89}Sr emit beta particles, which, in tissue, may ionize cellular molecules within a range of 1 cm, resulting in tissue damage and disruption of cellular function if the capacity of natural repair mechanisms is exceeded. Adverse health effects occur at high levels of exposure that significantly exceed background levels encountered by the general population. It should be noted that no discernable adverse health effects were detected in the general population from chronic low-level exposure to ^{90}Sr in fallout during the period of aboveground weapons testing.

^{90}Sr represents the most significant isotope of concern because of its relatively long half-life (29 years) and because of the bone-seeking properties of strontium. The most serious effects of oral exposure to absorbed radioactive strontium are necrotic lesions and cancers of bone and the adjacent tissues. High level acute exposures can destroy hematopoietic bone marrow, leading to acute radiation syndrome (see below), the primary cause of mortality in the short term. At lower doses, irradiation of bone marrow may lead to chronic suppression of immune function.

The consequences of inhalation exposures in animals vary depending on the solubility of the form of radiostrontium. Insoluble particles tend to be retained in the lung, resulting in pneumonitis; necrosis of the pulmonary, vascular, and adjacent myocardial tissues; pulmonary fibrosis; and, later, pulmonary and vascular cancers. Inhalation of soluble radiostrontium does not have these local effects because the material is absorbed and distributed in the skeleton. The effects of inhalation of soluble strontium are, therefore, similar to those described for the oral route: acute radiation syndrome and other hematopoietic effects, osteosarcoma, and immunosuppression.

External exposure to solid strontium sources placed near the skin or eye can cause local lesions when doses are significantly higher than background. Effects observed in clinical studies on the eye included

keratitis or scarring of the cornea, telangiectasis or scarring of the conjunctiva, iritis, conjunctivitis, mild irritation, and scleral thinning. Dermal effects in clinical studies range from erythema and pigmentation changes, dry and moist desquamation (which involves destruction of the basal epithelial cells), and telangiectasis and increased vascular permeability, to long-term responses such as epithelial and dermal hyperplasia, chronic fibrosis, and dermal atrophy.

There is inconclusive evidence in humans and definitive evidence in laboratory animals that exposure to radioactive strontium at very high doses *in utero* can lead to adverse developmental effects. Slight increases in developmental effects were noted in a population of the former Soviet Union whose drinking water (the Techa River) was contaminated with multiple radioactive elements released from a plutonium production plant between 1949 and 1956. These effects included slight increases in child mortality from chromosomal defects and from congenital anomalies of the nervous system, circulatory system, and other unspecified anomalies in the progeny of exposed individuals. However, the specific contribution of radiostrontium to these effects is not known. Developmental effects in laboratory animals were noted at extremely high doses, as if, on a kilogram body weight basis, individual pregnant females were receiving daily the entire amount of ^{90}Sr currently released from one nuclear power plant into the environment during a year (see Table 6-1). There is evidence that maternal oral exposure to radioactive strontium can lead to reduced fetal and postnatal survival in the offspring, but there is no evidence for birth defects. At the very highest doses of radioactive strontium injected into pregnant females, the offpsring exhibit increases in birth defects (skeletal anomalies and partial atelectasis of the lungs), and cancers of soft tissues near bone (meningeal and pituitary tumors), as well as hyperplasia of lymph nodes and spleen and deficient hematopoiesis. Exposure to radioactive strontium in milk from dams injected at very high doses reduces the numbers of early-stage oocytes in the ovary of neonatal mice, but the effect is less severe than when offspring are exposed only *in utero*.

There is no evidence in humans that radioactive strontium leads to reproductive effects, but there is some evidence in laboratory animals. Although the Techa River populations received the highest known extended oral exposure to radioactive strontium (and other radionuclides) of any human group, there were no significant effects on reproductive parameters (birth rate, fertility, incidence of spontaneous abortion). An increase in fetal deaths was noted in some studies in rats, but no reproductive effects were noted in larger laboratory animals at equivalent oral doses. This difference appears to be related to the fact that in small animals, the bone marrow cavity diameters are not wide enough to leave the central hematopoetic tissues untouched by beta-irradiation emitted by radioactive strontium bound to bone. Exposure to high

doses of radioactive strontium by injection led to significant reproductive effects (reduced fertility, reduced gonadal cellularity, suppressed spermatocyte maturation) in mice.

Other effects of radioactive strontium have been observed sporadically in animal studies and are of unclear physiological significance. Anorexia, reduced body weight, and liver effects that were possibly secondary to radiation pneumonitis (chronic passive congestion of the liver and mild centrilobular hepatic fibrosis) were observed in beagles following a single inhalation exposure of insoluble ^{90}Sr particles at an initial lung burden of 25 μCi/kg.

The populations potentially most sensitive to radiostrontium exposure include the young and individuals that have poor nutrition or deficiencies in vitamin D. Infants and children are more vulnerable than adults because they absorb strontium through the gastrointestinal tract at slightly higher rates and because they have actively growing bones that incorporate more strontium than mature bones. Very high prenatal exposure levels may cause major developmental anomalies in the skeleton and adjacent areas if critical tissues are destroyed. In addition, since children have a higher proportion of mitotic cells than adults, their rates of genotoxic damage are higher. This is because genetic lesions become fixed mutations when mitosis occurs before genetic damage is repaired. Genetic lesions in genes controlling the cell cycle can lead to the development of cancer and may be the basis of excess cancer cases attributed to exposure to radioactive strontium. Individuals with poor nutrition or deficiencies in vitamin D, such as those with osteomalacia, are theoretically more vulnerable to radioactive strontium because their lower absorption of calcium results in relatively higher rates of strontium incorporation into bone during the remodeling process that continues throughout life. The level of incorporation of radiostrontium into bone can be somewhat reduced by ingestion of alginates soon after exposure. Removal from bone after incorporation is not feasible.

The major adverse effects of exposure to radioactive strontium, non-cancerous lesions of hematopoietic bone marrow tissue, cancer, and dystrophic lesions of the skeleton, are discussed below in greater detail. It should be noted that the large animal studies are more relevant than rodent studies to humans because the severity of bone marrow effects is inversely proportional to the diameter of the bone marrow cavity.

Non-Cancerous Bone Marrow Effects (Including Acute Radiation Syndrome). Bone marrow effects are the most serious immediate consequences of exposure to high levels of radioactive strontium by either the inhalation or oral route. When absorbed radioactive strontium incorporates into bone, irradiation of the bone marrow results in hypoplasia of the hemopoietic tissue and pancytopenia,

with the severity depending on the dose. At the highest doses, acute radiation syndrome (anorexia, bloody diarrhea) would be expected because of the virtual destruction of the bone marrow. Acute radiation syndrome was not observed in the orally-exposed Techa River population, but was observed in dogs several weeks after receiving long-term retained body burdens of ≥47 μCi ^{90}Sr/kg (≥1.74 MBq/kg) following a single exposure to soluble $^{90}SrCl_2$ by inhalation. Hemorrhaging is caused by the drastic depression in platelet counts; a severe drop in neutrophil counts precedes death. At lower exposure levels, pancytopenia is detectable, but is not immediately life-threatening. This was observed in dogs that received long-term retained burdens >10 μCi ^{90}Sr/kg (>0.37 MBq/kg) following a single inhalation exposure of soluble $^{90}SrCl_2$.

At lower levels of exposure, not all types of hematopoietic cells within bone marrow are affected, possibly because of differences in intrinsic rates of replacement. In the orally-exposed Techa River populations, milder chronic effects of bone marrow irradiation were reported in a small percentage of exposed individuals: leukopenia, thrombocytopenia, and granulocytopenia, as well as lymphopenia involving T lymphocytes and large granulocytic lymphocytes. Reduced lymphocyte counts, indicators of weakened immune function, in some individuals who received radiation to the bone marrow in excess of 30 rem (0.3 Sv) per year, were implicated as the cause of the higher incidences of infectious disease in those who developed radiation-induced cancers. Suppression of the immune system is also supported by studies in pigs exposed to 625 μCi ^{90}Sr/day (23.13 MBq/day) in feed for 4–9 months or in dogs receiving single inhalation exposures of soluble (long-term retained burden >10 μCi ^{90}Sr/kg [>370 kBq/kg]) or insoluble (initial lung burden ≥5 μCi ^{90}Sr/kg [≥185 kBq/kg]) radioactive strontium. Injection studies in mice indicate that natural killer cells were preferentially eliminated. Chronic myeloid metaplasia, possibly related to genotoxicity, was another effect of bone marrow irradiation in orally-exposed pigs that received cumulative doses in excess of 40 rad (0.4 Gy) and in a small percentage of dogs that received ≥0.4 μCi ^{90}Sr/kg/day (44.4 kBq/kg/day) from mid-gestation to 1.5 years.

Cancer. Radioactive strontium, like other radionuclides, is a genotoxic carcinogen. Mutations in genes controlling the cell cycle can lead to cancer if the damage is not repaired before the next cell division; rapidly dividing cells, such as the hematopoietic cells in bone marrow, are especially vulnerable. Incorporation of radioactive strontium into bone places bone and the adjacent soft tissues at risk for cancer. Chronic consumption of radioactive strontium (and other radionuclides), leading to estimated doses to bone marrow in excess of 10 rem (0.1 Sv), significantly increased the incidence of leukemia in the Techa River population, but this effect was not observed in offspring exposed *in utero* who received lower doses. Leukemia has also been observed in animals exposed orally or by inhalation to soluble

radioactive strontium. Other cancers observed in animal studies include osteosarcomas, hemangiosarcomas, cancers of other soft tissues near bone, and, in feeding studies, nasal, oral, and periodontal carcinomas. In dogs that inhaled insoluble ^{90}Sr, the particles lodged in the respiratory tract, causing cancers of the immediately surrounding tissues: hemangiosarcomas of the lung and heart and carcinomas of the respiratory tract. External exposure to ^{90}Sr (solid source) in mice induced skin cancers (squamous cell carcinoma, basal cell carcinoma, fibrosarcoma) and, in one study, osteosarcomas. Immature organisms are potentially more vulnerable than adults to radioactive strontium partly because they have a higher proportion of cells in mitotic phase and partly because they incorporate relatively more radiostrontium into bone. In a multigenerational swine study, doses that were not carcinogenic in the females exposed as adults induced osteosarcomas in the F1 or F2 generations exposed from conception. National Council on Radiation Protection and Measurements concluded that uncertainties remain regarding extrapolation from the high doses of ^{90}Sr known to cause cancer in animals to the lower doses that might increase the incidence of leukemia in humans. The Council suggested that more basic knowledge on the mechanism of cancer induction by ionizing radiation would be required to understand the risk of internal exposure to ^{90}Sr. EPA has determined that radioactive strontium is a known human carcinogen (Group A). EPA estimated that the risk of developing cancer following exposure to 8 pCi/L in drinking water is 1 in 100,000. The International Agency for Research on Cancer has determined that internally deposited radionuclides, such as radioactive strontium, are carcinogenic to humans (Group 1).

Skeletal Effects. Dystrophic lesions of the skeleton occur when the level of oral exposure of soluble radioactive strontium is high enough that the amount incorporated into bone results in irradiation of the bone at levels exceeding natural repair mechanisms. The effect could occur by acute exposure to a very high dose, by intermediate-duration exposure at a moderate dose, or by chronic-duration exposure at a lower dose. Such lesions, primarily affecting articular and periarticular tissues, were reported in the Techa River populations that received mean radiation doses to the surface of bone in excess of 200 rem (2 Sv) following chronic oral exposure to radiostrontium, but not at the lower doses.

Animal oral exposure studies support the findings in humans. Skeletal or dental effects in adults are less severe than in developing animals because in adults, incorporation of radioactive strontium is mainly restricted to the surfaces of bone or teeth. Incorporation throughout the developing bone renders it vulnerable to weakening as a result of focal necrosis from long-term irradiation. Intermediate-exposure at 6 μCi/kg/day for 1–10 months reduced numbers of osteocytes and damaged blood vessels in the bone of adult rabbits. More severe effects damaging the bone structure (necrosis of vasculature, impaired transformation into cortical bone, and fracturing) were observed in dogs exposed *in utero* and chronically

into adulthood at 0.4 µCi/kg/day. Damage to developing teeth (disordered tooth structure and increased cell death of differentiating odontoblasts and pulp cells) has been reported in rabbits following injection of a very high dose (600 µCi ^{90}Sr/kg), but effects were less severe in mature teeth.

2.3 MINIMAL RISK LEVELS

Inhalation MRLs

Stable Strontium. Data on the toxicity of inhaled stable strontium are not suitable for derivation of an inhalation MRL: one case report of a woman exposed to an undetermined concentration of strontium mixed with other chemicals in smoke from an ignited flare (Federman and Sachter 1997).

Radioactive Strontium. The main sources on the toxicity of inhaled radioactive strontium are two acute-duration studies in dogs reporting severe hematological and immunological effects following a single nose-only exposure to ^{90}Sr as fused clay particles for several minutes (Jones et al. 1976) or strontium chloride (Gillett et al. 1987a). Inhalation of ^{90}Sr fused-clay particles leading to initial lung burdens of 5 µCi ^{90}Sr/kg (185 kBq/kg) resulted in chronic significant depression of lymphocyte counts and suppression of immune function (Jones et al. 1976). Chronic thrombocytopenia and neutropenia, which persisted for 1,000 days in dogs at all tested exposure levels (long-term retained burdens at or above 1 µCi ^{90}Sr/kg; 0.04 MBq/kg), was observed in dogs exposed to soluble $^{90}SrCl_2$ (Gillett et al. 1987a). These data were not considered adequate for derivation of an acute-duration inhalation MRL because the observed hematological and immunological effects were considered severe adverse effects.

Oral MRLs

Stable Strontium.

- An MRL of 2.0 mg/kg/day has been derived for intermediate-duration oral exposure (15–364 days) to stable strontium and its compounds.

The most consistent effects of oral exposure to excess stable strontium are rickets (impaired cartilage calcification) and osteomalacia (impaired bone mineralization), especially in the young. One Turkish epidemiological study provided indirect evidence that excess oral exposure to strontium (in the presence of other predisposing factors) may contribute to the development of rickets in children (Ögzür et al. 1996). Overall, animal studies on strontium have concentrated on the evaluation of skeletal effects, with

occasional consideration to body weight and serum chemistry. In young rodents, typical effects of excess strontium included an abnormal widening of the cartilaginous epiphyseal plates of the long bones, a lack of bone calcification, and abnormal deposition of unmineralized bone matrix or osteoid (Johnson et al. 1968; Kshirsagar 1976; Marie and Hott 1986; Morohashi et al. 1994; Neufeld and Boskey 1994; Storey 1962). The skeletal effects of strontium are known to be related to its chemical similarity to calcium and its suppression of vitamin D metabolism and intestinal calcium absorption (Armbrecht et al. 1998). Effects are more severe in young rats than in adults because the rate of skeletal incorporation of strontium is higher in young animals (see Section 3.5.2.2).

A lowest-observed-adverse-effect level (LOAEL) of 550 mg strontium/kg/day is identified for bone mineralization abnormalities in weanling rats that were exposed to dietary strontium carbonate for 20 days (Storey 1961). The epiphyseal plates of long bones were irregular and abnormally thick. Furthermore, areas of uncalcified bone matrix were deposited in the distal ends of the metaphyseal trabeculae and proximal end of the diaphyses. Irregularities in the organization of the cells of the hypertrophic zone, in the pattern of calcification, and in the deposition of osteoid were more conspicuous with increasing dose. In tibias, the dry weight, ash weight, ash percentage, and calcium in ash were significantly reduced with increased strontium intake. No effects on bone mineralization occurred in weanling rats ingesting 140 mg strontium/kg/day, the NOAEL for intemediate-duration exposure. In adult rats examined in this study, the effects of strontium ingestion were less severe in that higher doses were required to produce the same effect. The no-effect level in adults was 690 mg strontium/kg/day, which was higher than the LOAEL for weanlings. In adults, changes in tibial histology, such as abnormal thickening of the epiphyseal cartilages and abnormally widened metaphyseal osteoid seams, were noted at or above 1,370 mg strontium/kg/day. At 2,750 mg strontium/kg/day, osteoid tissue was deposited near vascular canals and the areas of bone resorption were reduced. In adult rat tibias, the dry weight, ash weight, ash percentage, and calcium in ash were only significantly affected at the highest dose. This study demonstrates the difference in sensitivity to strontium between young and old animals, which is caused by the higher rate of strontium incorporation into the developing skeleton in young animals.

The critical dose levels identified in the Storey (1961) study are supported by other studies in rodents. Similar LOAELs (500–565 mg strontium/kg/day) for abnormal bone mineralization are identified in several studies on weanling rats exposed to strontium carbonate (Morohashi et al. 1994; Neufeld and Boskey 1994) or an unspecified form of strontium (Johnson et al. 1968). Slight skeletal effects were noted in mice exposed to 350 mg strontium/kg/day as strontium chloride (Marie and Hott 1986). In addition, similar no-observed-adverse-effect levels (NOAELs) in the range of 110–168 mg

strontium/kg/day for skeletal effects were identified from studies in weanling rats exposed to an unspecified form of strontium (Grynpas et al. 1996), strontium chloride hexahydrate (Kroes et al. 1977), or strontium carbonate (Morohashi et al. 1994). The study by Storey (1961) is preferred as the basis for the intermediate MRL because both young and adult animals were tested, the administered doses included NOAELs and LOAELs for both age groups, and the evaluation of skeletal effects included histopathological analysis. Some of the other studies have serious deficiencies that render them unsuitable for deriving an MRL. Two studies administered single doses of 166–168 mg/kg, but reported no adverse effects (Grynpas et al. 1996; Kroes et al. 1977); although the results support the NOAEL by Storey (1961), the lack of higher doses causing positive results raises uncertainty about the experiments. The study by Johnson et al. (1968) administered a single dose of 565 mg/kg that was a serious LOAEL for increased mortality. Three of the other studies had deficiencies that rendered them less suitable than Storey (1961). The study by Morohashi et al. (1994) did not analyze bone histopathology. Studies by Marie and Hott (1986) and Neufield and Boskey (1994) administered single doses of 350 and 500 mg/kg, respectively, which were LOAELs for skeletal effects, but the studies provided no information on no-effect levels or effects at higher doses. Therefore, the NOAEL of 140 mg strontium/kg/day for skeletal effects in weanling rats (Storey 1961) would appear to be the most appropriate basis for calculating an intermediate MRL. The NOAEL of 140 mg strontium/kg/day was divided by an uncertainty factor of 30 (10 for extrapolation from animal to human and 3 for human variability) and a modifying factor of 3 (for short study duration and limited end point examination). A partial uncertainty factor was used to account for human variability because the selected NOAEL was based on the response of juveniles, which is also the most sensitive human group. The resulting MRL is calculated to be 2.0 mg strontium/kg/day, which is approximately 40 times higher than the total estimated daily exposure to stable strontium of 0.047 mg/kg/day. The MRL represents an estimate of daily human exposure that is likely to be without an appreciable risk of adverse health effects. Since the MRL is based on effects in young rats, it is considered to be protective of children, who are similar with respect to immaturity of the skeleton and high intestinal rates of strontium absorption.

MRLs were not derived for acute- or chronic-duration oral exposures to stable strontium. The relevant acute data are limited to two lethality studies in mice (Ghosh et al. 1990; Llobet et al. 1991a) and two toxicity studies in rats (Kshirsagar 1976; Kroes et al. 1977). The rat studies were not considered suitable for MRL derivation. In the Kshirsagar (1976) study, the only administered dose, 3,000 mg strontium per kg/day as strontium phosphate, resulted in severe body weight effects (62% reduction in body weight gain) and was higher than the LD_{50} values reported for mice (Ghosh et al. 1990; Llobet et al. 1991a). The Kroes et al. (1977) study did not identify an adverse effect level. Limited data on the chronic toxicity of

stable strontium are available for humans and no data are available for animals. The available data involve patients with osteoporosis or other disorders of bone mineralization who were treated for several years with low doses of strontium in the form of strontium salts: strontium lactate (Shorr and Carter 1952), strontium gluconate or strontium carbonate (Skoryna 1981a, 1984), and strontium ranelate (Meunier et al. 2002, 2004; Reginster 2002, 2003, Reginster et al. 2002). None of the studies reported adverse effects on bone or significant increases in side-effects related to treatment, but reporting was poor in some of the studies (Shorr and Carter 1952; Skoryna 1981a, 1984). These data are not suitable for MRL derivation for several reasons. All subjects in these studies were co-administered calcium and some were given vitamin D, both of which are known to interfere with strontium toxicity. In addition, all of the subjects were adults, the majority being postmenopausal women with osteoporosis. Considering that the intermediate oral MRL is based upon bone effects in juvenile rats, there is reason to suspect that a chronic oral MRL based on these data would not be protective of the most sensitive population (juveniles).

Radioactive Strontium. No MRLs were derived for oral exposure to radioactive strontium, although the database includes chronic-duration human studies and acute-, intermediate-, and chronic-duration animal studies in several species. Strontium dosimetry information is available for the populations affected by contamination of the Techa River, but these exposures included simultaneous external gamma radiation from ^{137}Cs, ^{106}Ru, and ^{95}Z and internal radiation from ^{137}Cs, in addition to ^{89}Sr and ^{90}Sr (Kossenko et al. 1994). The combined exposure studies are not suitable for the derivation of MRLs. An increase in the incidence of leukemia was reported for Techa River individuals receiving estimated bone marrow doses, attributed to radioactive strontium, in excess of 10 rem (0.1 Sv) (Kossenko 1996; Kossenko et al. 1997, 2000, 2002). Dystrophic lesions of the skeleton were observed in individuals with mean radiation doses to the surface of bone in excess of 200 rem (2 Sv) (Akleyev et al. 1995). Studies on rodents are not suitable models for establishing MRL levels for human exposure to radioactive strontium because of their relatively smaller bone diameter which places their bone marrow tissues at greater risk of radiation damage. Most of the large animal studies reported serious hematological effects at all dose levels. Immunosuppression was observed in pigs fed 625 μCi ^{90}Sr/day (23.13 MBq/day) for 4–9 months (Howard 1970; Howard and Clarke 1970). Chronic myeloid metaplasia was another effect of bone marrow irradiation in orally-exposed pigs that received cumulative doses in excess of 40 rad (0.4 Gy) and a small percentage of dogs that received ≥0.4 μCi ^{90}Sr/kg/day (44.4 kBq/kg/day) from mid-gestation to 1.5 years (Dungworth et al. 1969; Howard 1970; Howard and Clarke 1970). These serious effects are not suitable bases for determining MRL levels.

3. HEALTH EFFECTS

3.1 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 on the toxicology of strontium. It contains descriptions and evaluations of toxicological studies and epidemiological investigations and provides conclusions, where possible, on the relevance of toxicity and toxicokinetic data to public health.

A glossary and list of acronyms, abbreviations, and symbols can be found at the end of this profile. Appendix D contains background information on radiation physics, chemistry, and biology.

Naturally occurring strontium is a mixture of four stable (nonradioactive) isotopes, ^{84}Sr, ^{86}Sr, ^{87}Sr, and ^{88}Sr, the last being the most abundant. Section 3.2 contains a discussion of the chemical toxicity of stable strontium; radiation toxicity associated with exposure to radiostrontium (primarily ^{90}Sr and ^{89}Sr) is discussed in Section 3.3. The chemical properties of stable and radioactive strontium isotopes are identical and are described in Chapter 4.

Strontium is fairly reactive and therefore is rarely found in its pure form in the earth's crust. Examples of common strontium compounds include strontium carbonate, strontium chloride, strontium hydroxide, strontium nitrate, strontium oxide, and strontium titanate. The most toxic strontium compound is strontium chromate, which is used in the production of pigments and can cause cancer by the inhalation route. Strontium chromate is not included in the Levels of Significant Exposure (LSE) tables for strontium since the carcinogenic effects of the compound are a function of the concentration of hexavalent chromium, and strontium only contributes to solubility. The Toxicological Profile for Chromium (Agency for Toxic Substances and Disease Registry 2000) should be consulted for additional information on the health effects of strontium chromate.

There is no direct evidence that strontium is toxic to humans, but there is suggestive epidemiological evidence that the oral toxicity observed at high doses in juvenile laboratory animals may pertain to humans under special circumstances. Stable strontium is of relatively low toxicity. It comprises about 4.6 ppm by weight of the human body, but does not have any recognized essential biological role. Human exposure to strontium is primarily by the oral route (via fruits, vegetables, and drinking water),

although inhalation exposures are also possible. No toxic effects of stable strontium have been reported for the exposure levels normally encountered in the environment. Strontium is not readily absorbed through intact skin, but is absorbed through abraded skin and through puncture wounds. The biological effects of strontium are related to its chemical similarity to calcium, with both elements being found in Group 2 of the periodic table and forming divalent cations. However, since strontium is not the same size as calcium, it does not substitute precisely for calcium in biological processes. At different stages of the life cycle, organisms vary in their ability to discriminate between strontium and calcium, which may cause age-related differences in gastrointestinal absorption, and therefore in health effects. Because of its similarity to calcium, strontium accumulates to a high degree in bone, and, in high concentrations, may seriously interfere with the normal process of bone development. The young are particularly vulnerable because a lack of discrimination between calcium and strontium occurs during a dynamic period of bone formation and growth. For this reason, body burdens of strontium will be higher in children than in adults, and the health effects associated with high exposure levels would be more severe. As suggested in one human study and demonstrated in several animal studies, strontium 'rickets' is one potential consequence of childhood exposure to excess stable strontium.

Beta emissions from ^{90}Sr have a limited ability to penetrate through tissue (see Appendix D Section D.2.3). For that reason, radiostrontium must be internalized or placed in close contact with skin before adverse health effects will occur. The 'bone-seeking' behavior of strontium is the basis for concern regarding oral or inhalation exposures to the radioactive isotopes, particularly ^{90}Sr, with its long half-life of 29 years and highly energetic 0.546 MeV beta particles, plus the 2.2 MeV beta particles of its short-lived ^{90}Y decay product isotope. Radioactive strontium isotopes incorporate into bone and irradiate the bone cells, the hemopoietic bone marrow, and potentially, the soft tissues surrounding bone, especially in the skull. Human populations accidentally exposed to high levels of radiation from radiostrontium (and other radionuclides and external radiation) experienced chronic radiation sickness (postirradiation changes in hematological parameters) and increased leukemia and cancer mortality in the decades following exposure. In animal studies, high-level exposures to ^{90}Sr led to death within weeks because of radiation damage to hemopoietic tissues. Longer-term lower level exposures that overcome genetic repair mechanisms may lead to myeloid leukemia, osteosarcoma, and lymphoma (only observed in some rodent studies). It should be understood that because strontium is retained for a long time in the skeleton, acute- or intermediate-duration uptakes (i.e., absorption events occurring within a period of <2 weeks or <1 year, respectively) can result in decade-long (i.e., chronic) effects from internal exposure to the radiation emitted from the retained isotopes. Children would appear to have a higher lifetime risk for cancer effects per unit uptake, because of their relatively higher rate of skeletal incorporation of

strontium and potentially longer radiation exposure period. Immediately nonlethal exposures to high levels of radioactive strontium may contribute to suppression of the immune system.

Limited human data are available regarding health effects that can be exclusively associated with exposure to radioactive strontium sources such as ^{90}Sr and ^{89}Sr. These radionuclides are products of nuclear fission and may, therefore, be released from sites where nuclear fission occurs, from radioactive material removed from such sites, or from leakage of radioactive strontium sources. Both ^{90}Sr and ^{89}Sr emit beta radiation that travels short distances and can penetrate the skin and superficial body tissues. The radiation dose from these radionuclides can be classified as either external (if the source is outside the body) or internal (if the source is inside the body).

The external dose from strontium radionuclides emitting beta radiation outside the body is normally of little health concern unless the radioactive material contacts the skin. Skin contact can allow the beta radiation to pass through the epidermis to live dermal tissue where it becomes a major contributor to a radiostrontium-generated radiation dose to the skin. At very high doses, the beta radiation can cause such adverse effects as erythema, ulceration, or even tissue necrosis.

Once radioactive strontium is internalized, it is absorbed, distributed, and excreted in the same manner as stable strontium; the chemical similarity of strontium to calcium results in deposition of radioactive strontium in bone. The internal radiation dose from strontium is actually a measure of the amount of energy that the beta emissions deposit in tissue. The short-range beta radiation produces a localized dose, generally to bone and the soft tissues adjacent to bone; hemopoietic bone marrow is the most biologically significant target of radioactive strontium emissions. Molecular damage results from the direct ionization of atoms that are encountered by beta radiation and by interactions of resulting free radicals with nearby atoms. Tissue damage results when the molecular damage is extensive and exceeds the capacity of natural repair mechanisms.

In radiation biology, the term *absorbed dose* is the amount of energy deposited by radiation over time per unit mass of tissue, expressed in units of rad or gray (Gy) (see Appendix D for a detailed description of principles of ionizing radiation). The term *dose equivalent* refers to the biologically significant dose, which is determined by multiplying the absorbed dose by a quality factor for the type and energy of the radiations involved. Dose equivalent is expressed in units of rem or sievert (Sv). The quality factor is considered to be unity for the beta radiation emitted from ^{90}Sr and ^{89}Sr, so for these radionuclides, the absorbed dose (in rad or gray) is numerically identical to the dose equivalent (in rem or sievert). The dose

equivalent from internalized strontium radionuclides is estimated using the quantity of material entering the body (via ingestion or inhalation), the biokinetic parameters for strontium (retention, distribution, and excretion), the energies and intensities of the beta radiation emitted, and the parameters describing the profile of absorbed radiation energy within the body. If, for example, a person ingests a given activity of radiostrontium (measured in curies [Ci] or becquerels [Bq]), the tissues of the body will absorb some of the energy of the emitted beta radiation in a pattern reflecting the kinetics of distribution and elimination of the ingested radiostrontium, the rate at which the radioactive isotope decays to a stable form, and the age of the person at the time of ingestion (which affects both the biokinetics of the radiostrontium and the potential length of time over which the tissues can be exposed to the radiation). Each tissue, therefore, can receive a different dose equivalent. The total dose equivalent for the body will reflect the integration of the dose equivalents for the various tissues using a weighting scheme for the relative sensitivities of tissues and organs.

The EPA has published a set of internal dose conversion factors for standard persons of various ages (newborn; 1, 5, 10, or 15 years of age; and adult) in its Federal Guidance Report No. 13 supplemental CD (EPA 2000e). For example, the EPA has estimated that the dose equivalents following ingestion of 1 Bq of ^{90}Sr are 2.77×10^{-8} and 2.77×10^{-7} Sv, respectively, for the adult and infant (assuming an integration time of 50 years for an adult following the initial exposure). For ^{89}Sr, these values are 2.57×10^{-9} Sv and 3.59×10^{-8} Sv, respectively. Age-specific dose coefficients for inhalation and ingestion of any of the radioactive isotopes of strontium by the general public can be found in ICRP publications 71 (ICRP 1995) and 72 (ICRP 1996), respectively. Dose coefficients for inhalation and ingestion of strontium radionuclides can be found in U.S. EPA Federal Guidance Report No. 11 (EPA 1988). Dose coefficients for external exposure to radioisotopes of strontium in air, surface water, or soil contaminated to various depths can be found in U.S. EPA Federal Guidance Report No. 12 (EPA 1993b).

Unless otherwise stated, exposure levels in the text are presented per kg of body weight. In Appendix D, standard and SI units of radiation activity (curies, becquerels) and absorbed dose (rad, gray) are compared in Table D-5 and are discussed in Sections D.2.2 Half-Life and Activity and D.3.1.2 Absorbed Dose and Absorbed Dose-Rate.

3.2 DISCUSSION OF HEALTH EFFECTS OF STABLE STRONTIUM BY ROUTE OF EXPOSURE

Section 3.2 discusses the chemical toxicity of strontium. Radiation toxicity resulting from exposure to radiostrontium is discussed in Section 3.3.

To help public health professionals and others 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, reproductive, developmental, genotoxic, and carcinogenic effects). These data are discussed in terms of three exposure periods: acute (14 days or less), 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 no-observed-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. "Serious" effects are those that evoke failure in a biological system and can lead to morbidity or mortality (e.g., acute respiratory distress or death). "Less serious" effects are those that are not expected to cause significant dysfunction or death, or those whose significance to the organism is not entirely clear. ATSDR acknowledges that a considerable amount of judgment may be required in establishing whether an end point should be classified as a NOAEL, "less serious" LOAEL, or "serious" LOAEL, and that in some cases, there will be insufficient data to decide whether the effect is indicative of significant dysfunction. However, the Agency has established guidelines and policies that are used to classify these end points. ATSDR believes that there is sufficient merit in this approach to warrant an attempt at distinguishing between "less serious" and "serious" effects. The distinction between "less serious" effects and "serious" effects is considered to be important because it helps the users of the profiles to identify levels of exposure at which major health effects start to appear. LOAELs or NOAELs should also help in determining 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 Levels of Significant Exposure (LSE) tables and figures may differ depending on the user's perspective. Public health officials and others 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 (LOAELs) or exposure levels below which no

adverse effects (NOAELs) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels or MRLs) may be of interest to health professionals and citizens alike.

Levels of exposure associated with carcinogenic effects (Cancer Effect Levels, CELs) of strontium are indicated in Tables 3-2, 3-3, and 3-4 and Figures 3-2 and 3-3. Because cancer effects could occur at lower exposure levels, Figures 3-2 and 3-3 also show a range for the upper bound of estimated excess risks, ranging from a risk of 1 in 10,000 to 1 in 10,000,000 (10^{-4} to 10^{-7}), as developed by EPA.

Estimates of exposure levels posing minimal risk to humans (Minimal Risk Levels or MRLs) have been made for strontium. An MRL is defined as an estimate of daily human exposure to a substance that is likely to be without an appreciable risk of adverse effects (noncarcinogenic) over a specified duration of exposure. MRLs are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration within a given route of exposure. MRLs are based on noncancerous health effects only and do not consider carcinogenic effects. MRLs can be derived for acute, intermediate, and chronic duration exposures for inhalation and oral routes. Appropriate methodology does not exist to develop MRLs for dermal exposure.

Although methods have been established to derive these levels (Barnes and Dourson 1988; EPA 1990), 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.

A User's Guide has been provided at the end of this profile (see Appendix B). This guide should aid in the interpretation of the tables and figures for Levels of Significant Exposure and the MRLs.

3.2.1 Inhalation Exposure

3.2.1.1 Death

The only studies located regarding death in humans following inhalation exposure to stable strontium are related to strontium chromate. Strontium chromate has been implicated as a cause of increased deaths from lung cancer in occupational studies (Davies 1979, 1984) (see Section 3.2.1.7). The toxicity of strontium chromate is attributed to hexavalent chromium ion, which enters lung cells and is metabolized to a genotoxic agent. Strontium itself contributes to solubility of strontium chromate, but any associated health effect is expected to be masked by that of the chromate. No studies were located regarding death in animals following inhalation exposure to stable strontium.

3.2.1.2 Systemic Effects

No data are available regarding systemic effects following inhalation exposure to stable strontium for which the exposure levels are known. For that reason, no LSE table has been created for stable strontium. No studies were located that described gastrointestinal, hematological, hepatic, renal, body weight, metabolic, endocrine, dermal, or ocular effects in humans or animals following inhalation exposure to stable strontium.

Respiratory Effects. The only report of adverse respiratory effects in humans resulting from the inhalation of stable strontium is a case report of an anaphylactic reaction to smoke from an ignited roadside flare (Federman and Sachter 1997). The flare contained approximately 75% strontium nitrate (31% strontium), among other known irritating ingredients, and the exact contribution of strontium to the effect is uncertain. The anaphylactic reaction to the smoke included coughing, wheezing, and severe respiratory difficulties. This case report is discussed in Section 3.2.1.3 Immunological and Lymphoreticular Effects. No other reports were located describing longer-term respiratory effects following inhalation of stable strontium compounds by humans or animals.

Cardiovascular Effects. A single study documented adverse cardiovascular effects in humans resulting from the inhalation of stable strontium in smoke from an ignited roadside flare (Federman and Sachter 1997). Extreme tachycardia resulted as part of an anaphylactic reaction to the smoke, which contained ~31% strontium as strontium nitrate, in addition to other known irritants. The role of strontium

in this reaction is not established. No other reports were located describing longer-term cardiovascular effects following inhalation of stable strontium compounds by humans or animals.

3.2.1.3 Immunological and Lymphoreticular Effects

The single located study of immunological effects in humans following inhalation exposure to stable strontium is a case report of an anaphylactic reaction to smoke from an emergency roadside flare (Federman and Sachter 1997). A 35-year-old female paramedic developed a sudden, severe reaction upon inhaling fumes from a flare that contained approximately 31% strontium as strontium nitrate. Initial symptoms included coughing, wheezing, and shortness of breath that was not responsive to albuterol, epinephrine, or steroids; recovery ultimately required sedation, intubation, and intensive care for several days. Although the paramedic had been unsymptomatic before the incident, her medical history included several significant contributory factors: rheumatic fever requiring penicillin prophylaxis until age 12, a severe anaphylactic reaction to a bee sting at age 23, and adult-onset asthma at age 32. The ingredients of the flare (Road Fusee®; Standard Fusee Corporation, Easton, Maryland) included ±75% strontium nitrate (~31% strontium), ±10% potassium perchlorate, ±10% sulfur, and ±10% sawdust/oil binder. Upon combustion, each of these would yield products known to be irritating to the respiratory tract: strontium oxide, nitrous oxide, potassium oxide, chlorine gas, sulfur dioxide, and particulates. Thus, the exact contribution of strontium to the development of anaphylaxis in this case is uncertain. However, see Section 3.6.2 for a possible mechanism by which strontium could contribute to an immunological effect. No studies were located regarding immunological effects in animals following inhalation exposure to stable forms of strontium.

No studies were located regarding the following effects in humans or animals following inhalation exposure to stable strontium:

3.2.1.4 Neurological Effects

3.2.1.5 Reproductive Effects

3.2.1.6 Developmental Effects

3.2.1.7 Cancer

There were no reports regarding cancer in humans or animals resulting from inhalation exposure to stable strontium compounds except for strontium chromate. In an epidemiological study, no excess risk for lung cancer was found among workers in two Japanese factories who were involved in the production of strontium chromate pigment (Kano et al. 1993). However, exposures to strontium chromate in the factories may have been low because of suitable industrial hygiene procedures. Another epidemiological study examined workers in British chromate pigment manufacturing plants (Davies 1979, 1984). In one factory, both lead and zinc chromate were produced until 1976, and strontium chromate was produced from 1950 to 1968. For lung cancer deaths in workers exposed to 'high' and 'medium' levels of chromates before 1961, when industrial hygiene improvements were introduced, the observed/expected ratio (O/E) was 6/1.61, with a standard mortality ratio (SMR) of 373 ($p<0.01$). For workers exposed to 'high' and medium' levels from 1961 to 1967, the values were O/E=5/089, SMR=562 ($p<0.01$). The contribution of strontium to toxicity in these studies was not addressed.

No standard inhalation study of strontium chromate in animals was located. However, Levy et al. (1986) used an intrabronchial pellet implantation technique to evaluate the carcinogenicity of 23 different commercially available chromates, including two batches of strontium chromate. Metal pellets were coated with a mixture of cholesterol and strontium chromate and implanted into the left bronchus of male and female young rats (100 per group). Of 198 lungs treated with strontium chromate, 105 (53%) had a primary keratinizing squamous carcinoma of the bronchial epithelium. The authors indicated that carcinogenicity was associated with sparingly soluble hexavalent chromium compounds such as strontium, calcium, or zinc chromates.

3.2.2 Oral Exposure

There are no direct dose-response data for adverse effects of exposure to stable strontium in humans, but one epidemiological study suggests that the skeletal toxicity observed at high oral doses in juvenile animals may be relevant to humans (see Musculoskeletal Effects). At low exposure levels, ingestion of stable strontium poses no harm to organisms with access to adequate calcium, phosphorus, and vitamin D. At higher exposure levels, especially under conditions of inadequate calcium, phosphorus, and vitamin D, stable strontium will interfere with normal bone development, causing 'strontium rickets' of variable severity.

3.2.2.1 Death

No deaths in healthy humans have been reported after oral exposure to stable strontium. Stable strontium caused death in laboratory animals only at doses that are very high compared to normal human exposure. In acute exposure studies in mice, the oral LD_{50} for strontium nitrate was reported to be 2,350 mg strontium/kg in males (Llobet et al. 1991a). For strontium chloride administered by gavage, the acute oral LD_{50} in albino mice was reported to be 2,900 mg strontium/kg for males and 2,700 mg strontium/kg for females (Ghosh et al. 1990).

In intermediate-duration animal studies, ingestion of excess stable strontium resulted in increased mortality. The premature death rate was 40% among weanling male Sprague-Dawley rats fed stable strontium (form not specified) at a dose level of 565 mg strontium/kg/day for 43 days (Johnson et al. 1968). Weanling male Wistar rats exposed to strontium phosphate in the diet at a dose level of 2,820 mg strontium/kg/day for 4–6 weeks had a mortality rate of 30%, but no mortality occurred at 580 or 1,270 mg strontium/kg/day (Kshirsagar 1976). From an analysis of a pair-fed group (food intake matched to the high-dose group), the author concluded that the increased mortality in the high-dose group was not related to reduced food intake, but rather to the ingestion of strontium. No studies were located regarding death in animals following chronic-duration oral administration of stable strontium.

All reliable LOAEL values for death from stable strontium in each species and duration category are recorded in Table 3-1 and plotted in Figure 3-1.

3.2.2.2 Systemic Effects

No studies were located regarding dermal or ocular effects in humans or animals following oral exposure to stable strontium. The highest reliable NOAEL and all LOAEL values for the systemic effects from oral exposure to stable strontium in each species and duration category are shown in Table 3-1 and plotted in Figure 3-1.

Respiratory Effects. No studies were located regarding respiratory effects in humans following oral exposure to stable strontium. No studies were located regarding acute or chronic respiratory effects in animals following exposure to stable forms of strontium. In one intermediate-duration study, respiratory difficulties were noted in rats following lethal ingestion of 565 mg strontium/kg/day of stable strontium

Table 3-1 Levels of Significant Exposure to Strontium - Chemical Toxicity - Oral

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
	ACUTE EXPOSURE						
	Death						
1	Mouse (albino)	once (GW)				2900 M (LD50) 2700[c] F (LD50)	Ghosh et al. 1990 Strontium chloride
2	Mouse (NS)	NR (NS)				2350 M (LD50)	Llobet et al. 1991a Strontium nitrate
	Systemic						
3	Rat (Wistar)	2 wks ad lib (F)	Hemato	110			Kroes et al. 1977 Strontium chloride 6H2O
			Musc/skel	110			
			Hepatic	110			
			Renal	110			
			Bd Wt	110			

Table 3-1 Levels of Significant Exposure to Strontium - Chemical Toxicity - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
4	Rat (Wistar)	2 wks ad lib (F)	Gastro		3000 M (small intestine: decr acid & alkaline phosphatase; reversible)		Kshirsagar 1976 Strontium phosphate
			Musc/skel		3000 M (bone: incr alkaline phosphatase; reversible)		
			Hepatic		3000 M (incr alk phosphatase, decr acid phosphatase; reversible)		
			Bd Wt			3000 M (bd wt gain decr 62%)	
	INTERMEDIATE EXPOSURE						
	Death						
5	Rat (Sprague-Dawley)	PND 21-64 ad lib (F)				565 M (40% mortality)	Johnson et al. 1968 (NS)
6	Rat (Wistar)	4-6 wks ad lib (F)				2820 M (30% mortality)	Kshirsagar 1976 Strontium phosphate

Table 3-1 Levels of Significant Exposure to Strontium - Chemical Toxicity - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
	Systemic						
7	Rat (Sprague-Dawley)	8 wks ad lib (W)	Musc/skel	168 M			Grynpas et al. 1996 (NS)
			Bd Wt	168 M			
			Metab	168 M			
8	Rat (Sprague-Dawley)	PND 21-64 ad lib (F)	Resp			565 M (unspecified difficulties)	Johnson et al. 1968 NS
			Musc/skel			565 M (rickets)	
9	Rat (Wistar)	90 d ad lib (F)	Hemato	166 F			Kroes et al. 1977 Strontium chloride 6H2O
			Musc/skel	166 F			
			Hepatic	166 F			
			Renal	166 F			
			Bd Wt	166 F			
			Metab	166 F			

Table 3-1 Levels of Significant Exposure to Strontium - Chemical Toxicity - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
10	Rat (Wistar)	4-6 wks ad lib (F)	Cardio			2820 M (hemorrhage)	Kshirsagar 1976 Strontium phosphate
			Gastro	580 M	1270 M (small intestine: reversible decr alkaline phosphatase)		
			Musc/skel	580 M	1270 M (bone: incr alkaline phosphatase, reversible)		
			Hepatic	1270 M	2820 M (reversible decr alkaline phosphatase)		
			Bd Wt	580 M	1270 M (reversible decr in wt gain)		
11	Rat (Sprague-Dawley)	9 wks ad lib (W)	Musc/skel	524 M	633 M (bone calcification rate decr by 17%)		Marie et al. 1985 Strontium chloride
			Bd Wt	633 M			
			Metab	633 M			

Table 3-1 Levels of Significant Exposure to Strontium - Chemical Toxicity - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
12	Rat (Wistar)	4 wk ad lib (F)	Musc/skel			1970 M (tibiae: length decr 33%, epiphyseal plates 5 x wider, decr mineralization)	Matsumoto 1976 Strontium carbonate
			Bd Wt			1970 M (bd wt gain decr by 60%)	
13	Rat (Wistar)	27 d ad lib (F)	Gastro	102	510 F (20% decr net intestinal Ca2+ absorption)		Morohashi et al. 1994 Strontium carbonate
			Musc/skel	102	510 F (decr bone formation, resorption, Ca2+ content of bone)		
			Bd Wt	510 F			
			Metab	102 F	510 F (hypocalcemia)		
14	Rat (Sprague-Dawley)	3 wk ad lib (F)	Musc/skel		500 M (abnormal bone mineralization)		Neufeld and Boskey 1994 Strontium carbonate
			Bd Wt	500 M			
			Metab	500 M			

Table 3-1 Levels of Significant Exposure to Strontium - Chemical Toxicity - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
15	Rat (England Wright Y)	PND 21-41 ad lib (F)	Musc/skel			1850 M (epiphyseal cartilage histopathology)	Reinholt et al. 1984 (NS)
			Bd Wt			1850 M (28% decr bd wt gain)	
			Metab	1850 M			
16	Rat (NS)	20 d ad lib (F)	Musc/skel	140 F[b]	550 F (tibial epiphyseal cartilage abnormally wide)		Storey 1961 Strontium carbonate
			Bd Wt	1460 F		2220 F (24% decr bd wt gain)	
			Metab	4975 F			
17	Rat (NS)	20 d ad lib (F)	Musc/skel	690 F	1370 F (tibial epiphyseal cartilage abnormally wide; incr metaphyseal osteoid)		Storey 1961 Strontium carbonate
			Bd Wt	2750 F			
			Metab	2750 F			

Table 3-1 Levels of Significant Exposure to Strontium - Chemical Toxicity - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
18	Rat (NS)	up to 7 months ad lib (F)	Musc/skel			2160 (rickets)	Storey 1962 Strontium carbonate
			Bd Wt			2160 (30% decr bd wt gain)	
19	Rat (NS)	>7 mo ad lib (F)	Musc/skel			1570 (rickets: abnormal bone mineralization)	Storey 1962 Strontium carbonate
20	Rat (Sprague-Dawley)	26 d ad lib (F)	Musc/skel			1520 M (rickets)	Svensson et al. 1987 Strontium chloride
			Endocr	1520 M			
			Bd Wt		1520 M (16% decr bd wt gain)		
			Metab	1520 M			
21	Mouse (C57BL/6J)	29 d ad lib (W)	Musc/skel		350 M (11% decr number of osteoclasts; decr bone resorption; 10% incr osteoid surface)		Marie and Hott 1986 Strontium chloride
			Bd Wt	350 M			
			Metab	350 M			

Table 3-1 Levels of Significant Exposure to Strontium - Chemical Toxicity - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
	Neurological						
22	Rat (Sprague-Dawley)	PND 21-64 (F)				565 M (paralysis of hindlimbs)	Johnson et al. 1968 NS

[a] The number corresponds to entries in Figure 3-1.

[b] Used to derive an intermediate oral MRL of 2.0 mg/kg/day. The MRL was derived by dividing the NOAEL by an uncertainty factor of 30(10 for extrapolation from animals to humans, and 3 for human variability), and by a modifying factor of 3(for limited endpoint examination and short duration).

[c] Differences in levels of health effects and cancer effects between males and females are not indicated in Figure 3-2. Where such differences exist, only the levels of effect for the most sensitive gender are presented.

Ad lib - ad libitum; Bd Wt = body weight; Cardio = cardiovascular; d = day(s); decr = decreased; (F) = food; Gastro = gastrointestinal; (GW) = gavage in water; Hemato = hematological; hr = hour(s); incr = increased; LD50 = lethal does, 50% kill; LOAEL = lowest-observed-adverse-effect level; Metab = metabolic; Musc/skel = musculoskeletal; NOAEL = no-observed-adverse-effect level; NR = not reported; (NS) = not specified; PND = post natal day; wk = week(s); x = time(s); yr = year(s)

Figure 3-1 Levels of Significant Exposure to Strontium - Chemical Toxicity - Oral

Acute (≤14 days)

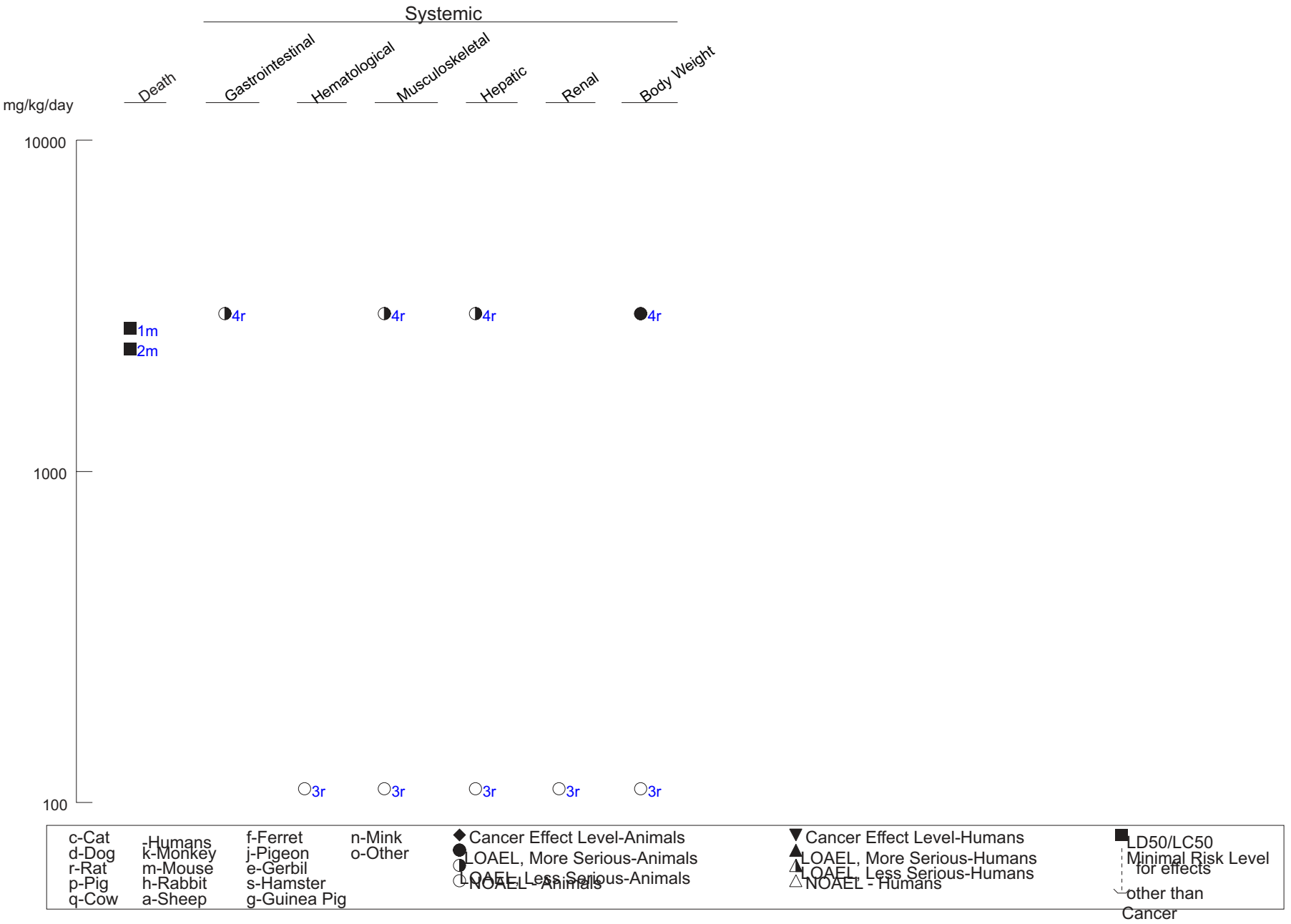


Figure 3-1 Levels of Significant Exposure to Strontium - Chemical Toxicity - Oral (*Continued*)

Intermediate (15-364 days)

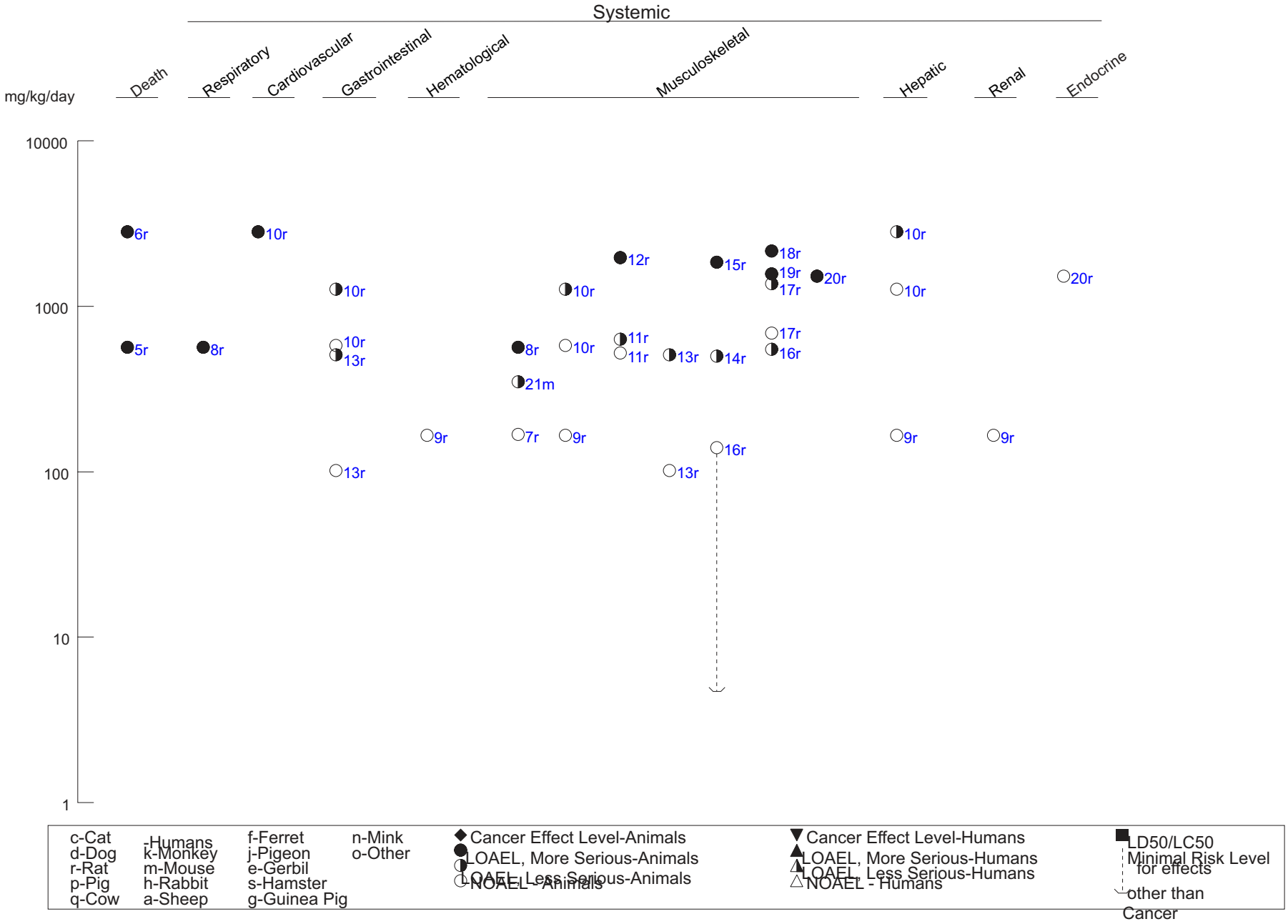
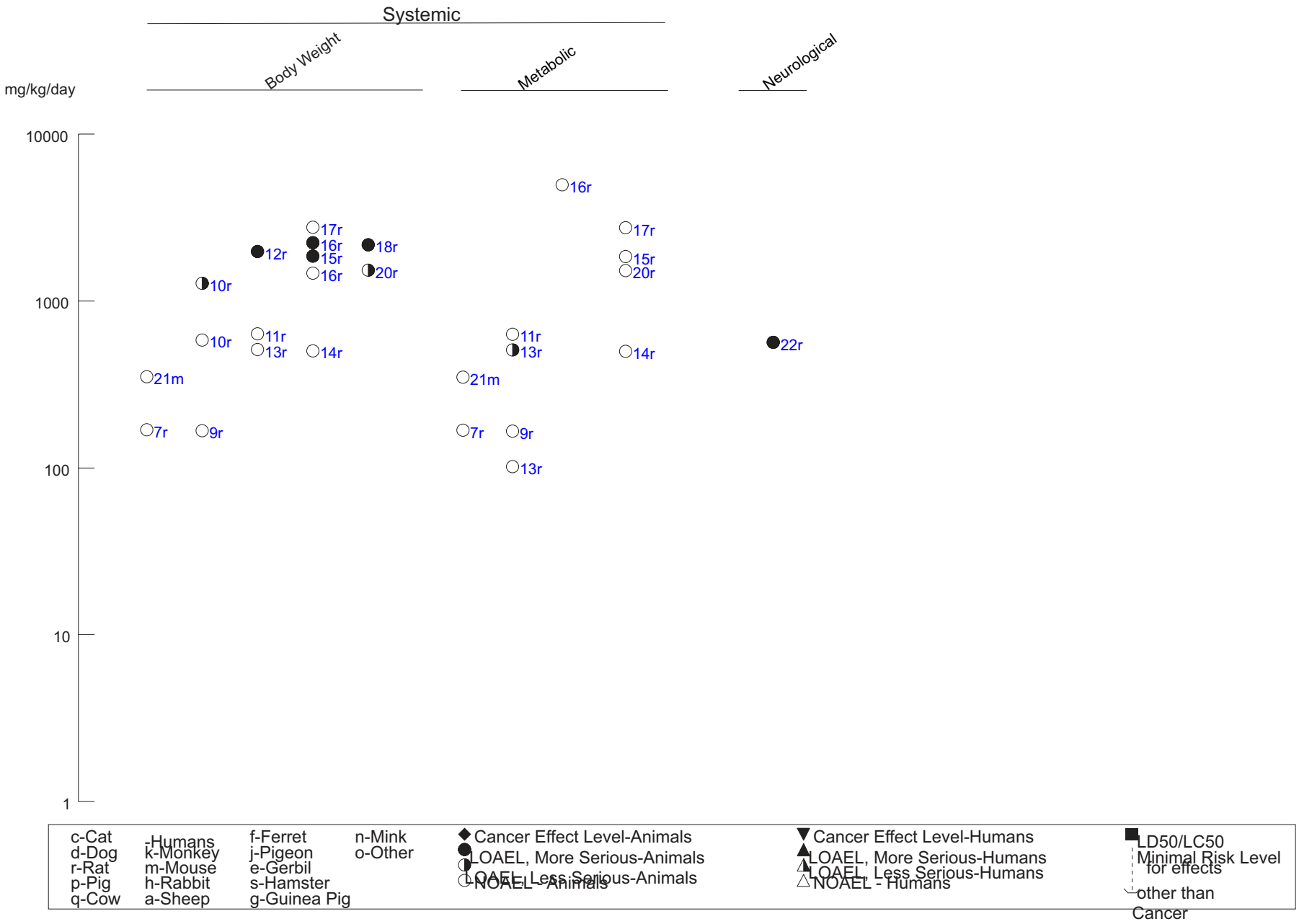


Figure 3-1 Levels of Significant Exposure to Strontium - Chemical Toxicity - Oral (*Continued*)

Intermediate (15-364 days)



(form unspecified) for 4–6 weeks (Johnson et al. 1968). No description of the respiratory effects or incidence data were reported.

Cardiovascular Effects. No studies were located regarding cardiovascular effects in humans following acute- or intermediate-duration oral exposure to stable strontium.

One epidemiological study examined the relationship between trace metals, including strontium, in drinking water and the rates of various kinds of vascular disease in 24 communities in the lowest quartile of the economic scale in Texas (Dawson et al. 1978). The concentration of strontium was measured in samples of drinking water and 2,187 urine samples from subjects (aged 5–97 years) in families that had resided within their respective communities for at least 10 years. There was a significant correlation between mean strontium levels in drinking water and in the urine. However, the only statistically significant product-moment correlationship for strontium (in urine and in drinking water) was for a decreased community mortality rate (in people over 45 years old) for hypertension with heart disease. There was no correlation found between strontium and mortality from arteriosclerotic and degenerative heart disease, other heart diseases, hypertension, general arteriosclerosis, or vascular diseases of the central nervous system.

No studies were located regarding cardiovascular effects after acute- or chronic-duration oral exposure in animals. In male weanling Wistar rats (5–6 per group) given strontium as strontium phosphate in the diet for 4–6 weeks, hemorrhage (unspecified) occurred at 2,820 mg strontium/kg/day, possibly related to the increased mortality at this dose level, but not at or ≤1,270 mg strontium/kg/day (Kshirsagar 1976).

Gastrointestinal Effects. No studies were located regarding gastrointestinal effects in humans following oral exposure to stable strontium.

No studies were located regarding gastrointestinal effects in animals following chronic-duration oral exposure to various forms of stable strontium. Acute- and intermediate-duration oral studies in animals have examined gastrointestinal effects that would be likely to influence calcium and phosphorus metabolism. Decreases in acid and alkaline phosphatase activities were observed in the small intestine of 5–6 male weanling (21 days old) Wistar rats given 3,000 mg strontium/kg/day as strontium phosphate for 2 weeks (Kshirsagar 1976). These effects were reversed by giving the rats a normal low-strontium diet for 2 weeks. The biological significance of the decreased phosphatase activities is not known. Studies in

chickens first demonstrated the relationship between strontium toxicity, calcium, and vitamin D. In male white Leghorn chickens raised on a diet deficient in vitamin D for the first 2 weeks of life, ingestion of >2,300 mg strontium/kg/day as strontium carbonate in a low-calcium, low-vitamin D diet for 11–14 days, affected calcium transport in the duodenum (Omdahl and DeLuca 1972). Strontium ingestion reduced the duodenal activation of vitamin D_3 (conversion of 25-hydroxycholecalciferol to 1,25-dihydroxy-cholecalciferol), reduced the activity of calcium binding protein, and reduced the absorption of calcium by the duodenum. Similar effects were observed in chickens given excess strontium in a diet with adequate vitamin D, but deficient in calcium (0.01%) (Corradino and Wasserman 1970; Corradino et al. 1971a, 1971b). In addition, excess strontium ingestion significantly reduced the absorption of glucose, histidine, and alanine by the duodenum to levels typical of rachitic (vitamin D-deprived) chickens (Corradino et al. 1971b). The effects of strontium on calcium transport by the duodenum were reversed by transferring chickens to a normal low-strontium diet containing adequate amounts of vitamin D_3 and calcium. The chicken data are not included in Table 3-2, because the physiological rates are likely to be very different from mammals, and also because health risk assessment methodology is currently limited to mammals. However, these phenomena were confirmed in a recent study in rats (Armbrecht et al. 1998). Six days on a diet low in calcium, but containing 0.8% strontium, was sufficient to suppress the serum levels of activated vitamin D, the concentrations of calbindin D protein (two calcium-binding protein induced by vitamin D; see Sections 3.6.1 and 3.6.2), and the rates of calcium transport in the duodenum of young, adult, and old rats.

In male weanling (3 weeks old) Wistar rats (5–6 per group) given strontium phosphate in the diet for 6 weeks, a decrease in alkaline phosphatase activity in the small intestine occurred at 1,270 mg strontium/kg/day, but not at 580 mg strontium/kg/day (Kshirsagar 1976). This decrease in enzyme activity was partly reversed by feeding the rats a normal low-strontium diet for 2 weeks. As mentioned above, the biological significance of these changes in phosphatase activity is not known. In slightly older female juvenile Wistar rats (36 days old, 6–8 per group) that ingested 510 mg strontium/kg/day as strontium carbonate for 27 days, the net intestinal absorption of calcium was reduced by 20%, but no effects occurred at 100 mg strontium/kg/day (Morohashi et al. 1994). In male white Leghorn chickens fed 255 mg strontium/kg/day (probably as carbonate) in a diet low in vitamin D_3 for the first 16 days after hatching, the conversion of 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol and the transport of calcium were suppressed in the duodenum (Omhdahl and DeLuca 1971). This study is omitted from Table 3-1 because of probable differences in physiology.

Hematological Effects. No studies were located regarding hematological effects in humans following oral exposure to stable strontium.

No studies were located regarding hematological effects in animals following chronic-duration oral exposure to stable strontium. In adult Wistar rats given up to 110 mg strontium/kg/day as strontium chloride in the diet for 2 weeks, the total number of erythrocytes was slightly elevated in both sexes, and the leucocyte count was slightly elevated in males at the highest dose level at termination (Kroes et al. 1977). However, since the results were not reported quantitatively, the significance of this information is uncertain. No hematological changes were observed among weanling Wistar rats fed up to 166 mg strontium/kg/day as strontium chloride in the diet for 90 days (Kroes et al. 1977). However, the relatively high level of calcium (0.85%) in the diet given to these animals may have reduced absorption and therefore the effect of strontium.

Musculoskeletal Effects. No studies were located regarding musculoskeletal effects in humans after acute-duration oral exposure to stable strontium. The only long-term human exposure study is an epidemiological study that was carried out in the Ulaş Health Region of Sivas, Turkey (Özgür et al. 1996). This region has a high prevalence of childhood rickets, 32% compared to 4.4% nationally among children aged up to 5 years, and the study sought to determine whether higher levels of strontium in the soil might be a contributing factor. Soils surrounding 55 villages were characterized as to strontium concentration (Group 1, >350 ppm; Group 2, <350 ppm). A total of 2,140 children (ages 6–60 months) from these localities (613 in Group 1 and 1,527 in Group 2) were examined for one or more signs of rickets: craniotabes (localized craniomalacia or thinning of cranium), rachitic rosary (beadlike growths at the ends of ribs where they join cartilage), conspicuous bulging at the wrist, bony deformities of the legs (bowleg, knock-knee), and delayed closure of the fontanelles. A significantly higher proportion of Group 1 children had one or more rachitic signs than those in Group 2: 37.5 vs 19.5%. In addition, the severity of disease (number of rachitic signs per child) was proportionally higher in Group 1 ($p<0.001$). For each cohort, the incidence of rickets was higher in Group 1 than in Group 2 and the differences were statistically significant for ages 6–12, 13–18, 25–36, and 37–48 months (odds ratios 1.66–2.55). When the duration of breast feeding was considered, the incidence of rickets within the two groups did not differ for children breast fed for 24 months or longer. However, for shorter periods of breast feeding, between 0 and 24 months, the incidence of rickets was significantly higher in Group 1 (odds ratios 1.79–3.14). The implication of this study is that breast feeding may be protective against strontium toxicity in nursing infants, probably by providing both calcium and protein, both of which tend to reduce the incorporation of strontium into bone (see Sections 3.10, 3.11, and 3.12.2). The authors attributed the higher incidence of

rickets in Group 1 children to their diet, which, after weaning, is mainly based on grains grown in strontium-rich soil.

No studies were located regarding musculoskeletal effects in animals after chronic-duration oral exposure to stable strontium. Acute- and intermediate-duration studies in animals documented significant adverse effects of strontium on bone that were especially severe in the young. In an acute-duration study, there was no effect on bone in groups of adult SPF Wistar rats that ingested up to 110 mg strontium/kg/day as strontium chloride in the diet for 2 weeks (Kroes et al. 1977). Strontium was detected in bone following ingestion of 11 or 110 mg/kg/day, but not at lower doses (0.1 or 1.0 mg/kg/day). Among male weanling (21 days old) Wistar rats that ingested 3,000 mg strontium/kg/day as strontium phosphate in the diet for 2 weeks, alkaline phosphatase activity was significantly increased in bone compared to controls (Kshirsagar 1976). The author speculated that the observed increase in alkaline phosphatase activity may have been related to a stimulation of osteoblasts, which secrete osteoid and have a high alkaline phosphatase content. In acute studies on young chickens fed 2,300–2,400 mg/kg/day of strontium, and an inadequate level of calcium, severe defects in bone organization and decreased mineralization were observed within 1 or 2 weeks (Corradino and Wasserman 1970; Corradino et al. 1971a, 1971b; Omdahl and DeLuca 1972): abnormally wide hypertrophic cartilaginous zone and impaired endochondral ossification (the removal of hypertrophic cartilage and its replacement by bone). As noted above, the chicken data are omitted from Table 3-1.

Numerous abnormalities of bone structure and bone mineralization were observed in weanling male Sprague-Dawley rats (100–125 g) that ingested 500 mg strontium/kg/day as strontium carbonate in the diet for 3 weeks (Neufeld and Boskey 1994). In strontium-fed rats, the ash weight (mineral content) of metaphyseal bone was reduced and the complexed acidic phospholipid content (lipid nucleator of bone mineral) was significantly higher than in controls. Large areas of nonmineralized bone (osteoid) were observed in epiphyseal bone and secondary spongiosa. The epiphyseal plates were abnormally wide and the metaphyses were abnormally long and dense. The diaphyses contained localized areas of decreased bone density. The primary spongiosa of the proximal tibia was longer and the trabeculae was disorganized and apparently disconnected from the overlying calcified cartilage. The authors suggested that since the levels of complexed acidic phospholipids were high and vitamin D deficiency is known to increase complexed acidic phospholipid levels, that the effect of strontium was probably not mediated through its effect on vitamin D. They suggested the binding of strontium to the surface of initial hydroxyapatite crystallites reduced their further proliferation, resulting in a smaller crystal size.

Similarly, significant abnormalities of bone organization occurred in five weanling (21 days old) male England Wright Y rats that ingested 1,850 mg strontium/kg/day (form unspecified) for 20 days in a diet sufficient in calcium, phosphorus, and vitamin D (Reinholt et al. 1984). In treated rats, the mean thickness of the epiphyseal growth plate was 70% larger than normal. In the epiphyseal regions of long bones, the volume of each zone was larger than its normal counterpart, and in addition, the relative sizes were altered; the proportional volumes of the resting, proliferative, and calcifying zones were significantly smaller and that of the hypertrophic zone was significantly larger than normal. There was an increase in the volume of extracellular matrix in bone, suggested to be associated with a reduced rate of extracellular matrix vesicle degradation. Another study from this laboratory examined the biochemistry of epiphyseal cartilage in rats treated as above (Reinholt et al. 1985). In strontium-treated rats, alterations were observed in the proteoglycan composition (slightly higher galactosamine content), chondroitin sulfate chain lengths (larger), regional distributions of large and small chondroitin sulfate peptides, and regional distributions of both non-sulfated chondroitin sulfate disaccharides and hyaluronic acid-disaccharides. The authors suggested that these strontium-induced alterations in cartilage matrix might affect the process of mineralization.

No effects on bone histology were observed in young female rats (40–60 g) that were fed 140 mg strontium/kg/day as strontium carbonate for 20 days, but histological abnormalities were detected at doses between 550 and 4,975 mg/kg/day (Storey 1961). Alterations in the appearance of the cartilage plate (irregular, thicker, with areas of uncalcified bone matrix in the distal ends of the metaphyseal trabeculae and proximal end of the diaphysis) were observed at 550 mg strontium/kg/day. Irregularities in the organization of the cells of hypertrophic zone (distorting the usual parallel arrangement of intercellular matrix columns), in the pattern of calcification, and in deposition of osteoid were more conspicuous with increasing dose. At higher doses, bands of uncalcified cartilage matrix were isolated between areas of osteoid tissue. In tibias, the dry weight, ash weight, ash percentage, and calcium in ash were significantly reduced with increased strontium intake. In the same study, adult female rats given doses of 170–2,750 mg strontium/kg/day exhibited milder effects in bone. Histological changes in the tibia (thicker epiphyseal cartilage, increased width of metaphyseal osteoid seams) were noted at 1,370 or 2,750 mg strontium/kg/day only. Other significant effects seen only at 2,750 mg strontium/kg/day included the deposition of osteoid tissue near vascular canals, a reduction in the area of bone resorption, and reductions in the dry weight, ash weight, ash percentage, and calcium in ash of bone (Storey 1961).

A 24% reduction in bone formation rate, 28% reduction in bone resorption rate (based on ^{45}Ca uptake), and a significantly reduced calcium content in ashed femurs, but no change in ash weight were observed

after female juvenile Wistar rats (36 days old) ingested 510 mg strontium/kg/day as strontium carbonate in the diet for 27 days (Morohashi et al. 1994). These rats were also significantly hypocalcemic. No effects were observed at 50 or 100 mg strontium/kg/day other than an unexplained increase in calcium content of bone at 50 mg strontium/kg/day (Morohashi et al. 1994). Minor bone effects occurred in 21-day-old male C57BL/6J mice after ingesting 350 mg strontium/kg/day as strontium chloride in the drinking water for 29 days (Marie and Hott 1986). Strontium had no significant effect on tibial length or bone mineral content (percent ash, calcium, or phosphorus). In vertebrae, strontium had no effect on the osteoblastic surface (percent endosteal surface showing plump osteoblasts), bone matrix apposition rate, osteoid seam thickness (average width of all endosteal osteoid seams), or calcified bone volume. However, exposure to strontium resulted in a 10% increase in osteoid surface (percent endosteal surface covered by an osteoid seam) and an 11% reduction in the number of active osteoclasts.

There was radiographic evidence of abnormally thickened epiphyseal cartilage plates in the long bones of weanling male Wistar rats exposed to strontium phosphate in the diet at a dose level of 2,820 mg strontium/kg/day for 4–6 weeks, but no effect at 580 mg strontium/kg/day and little effect at 1,270 mg strontium/kg/day (Kshirsagar 1976). Ingestion of 565 mg strontium/kg/day for 43 days resulted in several bone abnormalities in young Sprague-Dawley rats (Johnson et al. 1968). The level of sodium in bone was significantly lowered, and the level of potassium was significantly increased, and the overall index of bone mineralization (percent bone ash) was decreased. Unmineralized osteoid was visible in histological sections of vertebrae. Rats became rachitic and osteomalacic and exhibited paralysis of the hindlimbs.

Beneficial effects of a low dose of strontium were noted on bone mineralization, such as a 17% increase in mineral bone volume and a 70% increase in the number of bone forming sites, with no adverse effect on the hydroxyapatite mineral particle size in 28-day-old male Sprague-Dawley rats ingesting 168 mg strontium/kg/day in an unspecified form for 8 weeks (Grynpas et al. 1996) or in young SPF Wistar rats fed doses up to 166 mg strontium/kg/day as strontium chloride in the diet for 90 days (Kroes et al. 1977). Stimulation of calcified bone growth was noted among male weanling Sprague-Dawley rats ingesting between 316 and 524 mg strontium/kg/day as strontium chloride for 9 weeks, but reduced bone calcification was observed at 633 mg/kg/day (Marie et al. 1985). In male weanling Sprague-Dawley rats ingesting 1,520 mg strontium/kg/day for 26 days, epiphyseal growth plates had abnormally thick hypertrophic zones and impaired calcification and resorption at the metaphyseal side (Svensson et al. 1985, 1987). In addition, cartilage from strontium-treated rats contained 75% less calcium and had a 60% lower rate of synthesis of glycosaminoglycans and collagen. When 4-week-old male Wistar rats (50–60 kg body weight) were fed 1,970 mg strontium/kg/day as strontium carbonate in a diet low in calcium

(0.04%), bone mineralization was significantly affected (Matsumoto 1976). This study is presented in detail in Section 3.2.2.6 Developmental Effects, as an example of skeletal anomalies in young animals resulting from strontium ingestion.

In another intermediate-duration animal study, young (50–70 g) rats ingested 2,160 mg strontium/kg/day and adult rats ingested 1,570 mg strontium/kg/day as strontium carbonate for 7 months (Storey 1962). At 3 weeks, young rats developed a rachitic gait, and subsequently, some rats (numbers not specified) developed spinal kyphosis, bent tibiae, and irregular discolored enamel on anterior teeth. Histological abnormalities in long bone differentiation included reduced calcification, excess growth of epiphyseal cartilage, abnormal deposition of osteoid (unmineralized bone) in the metaphysis, fragmentation of the epiphyseal plates, and isolated nodules of cartilage. Osteoid accumulation was observed in the skull. Adult rats were affected by strontium ingestion in the same way, but to a lesser degree than young animals. Abnormal depositions of osteoid in long bones and skull were not as extensive as in young rats. The epiphyseal plate did not become fragmented. Tooth enamel was abnormally white and pitted.

Hepatic Effects. No studies were located regarding hepatic effects in humans following oral exposure to stable strontium.

No studies were located regarding hepatic effects in animals after chronic-duration oral exposure to stable strontium. In acute- and intermediate-duration studies, in which the diet contained adequate amounts of calcium and vitamin D, few hepatic effects were reported. No histological changes were observed in the livers of adult Wistar rats given up to 110 mg strontium/kg/day as strontium chloride in the diet for 2 weeks (Kroes et al. 1977). Acid phosphatase activity decreased by about 8% in the livers of 5–6 male weanling (21 days old) Wistar rats given 3,000 mg strontium/kg/day as strontium phosphate for 2 weeks (Kshirsagar 1976). However, this effect was reversible by feeding the rats a normal, low-strontium diet for 2 weeks. In male weanling Wistar rats, ingestion of strontium phosphate in the diet for 4–6 weeks resulted in a >26% decrease in hepatic alkaline phosphatase activity at 2,820 mg strontium/kg/day, but no decrease at 1,270 mg strontium/kg/day (Kshirsagar 1976). The biological significance of these small, but statistically significant, changes in hepatic phosphatase activity is not known. Among weanling male and female Wistar rats fed strontium chloride in the diet for 90 days, the only hepatic effects were ‘slight histological changes’ (not described) and an ‘increase in peripheral glycogen’ in females at the highest dose (166 mg strontium/kg/day); no other hepatic effects were observed in either sex ≤146 mg strontium/kg/day (Kroes et al. 1977).

Renal Effects. No studies were located regarding renal effects in humans after oral exposure to stable strontium.

No studies were located regarding renal effects in animals after chronic-duration oral exposure to stable strontium. In acute- and intermediate-duration studies, in which the diet contained adequate amounts of calcium and vitamin D, no renal effects were reported. No organ weight or histological changes were observed in the kidneys of adult Wistar rats given up to 110 mg strontium/kg/day as strontium chloride in the diet for 2 weeks (Kroes et al. 1977). Similarly, no such changes were observed among weanling Wistar rats fed up to 166 mg strontium/kg/day as strontium chloride in the diet for 90 days (Kroes et al. 1977). In male white Leghorn chickens raised on a diet deficient in vitamin D for the first 2 weeks of life, ingestion of 2,350 mg strontium/kg/day in a low-calcium, low-vitamin D diet for 7 additional days, reduced the activation of vitamin D_3 in mitochondria of the kidney (Omdahl and DeLuca 1972). Because of physiological differences between birds and mammals, this study is omitted from Table 3-1.

Endocrine Effects. Few studies were located regarding endocrine effects in humans after oral exposure to stable strontium. Vezzoli et al. (1998) reported that strontium absorption was inversely correlated with parathyroid hormone levels.

No studies were located regarding endocrine effects in animals of acute- or chronic-duration oral exposure to stable forms of strontium. There were no histological changes in the parathyroid gland or alterations in parathyroid hormone levels observed in male weanling Sprague-Dawley rats given 1,520 mg strontium/kg/day in the diet for 26 days (Svensson et al. 1987). The authors cautioned that their biochemical methods could not distinguish between active and inactive forms of the hormone. A few organ weight changes were observed among weanling Wistar rats fed up to 166 mg strontium/kg/day as strontium chloride in the diet for 90 days (Kroes et al. 1977). The relative thyroid weight was significantly heavier in males at 36 and 146 mg strontium/kg/day and the relative pituitary weight was significantly decreased in females at 10 and 166 mg strontium/kg/day, but in neither case was there a clear dose-response. Slight histological changes in the thyroid were reported.

Body Weight Effects. No studies were located regarding body weight effects in humans after oral exposure to stable strontium.

No studies were located regarding body weight effects in animals after chronic-duration oral exposure to stable strontium. In acute- and intermediate-duration animal studies, the effective dose levels for body

weight effects were relatively high and young animals were more sensitive than adults. In an acute-duration study, there was no effect on body weight in groups of adult SPF Wistar rats that ingested up to 110 mg strontium/kg/day as strontium chloride in the diet for 2 weeks (Kroes et al. 1977). Body weight gain was reduced by 62% among male weanling (21-day-old) Wistar rats that ingested 2,820 mg strontium/kg/day as strontium phosphate in the diet for 2 weeks, but this effect was reversible by feeding rats a diet low in strontium for 2 weeks (Kshirsagar 1976). From an analysis of a pair-fed control group (food intake matched to this high-dose group), the author concluded that the severe effects were a result of excess strontium, and not the reduced diet. Ingestion of 1,090 or 1,630 mg strontium/kg/day as strontium lactate reduced body weight gain in 5-week-old albino rats within several days (Teree et al. 1965). However, it seems likely that the reduced body weight gains resulted from an observed (but not measured) reduction in food intake, possibly because of reduced palatibility at the higher dose levels. Since the reduction appears not to be a systemic effect of strontium ingestion, this study is omitted from Table 3-1.

Most of the intermediate-duration oral exposure studies in weanling rodents have reported no effect on body weight for exposures <633 mg strontium/kg/day (rats: Grynpas et al. 1996; Kroes et al. 1977; Marie et al. 1985; Morohashi et al. 1994; Neufeld and Boskey 1994; Skoryna 1981a; and mice: Marie and Hott 1986). Intermediate-duration exposures to stable strontium at levels above 1,000 mg/kg/day adversely affected body weight. A 15% reduction in body weight gain was observed among weanling (21-day-old) male Wistar rats that ingested 1,270 mg strontium/kg/day as strontium phosphate for 4–6 weeks, but no reduction was observed at 580 mg strontium/kg/day (Kshirsagar 1976). The body weight gain was 28% lower than controls in weanling (21-day-old) male England Wright Y rats that ingested 1,850 mg strontium/kg/day (form unspecified) for 20 days (Reinholt et al. 1985). The terminal body weight was 16% lower than normal in male weanling Sprague-Dawley rats that ingested 1,520 mg strontium/kg/day (form not specified in this paper, but other publications from this lab used strontium chloride) for 26 days (Svensson et al. 1987).

A >30% loss in body weight occurred in young female rats (40–60 g) that were fed 4,975 mg strontium/kg/day as strontium carbonate for 20 days (Storey 1961); body weight gain was reduced by 24% at 2,220 mg, but was unaffected at 1,460 mg strontium/kg/day. Food intake was not reported, so it is uncertain to what extent these results are attributable to unpalatability. Similarly treated adult female rats exhibited no significant body weight changes at 2,750 mg strontium/kg/day (Storey 1961). Body weight gain was about a third lower than controls in young (50–70 g) rats that ingested 2,160 mg

strontium/kg/day as strontium carbonate for 7 months (Storey 1962); no quantitative body weight data were reported for young or adult animals.

In acute- and intermediate-duration studies, strontium effects on body weight were more severe in animals on diets low in calcium. Reduced body weight gain was reported in young white Leghorn chicks following ingestion of a high strontium/low calcium diet for 1 or 2 weeks (Corradino and Wasserman 1970; Corradino et al. 1971a, 1971b). The body weight gain of male weanling Wistar rats was reduced by 60% after ingestion of strontium carbonate (1,960 mg strontium/kg/day) in a diet low in calcium (0.04%) for 4 weeks (Matsumoto 1976).

Metabolic Effects. No studies were located regarding metabolic effects in humans after oral exposure to stable strontium.

No studies were located regarding metabolic effects in animals after chronic-duration oral exposure to stable strontium. In animal studies, few metabolic effects resulted from acute- or intermediate-duration oral exposure to stable strontium. In chicks given a normal Vitamin D_3-containing diet for 2 weeks after hatching, ingestion of a diet containing excess strontium reduced the plasma concentration of calcium, probably a consequence of reduced calcium absorption by the duodenum (Corradino et al. 1971a). Intermediate-duration exposures to 150–1,850 mg strontium/kg/day as strontium carbonate or strontium chloride had no effects on the serum levels of calcium, phosphorus, or magnesium in young or adult rodents given adequate dietary calcium, phosphorus, and vitamin D (rats: Grynpas et al. 1996; Kroes et al. 1977; Marie et al. 1985; Neufeld and Boskey 1994; Svensson et al. 1985, 1987; Reinholt et al. 1984; Skoryna 1981a; and mice: Marie and Hott 1986). No effects on serum calcium levels were observed in young female rats (40–60 g) that were fed 4,975 mg strontium/kg/day as strontium carbonate for 20 days or in adult female rats similarly fed 2,750 mg strontium/kg/day (Storey 1961). At 4,975 mg strontium/kg/day in the young rats, the calcium/strontium ratio was 1, whereas the ratio at 2,750 mg strontium/kg/day in adult rats was 1.4. A 13% reduction in serum calcium was observed in female juvenile Wistar rats (36-day-old, 6–8 per group) that ingested 510 mg strontium/kg/day as strontium carbonate in the diet for 27 days, but no effect was observed at 100 mg strontium/kg/day (Morohashi et al. 1994).

3.2.2.3 Immunological and Lymphoreticular Effects

No studies were located that reported immunological or lymphoreticular effects in humans or animals following oral exposure to stable strontium.

3.2.2.4 Neurological Effects

No studies were located that reported neurological effects in humans following oral exposure to stable strontium. No behavioral effects were observed in rats that ingested strontium chloride at levels up to 110 mg strontium/kg/day for 2 weeks or 166 mg strontium/kg/day for 90 days (Kroes et al. 1977). Johnson et al. (1968) reported paralysis of the hindlimbs in weanling male Sprague-Dawley rats that were fed 565 mg/kg/day of stable strontium (form not specified) for 43 days. It is not clear whether the observed paralysis was neurological or muscular, but it could have been related to abnormal calcium signaling in muscle or nerve. It is unlikely that the paralysis was due to the deformation of the femora as severely rachitic and osteomalacic rodents are not generally paralyzed. The NOAEL and LOAEL are recorded in Table 3-1 and plotted in Figure 3-1.

3.2.2.5 Reproductive Effects

No studies were located regarding reproductive effects in humans or animals following oral exposure to stable strontium.

3.2.2.6 Developmental Effects

No studies were located regarding developmental effects in humans following acute- or intermediate-duration oral exposure to stable forms of strontium. The only chronic-duration study is the Turkish epidemiological analysis that found a relationship between the concentration of strontium in the local soil and the prevalence of rickets in children between the ages of 6 months and 5 years (Ögzur et al. 1996). A relatively short period of breast feeding, which presumably affected calcium intake, and soil levels of strontium higher than 350 ppm, which probably determined the level of strontium in dietary grains consumed after weaning, were associated with an increase in the prevalence and severity of rickets. This study is discussed above in Section 3.2.2.2 Musculoskeletal Effects.

No studies were located that examined the effect of exposure to stable strontium *in utero* following oral maternal exposure in animals. However, the studies discussed in Section 3.2.2.2 Musculoskeletal Effects address the effects of strontium on bone organogenesis, in particular, endochondral ossification, a developmental process that continues long after birth. For example, in a study in which 4-week-old male Wistar rats (50–60 g body weight) were fed 1,970 mg strontium/kg/day as strontium carbonate in a diet low in calcium (0.04%), bone mineralization was significantly affected (Matsumoto 1976). Tibial length was reduced by 33% and the tibial proximal and distal epiphyseal plates were both about 5 times wider than normal. Microradiographic and histological analyses of tibial proximal heads revealed that no mineralization was detectable, that the organization of chondroblasts was irregular, and that osteoid rather than mineralized bone was deposited. Other studies on weanlings were conducted for acute durations (rat: Kshirsagar 1976) and intermediate durations (rat: Grynpas et al. 1996; Kroes et al. 1977; Morohashi et al. 1994; Neufeld and Boskey 1994; Reinholt et al. 1984, 1985; Svensson et al. 1985, 1987; and mice: Marie and Hott 1986). Intermediate-duration studies on rats demonstrated that ingestion of strontium resulted in more severe skeletal effects in young animals than in adults (Storey 1961, 1962). These studies are described in Section 3.2.2.2 Musculoskeletal Effects and are listed in Table 3-1 and Figure 3-1 under that category.

3.2.2.7 Cancer

No studies were located that demonstrated cancer effects of stable strontium following oral exposure in humans or animals. In one case-control study, no association was found between the incidence of liver cancer in 1984 on Chongming Island in China and the levels of stable strontium detected in hair (Wang et al. 1990).

3.2.3 Dermal Exposure

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

3.2.3.1 Death

3.2.3.2 Systemic Effects

3.2.3.3 Immunological and Lymphoreticular Effects

3.2.3.4 Neurological Effects

3.2.3.5 Reproductive Effects

3.2.3.6 Developmental Effects

3.2.3.7 Cancer

3.2.4 Other Routes of Exposure

This section includes injection and *in vitro* studies that provide evidence for the biological basis of toxicity of stable strontium in humans and animals. Since these studies are not directly relevant to general population exposure conditions, no LSE tables have been created for this section.

Cardiovascular Effects. Cardiovascular effects of strontium have been investigated by intravenous infusion studies in dogs. Infusions of strontium (as chloride or gluconate) averaging 172 mg strontium/kg under conditions of lowered potassium induced accelerated ventricular escape beats, ventricular tachycardia, or atrial fibrillation (Foster et al. 1977). High levels of strontium also induced oscillatory potentials and prolonged depolarization (precursors to arrhythmia) in Purkinje fibers of isolated sheep hearts (Gonzalez and Vassalle 1990). Whereas intravenous infusions at 4 mg strontium/kg had no effect on cardiac physiology, infusions at ~15 mg strontium/kg that brought the strontium/Ca ratio above 1 had a temporary negative chronotropic effect, reduced cardiac output, increased pulmonary vascular resistance, and systemic vascular resistance, but had no effect on pulmonary or systemic arterial pressure or pulmonary wedge pressure (Barry et al. 1972; Skoryna et al. 1986). The concentrations of strontium used in these studies are very high relative to the mean concentration of strontium in human blood, 27 µg strontium/L (see Table 6-9).

Hematological Effects. Because of its molecular similarity to calcium, the association of stable strontium with several kinds of blood cells has been investigated in a number of *in vitro* experiments. Strontium ions were found to be transported across the cell membrane of human erythrocytes by means of an ATP-dependent calcium pump (de la Sierra et al. 1990; Olson 1979; Olson and Cazort 1969; Porzig 1973). In washed platelets from human and rabbit, strontium stimulated the secretion of

5-hydroxytryptamine (Best et al. 1981; Bone et al. 1980; Togna et al. 1989). Best et al. (1981) concluded that strontium activates the release of arachidonate from platelet membrane phospholipid, with the subsequent synthesis of thromboxane A_2, a reaction that was antagonized by aspirin. These authors also suggested that strontium, because of its smaller hydrated ionic radius compared to calcium, is able to enter the platelet and mimic the rise in cytosolic calcium concentration that normally serves to activate secretion of 5-hydroxytryptamine (Best et al. 1981). Strontium was also found to stimulate degranulation of human large granular lymphocytes, which resulted in the inhibition of natural killer (NK) cells (Neighbour et al. 1982). The content of strontium (and calcium) was found to be significantly elevated above healthy control levels in granulocytes isolated from Swedish patients with active rheumatoid arthritis or seronegative spondarthritis (Hällgren et al. 1984). The strontium overload was thought to be linked to the degree of inflammation, and was positively related to serum levels of the acute-phase protein haptoglobin; corticosteroid therapy differentially reduced the strontium content of granulocytes compared to calcium. The authors suggested that leukocyte endogenous mediator (LEM) regulated the accumulation of strontium in granulocytes.

Immunological and Lymphoreticular Effects. Several *in vitro* experiments have demonstrated that strontium, although less efficient than calcium, is able to stimulate histamine release from rat mast cells (Alm and Bloom 1981a, 1981b; Atkinson et al. 1979; Foreman 1977; Foreman and Mongar 1972a, 1972b; Foreman et al. 1977). This is probably relevant to humans, since strontium has been shown to degranulate human lymphocytes (Neighbor et al. 1982) and stimulate the release of 5-hydroxytryptamine by human platelets (Best et al. 1981) (see Hematological Effects above). In rabbit blood treated with strontium chloride in vitro, the bacterocidal properties of serum were reduced (Toshioka et al. 1974); this effect was attributed to the inhibition of complement.

Neurological Effects. *In vitro* studies have demonstrated subtle differences between strontium and calcium with respect to neurological function at the cellular level. In a calcium-free medium, strontium ion weakly supported the generation of excitatory postsynaptic potentials following stimulation of guinea pig superior cervical ganglia (i.e., the release of acetylcholine was less efficient than when calcium was present) (McLachlan 1977). Calcium is sequestered in mitochondria and smooth endoplasmic reticulum of isolated presynaptic nerve terminals in preference to strontium (Rasgado-Flores et al. 1987). Strontium ion inhibits the uptake of calcium by synaptic vesicles in vitro, thereby blocking the antiport-regulated release of H+ (Gonçalves et al. 1999). Strontium ion was slightly more efficient than calcium ion in supporting the release of neurotransmitter from synaptosomes induced by leptinotoxin-h (Madeddu et al. 1985). Strontium ion was found to support the asynchronous mode of transmitter release in isolated layer

V pyramidal cells of the prefrontal cortex (Aghajanian and Marek 1999). This is apparently mediated through calcium-binding protein synaptotagmin III, as strontium does not support the function of calcium-binding synaptotagmins I and II (Li et al. 1995).

Reproductive Effects. The results of one *in vitro* study suggest that stable strontium is not directly harmful to human spermatozoa. In developing an improved method to be used by fertility clinics for testing the functional capacity of human spermatozoa, it was found that inclusion of strontium chloride in the testing medium improved the rate of penetration compared to calcium chloride (Mortimer 1986; Mortimer et al. 1986).

Developmental Effects. Subcutaneous injection of up to 82 mg strontium/kg/day as strontium nitrate into female Wistar rats between days 9 and 19 of gestation had no teratogenic effect, no adverse effect on the ossification of the skeleton, and no effect on the number of resorptions (Lansdown et al. 1972).

3.3 DISCUSSION OF HEALTH EFFECTS OF RADIOACTIVE STRONTIUM BY ROUTE OF EXPOSURE

Section 3.3 discusses radiation toxicity associated with exposure to radionuclides of strontium and is organized in the same manner as that of Section 3.2, first by route of exposure (inhalation, oral, and external) and then by health effect (death, systemic, immunological, neurological, reproductive, developmental, genotoxic, and carcinogenic effects). These data are discussed in terms of three exposure periods: acute (14 days or less), 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 NOAELs or LOAELs reflect the actual dose (levels of exposure) used in the studies. Refer to Section 3.2 for detailed discussion of the classification of endpoints as a NOAEL, less serious LOAEL, or serious LOAEL.

Levels of exposure associated with carcinogenic effects (Cancer Effect Levels, CELs) of radiostrontium are indicated in Tables 3-2, 3-3, and 3-4 and Figures 3-2 and 3-3. Because cancer effects could occur at lower exposure levels, Figures 3-2 and 3-3 also show a range for the upper bound of estimated excess risks, ranging from a risk of 1 in 10,000 to 1 in 10,000,000 (10^{-4} to 10^{-7}), as developed by EPA.

Refer to Appendix B for a User's Guide, which should aid in the interpretation of the tables and figures for Levels of Significant Exposure.

3.3.1 Inhalation Exposure

The two major sources of data regarding health effects of inhaled radioactive strontium are long-term studies using beagles at the Lovelace Foundation, Albuquerque, New Mexico (now known as the Lovelace Respiratory Research Institute). One study examined the acute inhalation effects of a relatively soluble aerosol of $^{90}SrCl_2$, and the other examined the acute inhalation effects of relatively insoluble particles of ^{90}Sr fused to aluminum silicate ('^{90}Sr fused-clay particles').

In the soluble aerosol study, beagles were exposed by nose breathing for varying exposure durations (2–22 minutes) to graded concentrations (2.16–419 μCi ^{90}Sr/L; 0.08–15.5 MBq/L) of $^{90}SrCl_2$ to produce graded levels of initial body burdens. Individual variations in the degree to which aerosol was cleared from the respiratory tract and swallowed contributed to variability in the initial rapid rate of clearance during the first few days. Therefore, exposures were expressed in terms of the long-term retained burden (LTRB), which ranged from 1.08 to 119 μCi (0.04–4.4 MBq) ^{90}Sr/kg of body weight. Radiostrontium quickly passed through the lungs and was overwhelmingly retained in the skeleton, where initial skeletal dose rates were calculated to be 0.43–55 rad/day (0.0043–0.55 Gy/day). Clearance of radiostrontium from the skeleton was gradual. For that reason, the initial and long-term health effects were primarily related to hemopoietic bone marrow and osteogenic tissues. Reports relating to the $^{90}SrCl_2$ aerosol study include Benjamin et al. (1974b, 1975, 1976a, 1976c, 1979), Boecker et al. (1969, 1991), Fission Product Inhalation Project (1967a), Gillett et al. (1987a, 1987b), Hahn et al. (1991), McClellan et al. (1973, 1983a), and Muggenburg et al. (1977, 1978, 1979).

In the other study, beagles were exposed by nose-only inhalation to ^{90}Sr fused-clay particles for initial lung burdens ranging from 0.21 to 94 μCi ^{90}Sr/kg (0.008–3.5 MBq/kg) of body weight. Control animals were exposed to similar aluminosilicate clay particles fused to stable strontium. Early and late-occurring health effects of inhaled particulate radiostrontium were primarily associated with the lung. Some particles were cleared into the lung-associated lymph nodes, where radiation damage led to their entry into the circulatory system, leading to distribution to spleen, liver, and possibly other tissues. Trapping of radioactive particles by these tissues created possible sites for radiation damage and tumor development. The biological retention half-time for ^{90}Sr in fused-clay particles was approximately 490 (±320 days standard deviation). Reports relating to ^{90}Sr fused clay particles include Benjamin et al. (1974a, 1975),

Griffith et al. (1992), Hahn et al. (1983a), Hobbs et al. (1972), Jones et al. (1972, 1976), Scott (1980), and Snipes et al. (1974a, 1974b, 1976, 1977, 1978, 1979). A similar study with a smaller group of dogs was carried out by Benjamin et al. (1976c).

3.3.1.1 Death

No studies were located regarding death in humans following inhalation exposure to radioactive strontium. Information on the lethality of inhaled radioactive strontium is limited to acute exposure studies. Because of the bone-seeking behavior of strontium, an acute exposure to airborne ^{90}Sr results in chronic exposure to radiation from ^{90}Sr incorporated into bone. If insoluble radiostrontium compounds are inhaled, there could be long-term lung exposure (see discussion of the study by Willard and Snyder (1966) in Section 3.5.1.1).

In two different experiments briefly described in a report by the Lovelace Foundation (now known as the Lovelace Respiratory Research Institute), young male and female Holtzman rats were exposed once to ^{90}Sr by whole body inhalation for initial body burdens ranging from 170 to 1,660 μCi ^{90}Sr/kg (0.63–61.4 MBq/kg) of body weight and average skeletal radiation doses ranging from 12,600 to 19,000 rad (126–190 Gy) (Fission Product Inhalation Project 1967b). Survival was inversely proportional to dose, with rats receiving the lowest dose living for more than 700 days, and those receiving the highest dose living less than 200 days. In the two experiments, 77% of the rats that died and 47% of the rats that were killed in a moribund state were found to have osteosarcoma. Among rats dying with tumors, the average skeletal dose was 81 rad/day, compared to 62 rad/day for rats without tumors (0.81 vs 0.62 Gy/day). The small sample sizes in this study do not permit its inclusion in the LSE Table 3-2.

In acute inhalation studies in beagle dogs, high-dose radiation effects of inhaled $^{90}SrCl_2$ on bone marrow resulted in death within days or weeks of exposure, whereas lower doses reduced long-term survival through carcinogenetic effects. For all exposed dogs, the mean survival time was 3,000 days, compared to 4,500 days for the controls (Gillett et al. 1987b). Among dogs receiving high or medium doses (long-term retained body burdens between 47 and 120 μCi ^{90}Sr/kg (1.74 and 4.44 MBq/kg), 6/22 died within 32 days from severe hypoplasia of the bone marrow (Gillett et al. 1987a; Muggenburg et al. 1979). Individual neutrophil counts were the most reliable predictors of lethality. Death from primary bone tumors occurred from 2 to 10 years after exposure to inhaled $^{90}SrCl_2$ (Gillett et al. 1987b). Fibrosarcomas and metastasizing hemangiosarcomas occurred somewhat earlier than osteosarcomas and were the major

contributors to shortened mean survival times for the dogs exposed to inhaled $^{90}SrCl_2$ (Gillett et al. 1987b). Deaths from myelomonocytic leukemia and from bone-associated soft tissues of the skull were also concluded to be associated with radiostrontium; the long-term retained burdens were 9.2–27 μCi ^{90}Sr/kg (0.34–1.0 MBq/kg) and 21–35 μCi ^{90}Sr/kg (0.081–1.3 MBq/kg), respectively. These are extreme doses.

In beagle dogs exposed by acute inhalation to ^{90}Sr fused-clay particles, the pattern of mortality was different since the radioactive particles were initially embedded in the lung. No deaths occurred until the 5th month postexposure. Of 36 dogs with initial lung burdens ≥25 μCi ^{90}Sr/kg (925 kBq/kg) of body weight, 35 died within the first 2 years, primarily of radiation pneumonitis and/or pulmonary fibrosis (Snipes et al. 1979). Subsequently, within the 2nd to 7th years after exposure, deaths from hemangiosarcoma and carcinoma of the lung were common. None of the control dogs died during the 9 years following exposure (Snipes et al. 1979), indicating that the observed mortality was not caused by inhalation of nonradioactive aluminum silicate particles alone. Among dogs dying prematurely from neoplasms of the lung, the initial lung burdens were between 3.7 and 94 μCi/kg (0.14–3.5 MBq/kg) and the doses to the lungs ranged from 43,000 to 67,000 rad (430–670 Gy) (Benjamin et al. 1975).

The percent mortality values for dogs from exposure to radioactive strontium by the inhalation route are presented in Table 3-2 and plotted in Figure 3-2.

3.3.1.2 Systemic Effects

No studies were located that described endocrine, dermal, or ocular effects in humans or animals following inhalation exposure to radioactive strontium. The highest NOAEL values and all reliable LOAEL values in each species and duration category for systemic effects from radiation exposure to strontium by the inhalation route are presented in Table 3-2 and plotted in Figure 3-2.

Respiratory Effects. The only respiratory effects reported for the study in which beagle dogs were exposed to soluble aerosols of $^{90}SrCl_2$ (Boecker et al. 1969; Gillett et al. 1987b) were late primary cancers of the respiratory tract or tumors metastasizing to the lung. These effects are discussed in Section 3.2.1.7 Cancer.

Table 3-2 Levels of Significant Exposure to Strontium - Radiation Toxicity - Inhalation

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (µCi/kg)	LOAEL Less Serious (µCi/kg)	LOAEL Serious (µCi/kg)		Reference Chemical Form
	ACUTE EXPOSURE							
	Death							
1	Dog (Beagle)	2-22 min once				47	[LTRB] (6/24 died from bone marrow hypoplasia)	Gillett et al. 1987a Strontium-90 (chloride)
	Systemic							
2	Dog (Beagle)	once	Cardio			25	[ILB] (damaged pulmonary vasculature; hypertrophic right ventricle; congestive heart failure)	Benjamin et al. 1976c Sr-90 (fused-clay particles)
			Hepatic			25	[ILB] (all with chronic passive congestion; one with mild centrilobular fibrosis)	
			Bd Wt			25	[ILB] (emaciation)	
3	Dog (Beagle)	2-22 min once	Gastro			47	[LTRB] (anorexia, bloody diarrhea from acute radiation syndrome)	Gillett et al. 1987a Strontium-90 (chloride)
			Hemato			1.5	[LTRB] (60% decr platelet count)	
			Renal			47	[LTRB] (incr blood urea nitrogen, decr urine output from acute radiation syndrome)	

Table 3-2 Levels of Significant Exposure to Strontium - Radiation Toxicity - Inhalation (continued)

Key to figure	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (µCi/kg)	LOAEL Less Serious (µCi/kg)	LOAEL Serious (µCi/kg)		Reference Chemical Form
4	Dog (Beagle)	2-22 min once	Gastro			1.9	[LTRB] (malabsorption syndrome at age >11 yrs)	Muggenburg et al. 1977 Strontium-90 (chloride)
			Bd Wt			1.9	[LTRB] (decr bd wt)	
5	Dog (Beagle)	once	Resp			25	[ILB] (pulmonary pneumonitis, fibrosis)	Snipes et al. 1979 Sr-90 (fused-clay particles)
			Gastro			4.1	[ILB] (ulcerating lesion of pharynx; anorexia)	
	Immuno/ Lymphoret							
6	Dog (Beagle)	once				25	[ILB] (50% decr lymphocytes for 28 weeks)	Benjamin et al. 1976c Sr-90 (fused-clay particles)
7	Dog (Beagle)	2-22 min once				10	[LTRB] (22% decr lymphocyte count lasting 3 years)	Gillett et al. 1987a Strontium-90 (chloride)
8	Dog (Beagle)	once				5	[ILB] (lymphocyte counts decr 40% for two years)	Jones et al. 1976 Sr-90 (fused-clay particles)

Table 3-2 Levels of Significant Exposure to Strontium - Radiation Toxicity - Inhalation (continued)

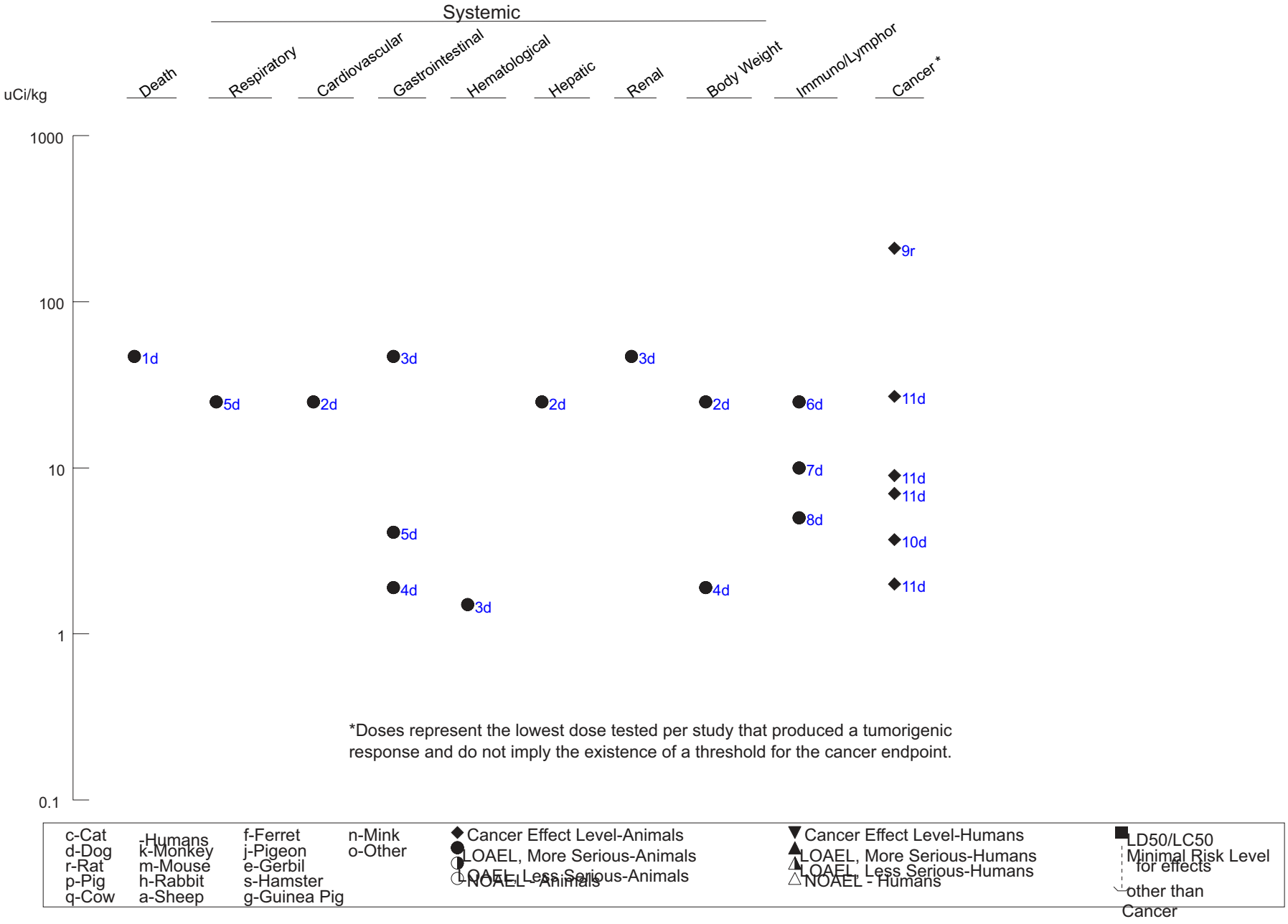
Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (µCi/kg)	LOAEL			Reference Chemical Form
					Less Serious (µCi/kg)		Serious (µCi/kg)	
	Cancer							
9	Rat (Holtzman)	once					210 (CEL: osteosarcoma)	Lovelace Foundation 1967 Strontium-90/yttrium-90
10	Dog (Beagle)	once					3.7 [ILB] (CEL: hemangiosarcoma of lung, heart)	Benjamin et al. 1975 Sr-90 (fused-clay particles)
11	Dog (Beagle)	2-22 min once					7 [LTRB] (CEL: osteosarcoma) 9 [LTRB] (CEL: leukemia) 27 [LTRB] (one premature death after 585 days from leukemia) 2 [LTRB] (CEL: nasal carcinoma)	Gillett et al. 1987b Strontium-90 (chloride)

[a] The number corresponds to entries in Figure 3-2.

Bd Wt = body weight; Cardio = cardiovascular; CEL = cancer effect level; decr = decreased; Gastro = gastrointestinal; (GW) = gavage in water; Hemato = hematological; hr = hour(s); [ILB] = initial lung burden; incr = increased; LOAEL = lowest-observed-adverse-effect level; [LTRB] = long-term retained burden; min = minute(s); NOAEL = no-observed-adverse-effect level; Resp = respiratory

Figure 3-2 Levels of Significant Exposure to Strontium - Radiation Toxicity - Inhalation

Acute (≤14 days)



Respiratory effects were more pronounced in beagle dogs that were exposed to ^{90}Sr fused-clay particles by inhalation (Benjamin et al. 1976c; Snipes et al. 1979). The primary cause of early death among dogs exposed to initial lung burdens ≥25 μCi ^{90}Sr/kg (925 kBq/kg) was radiation pneumonitis and/or pulmonary fibrosis (Snipes et al. 1979). No such effects were reported in control dogs exposed to nonradioactive aluminosilicate-fused clay particles (Snipes et al. 1979). Clinical signs included an increased respiratory rate, dyspnea, cyanosis, and dry and moist rales (Benjamin et al. 1976c). Radiographically, the dogs showed increased focal or diffuse lung-field densities. The pneumonitis was characterized by acute and chronic inflammation with increased numbers of alveolar macrophages, hypertrophy and hyperplasia of alveolar lining cells, degeneration of the bronchiolar epithelium and alveolar ducts, focal emphysema, and edema. The fibrosis involved the alveolar septa, pleura, and perivascular regions, with substantial scarring. Vascular damage in the lungs was characterized by congestion, hemorrhage (possibly related to thrombocytopenia), fibrin exudation, and occasional vessels with fibrinoid necrosis or intimal proliferation.

Cardiovascular Effects. Acute inhalation of radiostrontium was reported to lead to adverse cardiovascular effects in dogs. Among beagles that died within 5–15 months following inhalation exposure to ^{90}Sr fused-clay particles, most exhibited myocardial necrosis or degeneration, and fibrosis, primarily of the right atrium (Hobbs et al. 1972); these animals had initial lung burdens between 33 and 100 μCi/kg (1.2–3.7 MBq/kg) and cumulative beta radiation doses to the lung of 34,000 to 82,000 rad (340–820 Gy). In a later report of the same study, acute and chronic vascular lesions, characterized as inflammatory or degenerative, affected the elastic and muscular pulmonary arteries in dogs with initial lung burdens between 16 and 94 μCi/kg (0.6–3.5 MBq/kg) and doses to the lung between 40,000 and 96,000 rad (400–960 Gy) at the time of death (Snipes et al. 1977). Vascular damage in the lungs was characterized by congestion, hemorrhage, fibrin exudation, and occasional vessels with fibrinoid necrosis or intimal proliferation (Benjamin et al. 1976c). These effects were attributed to the direct effect of beta radiation (from radiostrontium particles embedded in the lung) on adjacent tissue. In addition, presumably as a consequence of radiation damage to the pulmonary vasculature, the right ventricle became dilated and hypertrophic with congestive heart failure. Hemangiosarcomas resulting from radiostrontium exposure in this study are discussed in Section 3.3.1.7 Cancer.

Gastrointestinal Effects. Gastrointestinal effects were observed in beagle dogs receiving single high doses (long-term retained body burdens between 47 and 83 μCi/kg; 1.74 and 3.07 MBq/kg) of soluble aerosols containing $^{90}SrCl_2$ (Gillett et al. 1987a). Anorexia and, 2 days before death, bloody diarrhea, developed in six dogs that died between 18 and 32 days after the extreme radiation dose rate

induced acute radiation syndrome (Gillett et al. 1987a). It is likely that severe thrombopenia, one of the features of radiation-induced bone marrow hypoplasia, contributed to hemorrhage in the gastrointestinal tract as elsewhere in the body. In addition, some effects could have been due to inhaled $^{90}SrCl_2$ droplets being transported from the mucoid, ciliated nasopharyngeal and tracheobronchial epithelia to the pharynx and then swallowed. The gastrointestinal epithelium then would have been exposed directly to beta emissions from radiostrontium for a day or two. Another report of the same study described three exposed dogs that died at age >11 years with a malabsorption syndrome (Muggenburg et al. 1977). All of the dogs exhibited chronic diarrhea with anorexia, and at necropsy, contained chronic degenerative and inflammatory lesions of the small intestines. Their long-term retained burdens were 1.9–9.6 μCi/kg (70.3–355.2 kBq/kg) and the absorbed doses to the skeleton were calculated to be 530–5,600 rad (5.3–56 Gy). Although the authors could not firmly establish whether the syndrome was a consequence of exposure or of age, the cumulative radiation dose to the digestive tract was likely to have been very low and this argues against ^{90}Sr as the cause.

One beagle dog that was exposed to ^{90}Sr fused-clay particles and had an initial lung burden of 4.1 μCi/kg (151.7 kBq/kg) and a cumulative radiation dose to the lung of 20,000 rad (200 Gy) died 9 years after exposure with anorexia and an ulcerative lesion to the pharynx (Snipes et al. 1979). Whether the pharyngeal lesion was related to exposure is uncertain, since the report was preliminary and no other response to radiation had been observed in this animal.

Hematological Effects. Profound hematological effects were observed in beagle dogs that were exposed once by inhalation either to soluble aerosols containing $^{90}SrCl_2$, or to ^{90}Sr fused to aluminosilicate particles that produced extremely large radiation dose rates and doses in the affected tissues sufficient to induce acute radiation syndrome.

Significant dose-related pancytopenia developed in dogs that were exposed to $^{90}SrCl_2$ aerosols and had long-term retained burdens >10 μCi (370 kBq) ^{90}Sr/kg (Gillett et al. 1987a). Profound decreases in platelet numbers were evident by 7 days and were maximal by 28 days. Drastic thrombocytopenia (platelets reduced >90%) probably contributed to widespread hemorrhaging and premature death in dogs with long-term retained burdens ≥47 μCi/kg (≥1.7 MBq/kg). Significant immediate reductions in platelet counts (>60%) occurred in surviving dogs with long-term retained burdens of ≥1.5 μCi/kg (≥0.56 MBq/kg). However, even dogs with the lowest long-term retained burdens (1–10 μCi/kg; 0.04–0.36 MBq/kg), which otherwise showed little immediate effect, exhibited long-term (>3 years) depression in platelet counts compared to controls. The pattern of neutropenia followed a similar exposure-response,

and profound neutropenia was the most accurate predictor of death. In surviving dogs that were immediately affected by exposure, neutrophil counts recovered, but in these dogs, as well as those immediately unaffected, significant long-term (>3 years) suppression was observed compared to controls. Similarly, lymphocyte counts were drastically reduced (by 75%) in dogs dying within weeks of exposure with long-term retained burdens ≥47 μCi/kg (≥1.7 MBq/kg). Surviving dogs with long-term retained burdens >10 μCi (370 kBq) ^{90}Sr/kg exhibited a long-term (>3 years) suppression of lymphocyte counts (>30%). Dogs with long-term retained burdens between 6 and 10 μCi/kg (0.26–0.36 MBq/kg) exhibited normal lymphocyte counts that were normal over 1,400 days except for periods of significant depression at 60–120 and 900–1,000 days. Dogs with long-term retained burdens between 1 and 3 μCi/kg (0.04–0.12 MBq/kg) had lymphocyte counts that were not significantly different from controls. Reduced erythrocyte mass, as exemplified by decreases in hematocrit, red blood cell counts, and hemoglobin levels, occurred between 2 and 3 weeks after exposure (slightly later than the depression in platelet and white cell counts). In the most severely affected dogs, red blood cell counts fell to 70–80% of pre-exposure values, with maximal depression at 32 days. Prolonged depression of erythrocyte counts was observed in surviving dogs with long-term retained burdens ≥27 μCi/kg (≥1 MBq/kg).

Significant suppression of peripheral lymphocyte counts was observed in beagle dogs that were exposed by inhalation to ^{90}Sr fused-clay particles (Jones et al. 1976). Lymphocytes declined gradually over time in all exposed groups (initial lung burdens ≥5 μCi/kg; ≥185 kBq/kg), and remained more than 50% lower than controls after 2 years.

Hepatic Effects. No studies were located that described hepatic effects in humans following inhalation exposure to radioactive strontium. All beagle dogs that died from radiation pneumonitis following a single inhalation exposure to high concentrations of ^{90}Sr fused-clay particles (25 μCi ^{90}Sr/kg of body weight; 925 kBq/kg) exhibited chronic passive congestion of the liver, and one had mild centrilobular fibrosis (Benjamin et al. 1976c).

Renal Effects. No studies were located that described renal effects in humans following inhalation exposure to radioactive strontium isotopes. Some beagle dogs in the terminal stages of acute radiation syndrome following inhalation exposure to aerosols of $^{90}SrCl_2$ (long-term retained burden 47–83 μCi ^{90}Sr/kg; 1.74–3.07 MBq/kg) had low urine output and elevated blood urea nitrogen (Gillett et al. 1987a).

Body Weight Effects No studies were located that described body weight effects in humans following inhalation of radiostrontium. Anorexia and reduced body weight were observed among beagle dogs with long-term retained burdens between 45 and 119 μCi/kg (1.7–4.4 MBq/kg) following inhalation of $^{90}SrCl_2$ aerosols (Gillett et al. 1987a; Muggenburg et al. 1977) or initial lung burdens between 25 and 32 μCi/kg (0.93–1.2 MBq/kg) following inhalation of ^{90}Sr fused-clay particles (Benjamin et al. 1976c).

3.3.1.3 Immunological and Lymphoreticular Effects

No studies were located regarding immunological effects in humans following inhalation exposure to radioactive strontium isotopes. However, profound effects on the immune system were a consequence of acute inhalation exposure to radiostrontium in dog studies. Effects in dogs exposed to soluble aerosols of $^{90}SrCl_2$ were sequelae of general irradiation of the bone marrow from ^{90}Sr incorporated into bone. Significant dose-related lymphopenia was observed in young adult beagle dogs (12–14 months old) after a single inhalation exposure to $^{90}SrCl_2$ at long-term retained burdens >10 μCi ^{90}Sr/kg (370 kBq/kg; Gillett et al. 1987a). Furthermore, there was some evidence of immunosuppression in dogs with average initial body burdens of 35 μCi ^{90}Sr/kg (1.3 MBq/kg) (Fission Product Inhalation Project 1967a); titers for infectious canine hepatitis and leptospira vaccines were depressed more than 30% following exposure to $^{90}SrCl_2$ aerosols. Effects in dogs exposed to relatively insoluble ^{90}Sr fused-clay particles were primarily a consequence of irradiation of the blood as it circulated through the lungs, although some damage to thoracic lymph nodes was observed. Among beagle dogs (17–20 months old) exposed by nose-only inhalation to ^{90}Sr fused clay particles (initial lung burdens 25–32 μCi ^{90}Sr/kg; 0.925–1.18 MBq/kg), the numbers of peripheral lymphocytes were depressed by more than 50% during the 12th through 28th weeks after exposure, although recovery was observed by week 44 (Benjamin et al. 1976c). The cumulative radiation dose to the lungs ranged from 35,000 to 43,000 rad (350–430 Gy). During the period of lymphocyte suppression, the immune response to phytohemagglutinin antigen tested *in vitro* was depressed 10-fold in the dog that had the highest initial lung burden (32 μCi/kg; 1.18 MBq/kg) and was the first to die. In this animal, the tracheobronchial and sternal lymph nodes, which received a significant radiation dose from ^{90}Sr, were depleted of lymphocytes, although peripheral nodes, which received much lower doses, were nearly normal. In the main study that employed 1-year-old beagles, the highest initial lung burdens of ^{90}Sr fused-clay particles resulted in severe atrophy and fibrosis of the tracheobronchial lymph nodes (Snipes et al. 1977). In other dogs, which had initial lung burdens averaging between 5 and 19 μCi/kg (185 and 703 kBq/kg), fluctuations in the peripheral lymphocyte numbers were observed, but the values remained depressed by 40% for 2 years following inhalation exposure (Jones et al. 1976).

Cumulative doses in these dogs ranged from 1,055 to 4,005 rad (10.5–40 Gy). None of the dog studies reported whether there was a NOAEL identified for immunological effects. Significant chronic suppression of the immune system is considered a serious effect because of the impaired resistance to infectious disease.

3.3.1.4 Neurological Effects

No studies were located that described neurological effects in humans following inhalation exposure to radioactive strontium. A beagle dog that was exposed to the highest concentration of $^{90}SrCl_2$ aerosol (long-term retained burden of 119 μCi/kg or 4.4 MBq/kg) succumbed with epileptic seizures, but the authors deemed these to be unrelated to exposure (Gillett et al. 1987b). Serious neurological effects (convulsions, paralysis) were observed in several dogs that were in the terminal stages of cancer following inhalation of ^{90}Sr fused clay particles (Snipes et al. 1977, 1978). No other studies addressed neurological effects in animals following inhalation exposure to radioactive strontium isotopes.

The highest NOAEL values and all reliable LOAEL values in each species and duration category for neurological effects from exposure to radioactive strontium by the inhalation route are presented in Table 3-2 and plotted in Figure 3-2.

No studies were located regarding the following effects in humans or animals following inhalation exposure to radioactive strontium:

3.3.1.5 Reproductive Effects

3.3.1.6 Developmental Effects

3.3.1.7 Cancer

No studies were located regarding cancer in humans following inhalation exposure to radioactive strontium isotopes, but several studies reported carcinogenetic effects in animals. The types of cancers produced varied with the form of strontium administered. In studies using soluble forms of radioactive strontium, (e.g., $^{90}SrCl_2$), bone-associated cancers were the predominant types, because absorbed strontium primarily incorporates into bone. Studies using relatively insoluble ^{90}Sr fused-clay particles

reported lung-related cancers as the major initial types, since the particles were initially embedded in the lungs. As particles slowly dissolved (releasing ^{90}Sr) or were cleared from the lungs, tumors were induced in other tissues.

In two different experiments described in a report by the Lovelace Foundation (now known as the Lovelace Respiratory Research Institute), young male and female Holtzman rats were exposed once to an aerosol of ^{90}Sr in cesium chloride by whole body inhalation for initial body burdens ranging from 170 to 1,660 μCi ^{90}Sr/kg (6.3–61.4 MBq/kg) of body weight (Fission Product Inhalation Project 1967b). The average skeletal radiation doses over their remaining lifespans averaged from 12,600 to 25,900 rad (126–259 Gy). In the two experiments, 77 or 47% of the rats that died or were euthanized in a moribund state were found to have bone tumors (osteosarcomas). Among rats dying with tumors, the average skeletal dose rate was 81 rad/day, compared to 62 rad/day for rats without tumors (0.81 vs 0.62 Gy/day).

Primary bone cancer was the most frequent cause of death in beagle dogs (30/66) given a single inhalation exposure to $^{90}SrCl_2$ aerosol and then observed for their lifespans (Benjamin et al. 1974a, 1976a, 1979; Gillett et al. 1987b; McClellan et al. 1973; Muggenburg et al. 1977, 1978, 1979). The cumulative absorbed doses of beta radiation to bone ranged from 12 to 1,200 rad (0.012–12 Gy) at 30 days and from 200 to 170,000 rad (2–1,700 Gy) at 1,000 days after exposure. In dogs with bone-related tumors, the long-term retained burdens ranged from 2 to 119 μCi ^{90}Sr/kg (0.081–4.4 MBq/kg) of body weight. Bone-tumor-related deaths occurred 759–3,472 days after exposure (median survival time of 1,702 days, compared to 4,500 days for controls). Twenty-seven tumors were classified as different subtypes of osteosarcoma, 14 as hemangiosarcomas, 3 as fibrosarcomas, and 1 as a myxosarcoma. Four additional animals developed carcinomas in soft tissues adjacent to the bones of the skull: invasive baso-squamous carcinoma, transitional carcinomas of the nasal cavity, and an adenocarcinoma in the maxilloturbinate region (Benjamin et al. 1979). In addition, two dogs died from myelomonocytic leukemia resulting from irradiation of bone marrow. Metastasis occurred from 21 tumors, in particular the hemangiosarcomas, with the lungs being the most frequent site of metastasis (76%).

Among 127 beagle dogs exposed by inhalation to ^{90}Sr fused-clay particles, deaths from primary pulmonary tumors were common: 19 dogs with hemangiosarcomas (one each also with bronchioalveolar carcinoma, nasal squamous cell carcinoma, or pulmonary epidermoid carcinoma), and one with pulmonary squamous cell carcinoma (Snipes et al. 1979). All 34 dogs exposed to ^{90}Sr fused clay particles with cumulative exposures of >29,000 rad (290 Gy) developed pulmonary hemangiosarcoma. The heart wall was the other primary location of hemangiosarcoma (11 dogs), the others being the mediastinum,

spleen, rib, lung-associated lymph nodes, and liver (Snipes et al. 1979). Hemangiosarcomas were metastatic in all but one affected dog. Among dogs dying prematurely from neoplasms of the lung, the initial lung burdens were 3.7–94 μCi/kg (0.14–3.5 MBq/kg) and the estimated cumulative doses to the lungs ranged from 43,000 to 67,000 rad (430–670 Gy) (Benjamin et al. 1975). Considering all dogs with tumors, pulmonary carcinomas or sarcomas occurred in 3/12 dogs that received cumulative radiation doses of 17,000–25,000 rad (170–250 Gy), but no pulmonary tumors were reported for three dogs with cumulative exposure levels of 11,000–15,000 rad (110–150 Gy; Hahn et al. 1983a).

The highest NOAEL values and all reliable LOAEL values in each species and duration category for cancer effects from exposure to radioactive strontium by the inhalation route are presented in Table 3-2 and plotted in Figure 3-2.

3.3.2 Oral Exposure

Upon ingestion, radioactive strontium isotopes become incorporated into bone, and irradiate the surrounding hard and soft tissues, resulting in hypoplasia of the bone marrow or various forms of cancer (osteosarcoma, leukemia). Adverse effects are associated with higher skeletal burdens of radioactive strontium. Younger organisms are more vulnerable to adverse effects of both stable and radioactive strontium. Maternal oral exposure to sufficient radioactive strontium can adversely affect the fetus.

The database for oral exposures to radioactive strontium is substantial. Human health effect data are derived primarily from long-term and ongoing studies of a population that was exposed to contaminated drinking water and food following the release of large quantities of radioactive materials into the Techa River from a Soviet nuclear weapons facility between 1949 and 1956. This population received a mixed exposure to external gamma radiation and to internal radiation from ^{89}Sr, ^{90}Sr, and ^{137}Cs (Akleyev et al. 1995; Kossenko et al. 2000). Animal data include several large, long-term studies in dogs, miniature pigs, and rodents. In addition to the papers cited below, interim reports and analyses for the beagle lifetime study (Laboratory for Energy-Related Health Research at the University of California at Davis) were published by Nilsson and Book (1987), Nilsson et al. (1985), Pool et al. (1972, 1973b), and Raabe et al. (1981a, 1981b, 1983, 1994).

3.3.2.1 Death

In the Techa River population that was exposed to radiostrontium and radiocesium in drinking water and food between 1949 and 1956, an increase in the number of deaths from leukemia and solid cancers was reported (Kossenko 1996). In the exposed group, the standardized mortality rate was 140 (95% CI: 131–150) per 100,000 compared to 105 (95% CI: 101–109) per 100,000 in the control group during the followup period (1950–1982). Absorbed doses to the red bone marrow in the study group were between 17.6 and 164 rad (0.176 and 1.64 Gy). No increase in cancer mortality was observed among offspring of exposed individuals. These data are omitted from Table 3-3 because the exposures were to multiple sources of radiation.

Oral exposure to radioactive strontium caused dose-related increases in mortality in animal studies. In general, younger animals were more sensitive to the effects of radiation than older animals. There was an increase in deaths in a small number (6 out of 7) of Rhesus monkeys given 100 μCi of ^{90}Sr per day (3.7 MBq/day) by gavage for 5 or 10 days (Casarett et al. 1962). One monkey given 11 μCi/kg/day (0.42 MBq/kg/day) for 5 days died 4 years after treatment from leukemia with a total skeletal dose of 4,300 rad (43 Gy). One monkey given a dose of 28 μCi/kg/day (1.0 MBq/kg/day) for 10 days died within 4 months of treatment from pancytopenia with an estimated skeletal dose of 4,500 rad (45 Gy). Two others exposed to an average of 18 μCi/kg/day (0.67 MBq/kg/day) for 10 days died from bone associated cancers within 36 months of treatment, and with estimated skeletal doses of 4,700–9,500 rad (47–95 Gy). Because of the small sample size and the fact that the animals were of different ages, this study serves as an indicator, but not as proof of dose-response effects of ingested radiostrontium.

In experiments in which weanling (30 days old) and adult Long-Evans rats were given ^{90}Sr in drinking water for 10 days, survival at 5 months was reduced by 80% in the weanlings consuming at least 297–386 μCi ^{90}Sr/kg/day (11 MBq/kg/day; total 464 μCi or 17 MBq), but was unaffected in adults consuming 64–194 μCi ^{90}Sr/kg/day (7.2 MBq/kg/day; total 650 μCi or 24.1 MBq; Casarett et al. 1962). The reduced survival of the weanlings was consistent with their higher skeletal burden at 5 months: >20 times higher than in the adults. In another acute study, six young female dairy cattle (three sets of twins from three different strains, ages 398 and 479 days and weighing 145–349 kg at the start of treatment) were given 44 μCi ^{90}Sr/kg/day (1.63 MBq/kg/day) 'orally' for 5 days (Cragle et al. 1969). The four youngest (398 days) and lightest heifers (145–212 kg), which were administered a total of 32–46 mCi (1.18–1.70 GBq), died of radiation sickness between 93 and 132 days after treatment was started, whereas the older and heavier animals (342–349 kg), which had received a total of 75–77 mCi of ^{90}Sr (2.78–

2.85 GBq), were still alive 3 years after treatment. In addition to age-related differences, strain differences may have contributed to the results; the older cows were Holsteins, which have more massive skeletons than the Brown Swiss and Jersey strains. The authors suggested that the larger animals survived because of the wider diameter of the marrow cavity, which possibly shielded the central marrow from beta radiation released from ^{90}Sr (and its ^{90}Y decay product) deposited at the periphery of the bone shaft.

In an intermediate-duration experiment, young (87-day-old) Long-Evans rats were treated with up to 104 μCi of ^{90}Sr per kg of body weight per day (3.8 MBq/kg/day) for 30 days over a period of 37 days (Casarett et al. 1962; Hopkins et al. 1966); the total amount administered was 790 μCi (29.2 MBq). In these rats, the estimated skeletal activity of ^{90}Sr at 5 months was 11 μCi (407 kBq) and survival was reduced by about 36%. In the young rats treated for 30 days, skeletal activity was higher and survival was reduced accordingly compared to the adult rats treated for 10 days (see previous paragraph), but the differences were out of proportion to the total amounts of ^{90}Sr administered to the two sets of rats. The total amount given to adults was 18% less than to the juveniles, but the skeletal doses in the adults were 82% less, suggesting age-related differences in incorporation.

In a lifetime study, adult CF-1 mice that were exposed to ^{90}Sr beginning at ages 110–250 days were less vulnerable to continuous exposure than mice that had been exposed since conception (Finkel et al. 1960). The adult lifespan was shortened by 17% in mice given 31 μCi ^{90}Sr/kg/day (1.15 MBq/kg/day), but was unaffected by administration of up to 16 μCi ^{90}Sr/kg/day (592 kBq/kg/day). In mice exposed from conception, the lifetime was shortened by 40% when given 36 μCi ^{90}Sr/kg/day (1.33 MBq/kg/day), and by 26% when given between 4 and 19 μCi ^{90}Sr/kg/day (148 and 703 kBq/kg/day), but was unaffected by 0.05–0.4 μCi ^{90}Sr/kg/day (1.85–14.8 kBq/kg/day). In albino rats that were fed 0.5 or 2 μCi ^{90}Sr/kg/day (18.5 or 74 kBq/kg/day) for their postweaning lifetime, the lifespan was shortened, by about 18 or 30%, respectively, compared to controls (Zapol'skaya et al. 1974). The authors calculated that the lifespan was shortened by 0.09 day per rad. A plot of mortality against absorbed dose showed maximum mortality (40%) against a skeletal absorbed dose of 4,000 rad (40 Gy). In a study in which eight weanling Dutch rabbits were fed approximately 6 μCi/kg/day (218 kBq/kg/day) in pellets once a day for 31–280 days, some died within a few weeks with bone marrow that was slightly hypoplastic (Downie et al. 1959). The bone marrow was entirely atrophic in rabbits dying several months later with osteogenic sarcoma.

Two related long-term oral exposure studies demonstrated dose-related effects of $^{90}SrCl_2$ on survival in beagle dogs. In the main study, groups of pregnant beagles were fed 0.002–3.6 μCi ^{90}Sr/kg/day (0.074–

133.2 kBq/kg/day) from gestational day 21 through lactation to postnatal day 44, and the pups were fed the same doses from weaning at day 42 through day 540 (Raabe et al. 1983; White et al. 1993). Survival of the pups was reduced by 18, 64, and 85% at the three highest levels (0.4, 1.2, and 3.6 μCi/kg/day or 14.8, 44.4, and 133.2 kBq/kg/day, respectively). Survival was not significantly different from the controls for exposures of 0.002–0.13 μCi/kg/day (0.074–4.8 kBq/kg/day). Mean absorbed skeletal absorbed doses at or below 2,250 rad (22.5 Gy) had no effect on mortality, whereas increased mortality was observed at or above 5,040 rad (50.4 Gy). The secondary study had a similar protocol, except that the dogs were given doses of 0.13–1.2 μCi/day (4.81–44.4 kBq/day) from gestational day 21 throughout their entire lifetime (Book et al. 1982). The mean lifetime absorbed skeletal doses were 2,840–11,190 rad (28.4–111.9 Gy). The median lifespans were reduced by 11–65%, which was similar to the results of the main study. This implies that irradiation after day 540 did not significantly change the survival rate and that survival was shortened because of exposure at a young age. The two main radiation-related causes of death in these studies were myeloproliferative syndrome and skeletal sarcomas (see Section 3.3.2.7 Cancer).

In a multigenerational study of female Pitman-Moore miniature swine, there were dose-related effects on mortality following chronic ingestion of ^{90}Sr in the form of strontium chloride (Clarke et al. 1970; McClellan et al. 1963; Ragan et al. 1973). Sows ingesting 3,100 μCi ^{90}Sr/day (114.7 MBq/day) from age 9 months did not survive their first pregnancy, succumbing from the destruction of hemopoietic tissue in the bone marrow. The sows developed anemia, leukopenia, thrombocytopenia, and terminal hemorrhagic syndrome (Clarke et al. 1972). Exposure to 25, 125, or 625 μCi ^{90}Sr/day (0.925, 4.625, or 23.13 MBq/day) significantly increased mortality after 11, 5, and 1 year(s), respectively, whereas exposure to 1 or 5 μCi ^{90}Sr/day (37 or 185 kBq/day) had no effect on survival. Effects on the F1 females exposed from the time of conception were more severe, even though, after weaning, their administered dose level was only a fraction of the maternal level until the age of 6 months. None of the F1 females exposed to 625 μCi ^{90}Sr/day (23.13 MBq/day) survived to the age of 9 months, whereas that dose was not immediately fatal to the parental generation of sows. Furthermore, the F1 females receiving 25 μCi ^{90}Sr/day (925 kBq/day) showed a significant increase in cumulative mortality after 7 years, rather than 11. However, the 1 and 5 μCi ^{90}Sr/day levels (37 and 185 kBq/day), as in the parental generation, had no effect on survival. In this study, the average attained body burden was 10, 50, 250, 1,250, and 4,700 μCi (0.37, 1.85, 9.25, 46.25, and 173.9 MBq) for the 1, 5, 25, 125, and 625 μCi ^{90}Sr/day (0.037, 0.185, 0.925, 4.625, and 23.13 MBq/day) levels, respectively.

All reliable LOAEL values for death from oral exposure to radioactive strontium in each species and duration category are recorded in Table 3-3 and plotted in Figure 3-3.

3.3.2.2 Systemic Effects

No studies were located regarding endocrine, dermal, or metabolic effects in humans or animals after oral exposure to radioactive strontium. The highest reliable NOAEL and all LOAEL values for the systemic effects from oral exposure to radioactive strontium are shown in Table 3-3 and plotted in Figure 3-3.

Respiratory Effects. No studies were located regarding respiratory effects in humans following oral exposure to radioactive strontium isotopes. No studies were located regarding respiratory effects in animals following acute- or intermediate-duration exposure to radioactive strontium. In a chronic-duration beagle study, animals exposed to 0.4 or 1.2 µCi/kg/day (14.8 or 44.4 kBq/kg/day) of ^{90}Sr *in utero* from gestational day 21, throughout lactation, and from weaning on day 42 to day 540 exhibited only secondary respiratory effects (Dungworth et al. 1969); lungs showed varying degrees of myeloid infiltration (see Section 3.3.2.7 Cancer). Since this effect is not the direct result of the action of radiostrontium on lung tissue, but rather a secondary effect of myeloid proliferation induced by irradiation of bone marrow, it is not categorized under Systemic: Respiratory Effects in Table 3-3.

Cardiovascular Effects. No studies were located regarding cardiovascular effects in humans after oral exposure to radioactive strontium isotopes. No studies were located regarding cardiovascular effects in animals after acute- or intermediate-duration oral exposure to radioactive strontium isotopes. Petechiae, ecchymoses, and gastrointestinal bleeding were found postmortem in some beagles in a chronic-duration study, in which animals were exposed to 0.002–1.2 µCi ^{90}Sr/kg/day (0.074–44.4 kBq/kg/day) *in utero* from gestational day 21, throughout lactation, and from weaning on day 42 to day 540 (Dungworth et al. 1969). These findings, observed in high dose animals (0.4 and 1.2 µCi/kg/day; 14.8 and 44.4 kBq/kg/day), indicated the presence of a hemorrhagic disorder related to thrombocytopenia (see Hematological Effects below).

The highest reliable NOAEL and all LOAEL values for cardiovascular effects from oral exposure to radioactive strontium in each species and duration category are shown in Table 3-3 and plotted in Figure 3-3.

Table 3-3 Levels of Significant Exposure to Strontium - Radiation Toxicity - Oral

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (uCi/kg/day)	LOAEL Less Serious (uCi/kg/day)	LOAEL Serious (uCi/kg/day)	Reference Chemical Form
	ACUTE EXPOSURE						
	Death						
1	Monkey (Rhesus)	5-10 d (GW)				28 M (1/1 dead within 4 months from pancytopenia; est skeletal dose at death =4,500 rad)	Casarett et al. 1962 Strontium-90
2	Rat (Long- Evans)	10 d ad lib (W)				297 M (lifespan decr 80%)	Casarett et al. 1962 Strontium-90
3	Cow	5 d 1 x/d				44 F (4/6 died within 5 months)	Cragle et al. 1969 Strontium-90
	Systemic						
4	Rat (Long- Evans)	10 d ad lib (W)	Hemato			297 M (hypoplasia of bone marrow)	Casarett et al. 1962 Strontium-90
			Musc/skel			297 M (failure of osteogenesis)	
5	Rat (Long- Evans)	10 d ad lib (W)	Hemato		64 M (slight hypoplasia of bone marrow)		Casarett et al. 1962 Strontium-90
6	Cow	5 d 1 x/d	Gastro			44 F (intestinal hemorrhage)	Cragle et al. 1969 Strontium-90
			Hemato			44 F (severe leukopenia, thrombocytopenia)	
	Reproductive						
7	Rat	once (G)				0.15 F (20% fetal mortality)	Howard and Clarke 1970 Strontium-90

Table 3-3 Levels of Significant Exposure to Strontium - Radiation Toxicity - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (uCi/kg/day)	LOAEL: Less Serious (uCi/kg/day)	LOAEL: Serious (uCi/kg/day)		Reference Chemical Form
	Cancer							
8	Monkey (Rhesus)	5-10 d 1 x/d (GW)				11	(CEL: leukemia in 1/1)	Casarett et al. 1962 Strontium-90
9	Rat (Long- Evans)	10 d ad lib (W)				300 M	(CEL: osteosarcoma)	Casarett et al. 1962 Strontium-90
10	Rat (Long- Evans)	10 d ad lib (W)				135 M	(CEL: 2 x incr in incidence of malignancies)	Casarett et al. 1962 Strontium-90
	INTERMEDIATE EXPOSURE							
	Death							
11	Rat (Long- Evans)	30 d ad lib (W)				74 M	(35% decr survival)	Casarett et al. 1962 Strontium-90
12	Rabbit (Dutch)	31-280 d 1 x/d (F)				6	(premature death from bone marrow hypoplasia)	Downie et al. 1959 Strontium-90
	Systemic							
13	Rat (Long- Evans)	30 d ad lib (W)	Hemato			74 M	(moderate bone marrow hypoplasia)	Casarett et al. 1962 Strontium-90
			Musc/skel			74 M	(damaged epiphyseal cartilage)	
14	Rabbit (Dutch)	31-280 d 1 x/d (F)	Hemato			6	(bone marrow hypoplasia; anemia, reduced platelets)	Downie et al. 1959 Strontium-90
			Musc/skel			6	(decr osteocytes, decr blood vessels of bone)	

Table 3-3 Levels of Significant Exposure to Strontium - Radiation Toxicity - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (uCi/kg/day)	LOAEL: Less Serious (uCi/kg/day)	LOAEL: Serious (uCi/kg/day)		Reference Chemical Form
	Reproductive							
15	Mouse (CF-1)	600 d ad lib (F)		31 F				Finkel et al. 1960 Strontium-90
	Cancer							
16	Rat (Long- Evans)	30 d ad lib (W)				74 M	(CEL: 28% osteosarcoma, 11% skin carcinoma, 6% leukemia compared to none in control group)	Casarett et al. 1962 Strontium-90
17	Rat (Long- Evans)	37 d 1 x 30 d ad lib (W)				74 F	(CEL: osteosarcoma)	Hopkins et al. 1966 90Sr
18	Rabbit (Dutch)	31-280 d 1 x/d (F)				6	(CEL: osteosarcoma; multiple myeloma)	Downie et al. 1959 Strontium-90
	CHRONIC EXPOSURE							
	Death							
19	Rat (albino)	372-620 d daily ad lib (F)				0.5	(18% mortality)	Zapol'skaya et al. 1974 Strontium-90
20	Mouse (CF-1)	600 d ad lib (F)				31 F	(survival decr 17%)	Finkel et al. 1960 Strontium-90
21	Mouse (CF-1)	GD0-PND 414 ad lib (F)				4 F	(survival decr 36%)	Finkel et al. 1960 Strontium-90

Table 3-3 Levels of Significant Exposure to Strontium - Radiation Toxicity - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (uCi/kg/day)	LOAEL Less Serious (uCi/kg/day)	LOAEL Serious (uCi/kg/day)	Reference Chemical Form
	Systemic						
22	Rat (albino)	372-620 d daily ad lib (F)	Hemato			0.5 (~21% leukopenia lasting 2 yrs)	Zapol'skaya et al. 1974 Strontium-90
23	Mouse (CF-1)	GD0-PND 414 ad lib (F)	Bd Wt	36 F			Finkel et al. 1960 Strontium-90
24	Dog (Beagle)	GD40-death ad lib (F)	Musc/skel			0.4 M (osteodystrophy)	Book et al. 1982 Strontium-90
25	Dog (Beagle)	GD40-PND540 ad lib (F)	Cardio			0.4 M (petechiae, ecchymoses, gastrointestinal bleeding)	Dungworth et al. 1969 Strontium-90
			Hemato			0.4 M (leukopenia, anemia, thrombocytopenia; poikilocytosis, anisocytosis, hypochromasia of erythrocytes)	
			Hepatic			0.4 M (periacinar lipidosis; terminal necrosis)	
			Bd Wt			0.4 M (progressive weight loss in anemic dogs)	
26	Dog (Beagle)	GD40-PND540 ad lib (F)	Musc/skel			0.4 M (osteolytic lesions, osteoporosis, cortical sclerosis and thickening, mottling)	Momeni et al. 1976 Strontium-90

Table 3-3 Levels of Significant Exposure to Strontium - Radiation Toxicity - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (uCi/kg/day)	LOAEL Less Serious (uCi/kg/day)	LOAEL Serious (uCi/kg/day)	Reference Chemical Form
	Immuno/ Lymphoret						
27	Dog (Beagle)	GD40-PND540 ad lib (F)				0.4 M (splenic myeloid metaplasia)	Dungworth et al. 1969 Strontium-90
	Developmental						
28	Mouse (CF-1)	600 d ad lib (F)				3 F (decr postnatal survival from cancer)	Finkel et al. 1960 Strontium-90
	Cancer						
29	Rat (albino)	372-620 d daily ad lib (F)				2 (CEL: lymphosarcoma, osteosarcoma)	Zapol'skaya et al. 1974 Strontium-90
30	Mouse (CF-1)	600 d ad lib (F)				0.03 F (CEL: reticular tumors)	Finkel et al. 1960 Strontium-90
31	Mouse (CF-1)	GD0-PND 414 ad lib (F)				36 F (CEL: 4x incr reticulocyte tumors; osteosarcoma)	Finkel et al. 1960 Strontium-90
32	Dog (Beagle)	GD40-death ad lib (F)				0.4 M (premature death from cancer)	Book et al. 1982 Strontium-90
33	Dog (Beagle)	GD40-PND540 ad lib (F)				1.3 M (CEL: osteosarcoma) 0.4 M (incr death from cancer)	White et al. 1993 Strontium-90

[a] The number corresponds to entries in Figure 3-3.

Ad lib - ad libitum; Bd Wt = body weight; Cardio = cardiovascular; CEL = cancer effect level; d = day(s); decr = decreased; (F) = food; (G) = gavage; Gastro = gastrointestinal; GD = gestational day; (GW) = gavage in water; Hemato = hematological; incr = increased; LOAEL = lowest-observed-adverse-effect level; min = minute(s); mo = month(s); Musc/skel = musculoskeletal; NOAEL = no-observed-adverse-effect level; PND = post natal day; (W) = water; wk = week(s); x = time(s); yr = year(s)

Figure 3-3 Levels of Significant Exposure to Strontium - Radiation Toxicity - Oral

Acute (≤14 days)

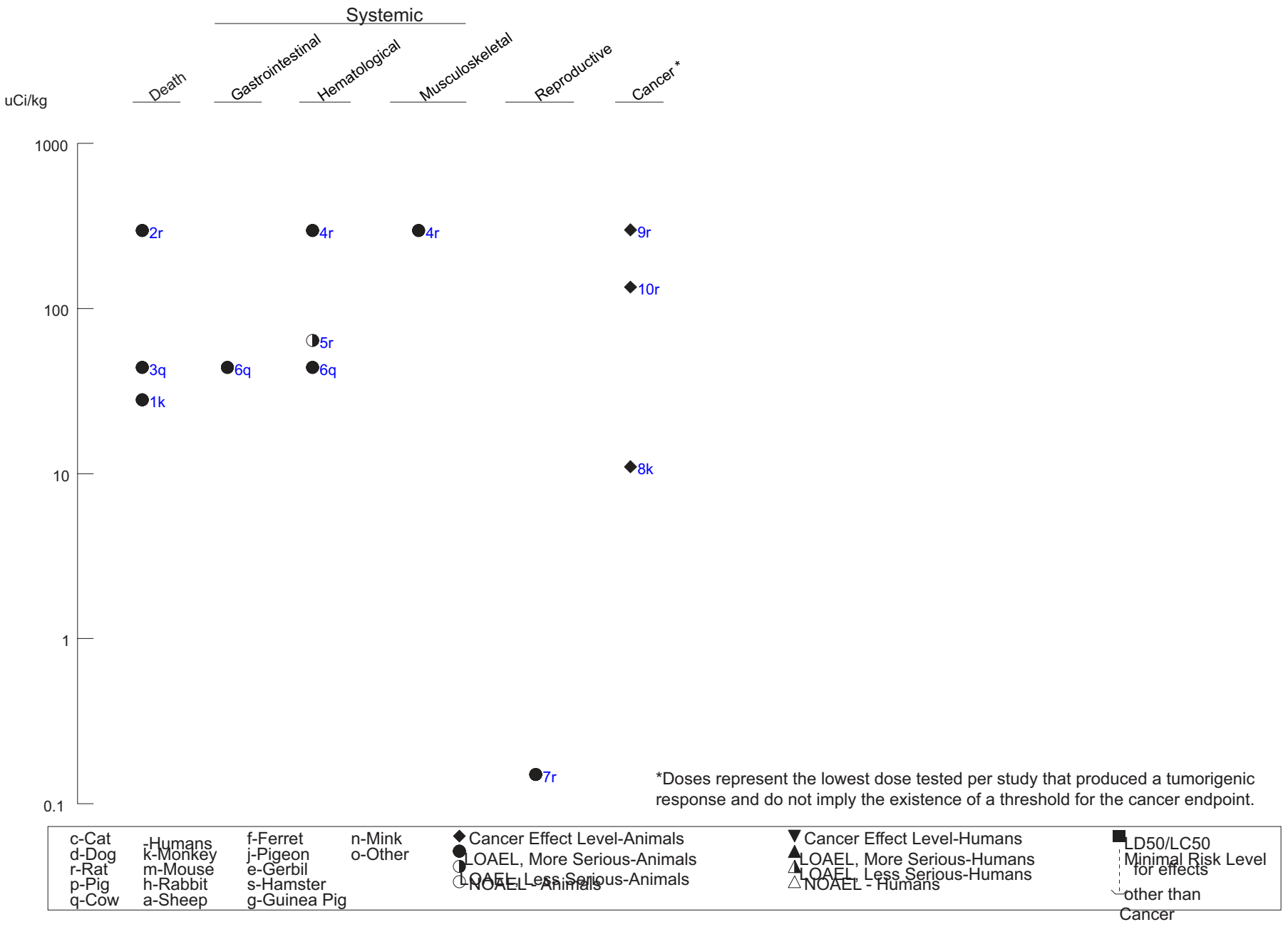


Figure 3-3 Levels of Significant Exposure to Strontium - Radiation Toxicity - Oral (*Continued*)

Intermediate (15-364 days)

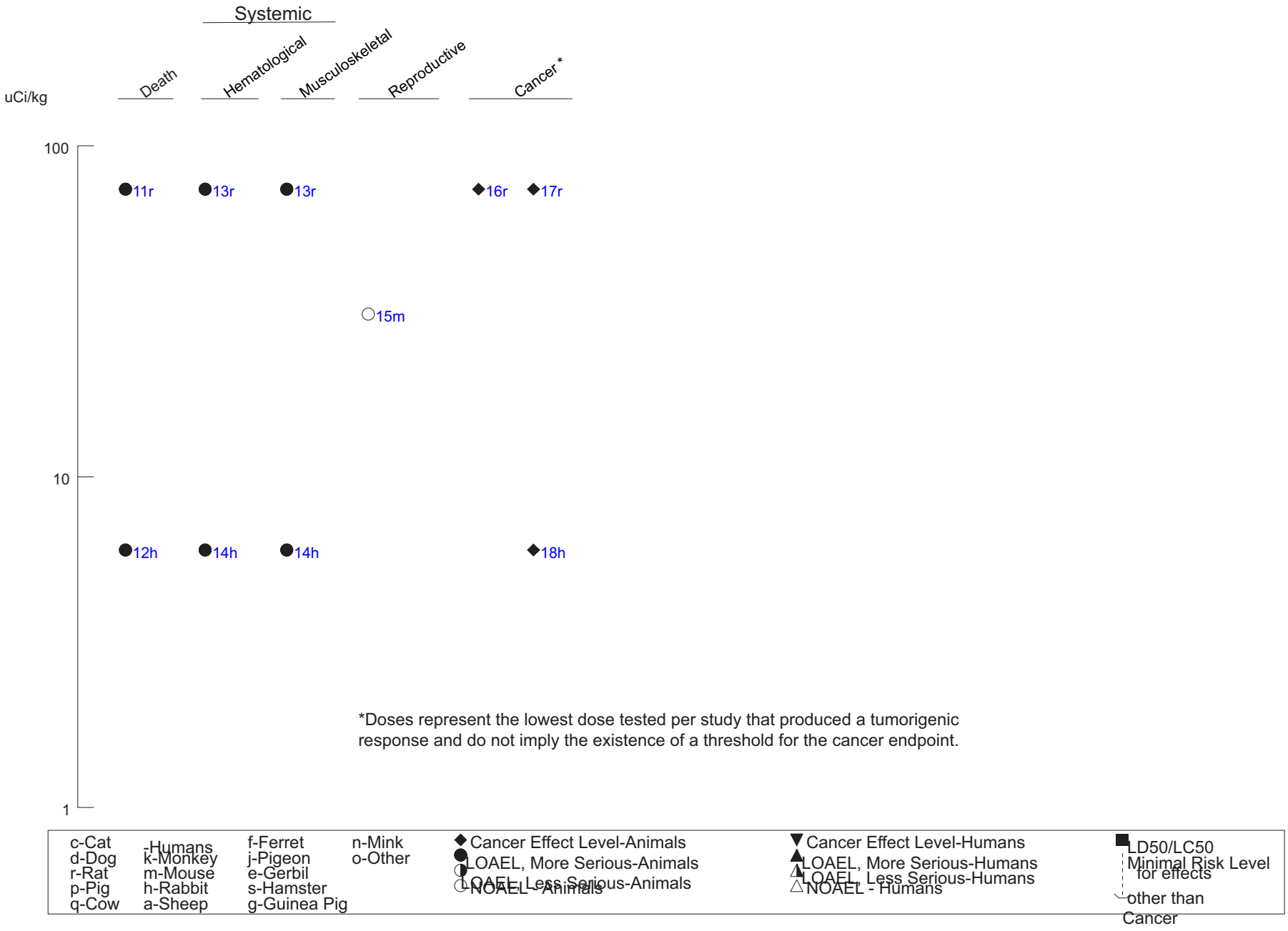
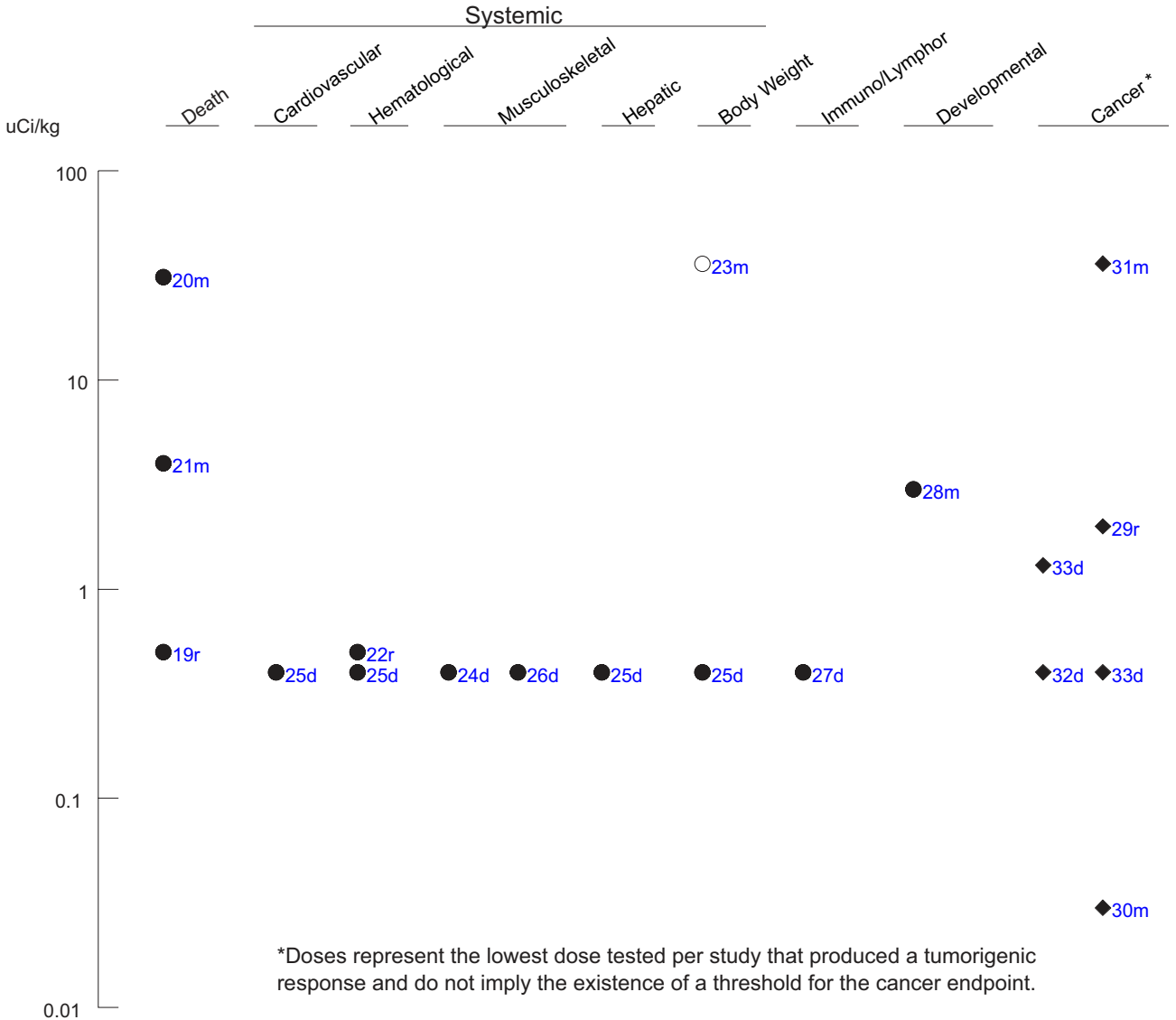


Figure 3-3 Levels of Significant Exposure to Strontium - Radiation Toxicity - Oral (*Continued*)

Chronic (≥365 days)



*Doses represent the lowest dose tested per study that produced a tumorigenic response and do not imply the existence of a threshold for the cancer endpoint.

c-Cat
d-Dog
r-Rat
p-Pig
q-Cow

-Humans
k-Monkey
m-Mouse
h-Rabbit
a-Sheep

f-Ferret
j-Pigeon
e-Gerbil
s-Hamster
g-Guinea Pig

n-Mink
o-Other

◆ Cancer Effect Level-Animals
● LOAEL, More Serious-Animals
◑ LOAEL, Less Serious-Animals
○ NOAEL - Animals

▼ Cancer Effect Level-Humans
▲ LOAEL, More Serious-Humans
◭ LOAEL, Less Serious-Humans
△ NOAEL - Humans

■ LD50/LC50
Minimal Risk Level for effects other than Cancer

Gastrointestinal Effects. No studies were located regarding gastrointestinal effects in humans after oral exposure to radioactive strontium. Intestinal hemorrhage occurred in cows succumbing to radiation sickness 3 months after ingesting 44 μCi ^{90}Sr/kg/day (1.63 MBq/kg/day) for 5 days (Cragle et al. 1969). It is likely that other reports of terminal hemorrhagic effects (see Hematological Effects below) following high doses of radiostrontium encompassed intestinal hemorrhage whether or not it was specifically mentioned.

Hematological Effects. In human and animal studies, adverse hematological affects were associated with beta radiation of bone marrow following incorporation of radiostrontium into bone.

The Techa River population exposed to chronic combined external gamma radiation and internal radiation due to ^{90}Sr and ^{137}Cs exhibited alterations in hematological parameters, including leukopenia, thrombocytopenia, and granulocytopenia (Akleyev et al. 1995). These effects were observed in a portion of the exposed population that received radiation doses to the bone marrow at rates in excess of 30–50 rem (0.3–0.5 Sv) per year. These data are omitted from Table 3-3 because exposures were to multiple sources of radiation.

Among Rhesus monkeys given 1,000 μCi (37 MBq) of ^{90}Sr over 10 days, the one with the highest dose on a kg body weight basis (28 μCi/kg/day; 1.0 MBq/kg/day) died from pancytopenia within 4 months of treatment (Casarett et al. 1962). Among young (30 days old) Long-Evans rats that were given >300 μCi ^{90}Sr/kg/day (11 MBq/kg/day) in drinking water for 10 days (total 460 μCi; 17 MBq), the bone marrow was extremely hypoplastic. Hypoplastic effects were slight among adult males given doses of 64 or 135 μCi/kg/day or adult females given 92 or 194 μCi/kg/day (total 330 or 650 μCi; total 12.2 or 24.1 MBq; Casarett et al. 1962). Skeletal radiation doses were about 15 times higher in the younger rats. In another acute study, six young female dairy cattle (three sets of twins, ages 398 and 479 days and weighing 145–349 kg at the start of treatment) were given 44 μCi ^{90}Sr/kg/day (1.63 MBq/kg/day) for 5 days (Cragle et al. 1969). All six heifers exhibited decreases in leukocyte and platelet counts by the first month. In surviving animals, the counts plateaued at about 60% of the normal value. In four animals, the youngest (398 days old) and lightest (145–212 kg) at the time of dosing, leukocyte and platelet counts dropped severely after 80 days, shortly before the onset of the terminal stages of radiation sickness.

In an intermediate-duration study in young Long-Evans rats, moderate hypoplasia of the bone marrow occurred among males (87 days old) given 74 μCi/kg/day and females given 104 μCi/kg/day (2.7 and

3.8 MBq/kg/day, respectively) of ^{90}Sr in drinking water for 30 days (total 790 μCi; 29.2 MBq) (Casarett et al. 1962). Hypoplasia of the bone marrow leading to anemia and thrombocytopenia developed in Dutch rabbits that were fed approximately 6 μCi ^{90}Sr/kg/day (218 kBq/kg/day) in pellets for 31–280 days (Downie et al. 1959).

Chronic-duration studies in several species reported suppression of hematopoiesis. In albino rats fed ≥0.5 μCi ^{90}Sr/kg/day (18.5 kBq/kg/day) for their post-weaning lifetime, hematopoiesis was significantly depressed (Zapol'skaya et al. 1974). Lymphocytes were the first cells affected, then neutrophils, thrombocytes, and after 1 year, erythrocytes. Morphological abnormalities included binucleation. At 0.5 μCi ^{90}Sr/kg/day (18.5 kBq/kg/day), leukocyte numbers remained 20% depressed by the end of the second year. The authors calculated that the minimal dose to induce leukopenia was 150–200 rad. The reduction in leucocytes plateaued at about 30–35% for absorbed doses between 400 and 2,000 rad. Hematological effects were reported in a chronic-duration beagle study, in which animals were exposed to 0.002–1.2 μCi/kg/day (0.074–44.4 kBq/kg/day) of ^{90}Sr *in utero* from gestational day 21, throughout lactation, and from weaning on day 42 to day 540 (Dungworth et al. 1969). Six years after exposure began, the following effects were observed at doses of 0.44 or 1.2 μCi/kg/day (14.8 or 44.4 kBq/kg/day): abnormal erythrocyte morphology (primarily poikilocytosis, anisocytosis, and hypochromasia, with some instances of macrocytosis), dose-related, radiation-induced leukopenia, an abnormal number of immature granulocytes, one case of unusual giant neutophils, a reduction in the number of platelets, anemia, and splenomegaly. Similarly, female Pitman-Moore miniature swine exposed to 3,100 μCi ^{90}Sr/day (114.7 MBq/day) as strontium chloride died within 3–4 months from destruction of hematopoietic tissue in bone marrow, which resulted in anemia, leukopenia, thrombocytopenia, and terminal hemorrhagic syndrome (Clarke et al. 1972). In addition, two animals in this group developed myeloid metaplasia.

Musculoskeletal Effects. Skeletal effects following oral exposure to radioactive strontium have been reported in humans and animals. Dystrophic lesions of the skeleton, primarily affecting articular and periarticular tissues, were observed in the Techa River populations that were chronically exposed to radiostrontium and other radionuclides in contaminated food and water (Akleyev et al. 1995). The incidence of skeletal lesions was significantly higher for mean radiation doses to the surface of bone in excess of 200 rem (2 Sv).

In an acute uptake, chronic radiation study, male and female 30-day-old Long-Evans rats that were given 300 or 390 μCi ^{90}Sr/kg/day, respectively (11 or 14.4 MBq/kg/day) in drinking water for 5–10 days (total 460 μCi; 17 MBq) exhibited signs of abnormal osteogenesis more than 10 months after administration

(Casarett et al. 1962). As marrow failed to invade into metaphyseal cartilage, the cartilage resumed active proliferation. Resorption failed to occur in metaphyseal cartilage and metaphyseal spongiosa failed to transform to lamellar bone. Often, cartilage and fibrous marrow were incorporated into cortical bone, sometimes causing fracture and deformation.

In an intermediate uptake, chronic radiation study on young (87 days old) Long-Evans rats, ingestion of 74 (males) or 104 (females) μCi ^{90}Sr /kg/day (2.7 or 3.8 MBq/kg/day) in drinking water for 30 days (total 790 μCi; 28.9 MBq) adversely affected the vasculature of the bone, which interfered with the normal transformation of cartilage into bone (Casarett et al. 1962). At the end of the long bones, the cartilage discs were damaged, with detachment of primary spongiosa and failure of resorption. In another intermediate-duration study, numbers of osteocytes (bone cells surrounded by a mineralized matrix and connected by a mesh-work of processes) were reduced in Dutch rabbits that ingested approximately 6 μCi ^{90}Sr/kg/day (218 kBq/kg/day) in pellets for 48 days (Downie et al. 1959).

Bone damage was a notable effect of chronic-duration oral exposure to radioactive strontium in dogs (Momeni et al. 1976). Groups of pregnant beagles were fed 0.002–3.6 μCi ^{90}Sr/kg/day (0.074–133.2 kBq/kg/day) from gestational day 21 through lactation to PND 44, and the pups were fed the same doses from weaning at day 42 through day 540 (Raabe et al. 1983; White et al. 1993). Ten years from the start of the study, dose-related skeletal effects included mild trabecular osteopenia, endosteal and periosteal cortical changes (sclerosis and thickening), and mottling or focal osteolytic lesions (Momeni et al. 1976). These occurred in all the dogs in the 3.6 μCi/kg/day group and also in the 1.2 and 0.4 μCi/kg/day groups (133.2, 44.4, and 14.8 kBq/kg/day, respectively). Radiation-induced osteodystrophy was noted in three out of four beagle dogs that received 1.2 μCi ^{90}Sr/kg/day (44.4 kBq/kg/day) for life beginning at midgestion (Book et al. 1982); the average dose rate (cumulative dose divided by lifespan) for these dogs was 4 rad/day (0.04 Gy/day). Radiation osteonecrosis was said to be a common finding among female Pitman-Moore miniature swine that died with hematopoietic disorders or bone marrow hypoplasia after ingesting $^{90}SrCl_2$ at levels between 1 and 3,100 μCi/day (0.37–114.7 MBq/day) until death (Clarke et al. 1972). The incidence of osteonecrosis at each dose level was not reported. Bone cancers that were reported in these chronic studies are discussed below in Section 3.3.2.7.

Hepatic Effects. No studies were located regarding hepatic effects in humans after oral exposure to radioactive strontium isotopes. No studies were located regarding hepatic effects in animals after acute- or intermediate-duration oral exposure to radioactive strontium isotopes. In a chronic-duration beagle

study, animals exposed to 0.4 or 1.2 µCi ^{90}Sr/kg/day (14.8 or 44.4 kBq/kg/day) *in utero* from gestational day 21, throughout lactation, and from weaning on day 42 to day 540 exhibited only secondary hepatic effects (Dungworth et al. 1969). Livers were sometimes enlarged from myeloid infiltration and periacinar lipidosis, sometimes with terminal necrosis, in dogs with severe anemia. Since the observed myeloid infilitration was a secondary effect resulting from irradiation of the bone marrow, it is not categorized under Systemic: Hepatic Effects in Table 3-3.

Renal Effects. No studies were located regarding renal effects in humans after oral exposure to radioactive strontium isotopes. Approximately 19% of adult Long-Evans rats ingesting 65 µCi ^{90}Sr/day (2.41 MBq/day; 135 or 194 µCi/kg/day, 5 or 7.2 MBq/kg/day for males and females, respectively) of in drinking water for 10 days developed chronic interstitial nephritis, a common disease in older rats, during their remaining lifespan (Casarett et al. 1962). It is very unlikely that the ingestion of radiostrontium was related to the occurrence of nephritis.

Ocular Effects. No studies were located regarding ocular effects in humans after oral exposure to radioactive strontium isotopes.

No studies were located regarding ocular effects in animals after acute- or intermediate-duration oral exposure to radioactive strontium isotopes. In one chronic-duration study, 2 out of 403 beagles that had been exposed to ^{90}Sr *in utero* from gestational day 21, during lactation, and from weaning on day 42 to day 540, developed a benign melanoma of the eye, but the dose-level was not reported (Raabe et al. 1994). Statistical analysis showed that these tumors (not found in controls, but also found in dogs irradiated through other exposure routes, or with other radionuclides) were significantly related to exposure to ionizing radiation. According to a 6-year report from the same chronic-duration beagle study, animals exposed to 0.4 or 1.2 µCi ^{90}Sr/kg/day (14.8 or 44.4 kBq/kg/day) *in utero* from gestational day 21, throughout lactation, and from weaning on day 42 to day 540 exhibited only indirect ocular effects (Dungworth et al. 1969). The eyes of dogs with a myeloproliferative disorder exhibited some slight degree of myeloid infiltration (see Section 3.3.2.7 Cancer). Since this was a secondary effect resulting from irradiation of bone marrow and not the direct response of the eye tissues to radiostrontium, it is not categorized under Ocular Effects in Table 3-3.

Body Weight Effects. No studies were located regarding body weight effects in humans after oral exposure to radioactive strontium isotopes. No studies were located regarding body weight effects in animals after acute- or intermediate oral exposure to radioactive strontium. No effect on body weight was

observed among female CF-1 mice that had been exposed to ^{90}Sr *in utero*, during lactation, and up to day 414 at doses of up to 36 μCi of ^{90}Sr/kg/day (1.33 MBq/day) (Finkel et al. 1960). Progressive weight loss was observed among beagle dogs that developed anemia after having been exposed to 0.4–1.2 μCi of ^{90}Sr/kg/day (148–444 kBq/kg/day) from mid-gestation to age 1.5 years (Dungworth et al. 1969).

3.3.2.3 Immunological and Lymphoreticular Effects

Immunological changes were reported in the Techa River population that was exposed to chronic combined external gamma radiation and internal radiation from ^{90}Sr and ^{137}Cs between 1949 and 1956 (Akleyev et al. 1995). Immunological disorders persisted for 30 years and included decreased expression of antigens of differentiating T-lymphocytes, decreased T-lymphoblast transformation, and reduced counts of large granulocytic lymphocytes. Granulocytopenia developed in a portion of the exposed population that received radiation to the bone marrow at rates in excess of 30–50 rem (0.3–0.5 Sv) per year. Akleyev et al. (1995) suggested that radiation-induced immunodeficiency may have contributed to the higher incidence of leukemia in the exposed population (see Section 3.3.2.7 Cancer). Clinical manifestations of immune insufficiency in exposed cancer patients included 3-fold increases in the incidences of infectious diseases (chronic pneumonia, chronic bronchitis, pulmonary tuberculosis, and osteomyelitis) compared to a nontumor-bearing group. These data are omitted from Table 3-3 because of the mixed exposures.

No animal studies were located that described immunological effects following acute oral uptake of radiostrontium. Intermediate-to-chronic-duration exposures to radiostrontium resulted in impaired immune function in animals. In Pitman-Moore miniature pigs that were fed 625 μCi ^{90}Sr/day (23.13 MBq/day) as strontium chloride for 9 months, the antibody response to inoculated *Brucella abortus* (strain 19) antigen was determined by the plate agglutination test to be less than half that of controls (Howard 1970). In another test, peripheral leukocyte cultures were prepared from these same animals at monthly intervals, in medium containing phytohemagglutinin (PHA). In pigs that were fed 625 μCi ^{90}Sr/day (23.13 MBq/day) for 4–5 months, peripheral lymphocytes lost the ability to respond to PHA stimulation; this adverse effect was sustained for at least 6 months. The author attributed these immunological effects to exposure to ^{90}Sr. Myeloid metaplasia also afflicted female Pitman-Moore miniature swine that were fed 3,100 μCi ^{90}Sr/day (114.7 MBq/day) until the end of life at age 3–4 months (Howard and Clarke 1970). The cumulative doses at the time of death ranged from 40 to 10,000 rad (0.4–100 Gy).

In a 6-year status report of a chronic uptake study in which beagle dogs were exposed to ^{90}Sr from midgestion to age 1.5 years, 1.3% of dogs receiving 0.4 μCi ^{90}Sr/kg/day (14.8 kBq/kg/day) and 3.7% of dogs receiving 1.2 μCi ^{90}Sr/kg/day (44.4 kBq/kg/day) developed myeloid metaplasia of the spleen (Dungworth et al. 1969).

The highest reliable NOAEL values and all LOAEL values for immunological and lymphoreticular effects from oral exposure to radioactive strontium in each species and duration category are recorded in Table 3-3 and plotted in Figure 3-3.

3.3.2.4 Neurological Effects

Nervous system disorders (weakness, apathy, fatigue) were reported in the Techa River population that was chronically exposed to combined external gamma radiation and internal radiation from ^{90}Sr and ^{137}Cs (Akleyev et al. 1995). Neurological effects were observed at chronic dose rates in excess of 40–50 rad (0.4–0.5 Gy) per year and persisted for 14–20 years in the exposed population. However, it is not clear to what extent strontium-derived radiation contributed to neurological effects, compared to external gamma radiation. These data are omitted from Table 3-3 because of the mixed exposures.

No studies were located that reported neurological effects in animals following oral exposure to radioactive strontium isotopes.

3.3.2.5 Reproductive Effects

No significant reproductive effects were reported in the Techa River population that was exposed to combined external gamma radiation and internal radiation from ^{90}Sr and ^{137}Cs between 1949 and 1956 (Kossenko et al. 1994). Exposure had no effect on birth rate, fertility, or the incidence of spontaneous abortions in the study group that had received average doses to the gonads of up to 74 rem (0.74 Sv), primarily from external gamma radiation (Akleyev et al. 1995). An increase in the incidence of ectopic pregnancies was not dose-associated. These data are omitted from Table 3-3 because exposures were to multiple sources and it is probable that radiostrontium had a minor effect on the gonadal radiation dose.

In one acute study, female rats were given a single dose of 400 μCi ^{90}Sr/kg by gavage 1–10 days before impregnation (Moskalev et al. 1969). At the time of conception, the maternal skeletal dose was 800 rad

(8 Gy) and soft tissue dose was 10 rad (0.1 Gy). Fetuses received skeletal doses of 20 rad (0.2 Gy). Under these conditions, 22% of fetuses died. In an intermediate-duration study, groups of 230–339 female CF-1 mice were fed ^{90}Sr in the diet at doses between 0.03 and 31 μCi/kg/day (1.11 and 1,147 kBq/day; Finkel et al. 1960). Dams and males bred while on the radiostrontium diet, and dams were maintained on diet throughout gestation and lactation. Radiostrontium feeding had no effect on fertility, the number of live offspring, or the number of female offspring surviving at PND 35.

In a multigenerational study, 9-month-old female Pitman-Moore miniature swine were fed a diet containing between 1 and 3,100 μCi ^{90}Sr/day (0.037 and 114.7 MBq/day) and then were bred with males that were only exposed to ^{90}Sr during the period of mating (Clarke et al. 1970, 1972; McClellan et al. 1963). Ingestion of radioactive strontium had no effect on fertility or fecundity. Pregnant sows receiving 3,100 μCi ^{90}Sr/day (114.7 MBq/day) did not survive to the end of the period of gestation because of bone marrow hypoplasia, but their fetuses were apparently normal (McClellan et al. 1963). For doses between 1 and 625 μCi ^{90}Sr/day (0.037 and 23.13 MBq/day), there was no significant effect on litter size, percentage of stillborn, or birth weight. Exposure had no effect on frequency and duration of the estrus cycle or in the number of repeat breedings. However, the F1 offspring of the sows ingesting 625 μCi ^{90}Sr/day (23.13 MBq/day) did not survive to adulthood. Survival of the F2 offspring was apparently similar to the F1 generation, but their reproductive capacity was not reported, since later studies focused on cancer effects.

The highest reliable NOAEL values and all LOAEL values for reproductive effects from oral exposure to radioactive strontium in each species and duration category are recorded in Table 3-3 and plotted in Figure 3-3.

3.3.2.6 Developmental Effects

Few developmental effects were reported in the progeny of the Techa River population that was exposed to combined external gamma radiation and internal radiation from ^{90}Sr and ^{137}Cs between 1949 and 1956 (Kossenko et al. 1994). The cohort of women in the study received radiation doses to the gonads of up to 74 rem (0.74 Sv), primarily from external gamma radiation (Akleyev et al. 1995); the proportion of the dose attributable to radiostrontium was not specified, but is likely to have been relatively small. No increase in the incidences of spontaneous abortion, miscarriages, or stillbirths was observed. However, there were slight increases in child mortality from chromosomal defects and from congenital anomalies of

the nervous system, circulatory system, and other unspecified anomalies in the progeny of the exposed group compared to controls. Considering deaths from these anomalies, from labor complications, or from unspecified perinatal causes, the mortality coefficient of the offspring of parents with gonadal doses of 11 rem (0.11 Sv) was double that of the unexposed control group. Kossenko et al. (1994) calculated that the gonadal doses required to double the incidences of stillbirths, miscarriages, early neonatal mortality, or lethal developmental effects were rather high, ranging from 20 to 480 rem (0.2–4.8 Sv) for the different end points. These data are omitted from Table 3-3 because of the combined internal and external radiation exposures.

In one animal study, CF-1 mice were exposed to ^{90}Sr from the time of conception; breeding adults were fed a diet containing 0.03–31 μCi ^{90}Sr/kg/day (1.11–1,147 kBq/kg/day), and the dams were fed the same diet throughout gestation and lactation (Finkel et al. 1960). The offspring were fed the same diet throughout their lifetimes. Gestational exposure to radiostrontium did not affect litter size or early survival of offspring, and no teratogenic effects were noted. However, survival of the offspring was shortened at doses of 3 μCi ^{90}Sr/kg/day (111 kBq/kg/day) or higher, which was related to the higher incidence of bone-related cancer (see Section 3.3.2.7 Cancer). Autoradiographs demonstrated the uniform distribution of ^{90}Sr in the skeleton, which probably contributed to these effects.

In a large multigenerational study, 9-month-old female Pitman-Moore miniature swine were fed a diet containing between 1 and 3,100 μCi ^{90}Sr/day (0.037 and 114.7 MBq/day) and then were bred with males that were only exposed to ^{90}Sr during the period of mating (Clarke et al. 1970, 1972; McClellan et al. 1963). Ingestion of radioactive strontium had no effect on fertility or fecundity. Fetuses were apparently unaffected, even those of sows that died during pregnancy from bone marrow hypoplasia after ingesting 3,100 μCi ^{90}Sr/day (114.7 MBq/day; McClellan et al. 1963). For doses between 1 and 625 μCi ^{90}Sr/day (0.037 and 23.13 MBq/day), there was no significant effect on litter size, percentage of stillborn, or birth weight. In offspring of sows ingesting 625 μCi ^{90}Sr/day (23.13 MBq/day), the weaning weight was reduced because radiation-induced hematopoietic effects reduced the output of milk (Clarke et al. 1970). After weaning, the F1 offspring were fed ^{90}Sr in the diet at graded levels that, by 6 months, equaled the maternal level, 1–625 μCi ^{90}Sr/day (0.037–23.13 MBq/day). The 625 μCi ^{90}Sr/day (23.13 MBq/day) F1 females did not survive to be bred at 9 months. These results indicate an age-related vulnerability to ^{90}Sr, since the 625 μCi ^{90}Sr/day (23.13 MBq/day) dosage was not lethal to the parental generation (pigs exposed from age 9 months).

The highest reliable NOAEL values and all LOAEL values for developmental effects from oral exposure to radioactive strontium in each species and duration category are recorded in Table 3-3 and plotted in Figure 3-3.

3.3.2.7 Cancer

Epidemiological studies have found little or no association between oral exposure to radioactive strontium from fallout and cancer effects in humans. In an epidemiological study using the Danish cancer registry, no association was found between the incidence of thyroid cancer in Denmark between 1943 and 1988 and the levels of skeletal incorporation of ^{90}Sr from fallout (Sala and Olsen 1993). In another epidemiological study, data collected between 1959 and 1970 in a ^{90}Sr monitoring program in Glasgow, Scotland, were used to identify three cohorts with respect to the hypothetical risk for leukemia and non-Hodgkin's lymphoma, acute myeloid leukemia, all childhood cancers combined, and bone tumors (Hole et al. 1993). The three cohorts were a high risk group born in 1963–1966 (exposed to high levels of fallout, i.e., ^{90}Sr, at a young age), a medium risk group born in 1959–1962 (exposed to high levels at an older age), and a low risk group born after 1966. Cumulative incidences for all cancers, leukemia and non-Hodgkin's lymphoma, and acute myeloid leukemia all showed a secular (progressive, noncyclical) increasing trend for children born before 1982. However, the study found no evidence for increased risks of total cancers, leukemia and Non-Hodgkin's lymphoma, or acute myeloid leukemia for cohorts born during the period of highest fallout (radiostrontium) exposure. The few cases of bone tumors showed a statistically nonsignificant increase for children born during the 'high risk' period.

In contrast, the Techa River population that was exposed to contaminated water and food as a result of releases from a nuclear weapons facility exhibited a significant increase in the incidence of leukemia (Kossenko 1996; Kossenko et al. 1997, 2000, 2002). An excess of leukemia cases (0.85 excess cases per 10,000 person-year Gy (95% CI: 0.2; 1.5) was observed in groups of individuals with estimated bone marrow doses in excess of 10 rem (0.1 Sv), and the risk of mortality from leukemia increased with increasing dose (Kossenko, 1997, 2002). This finding can be related to the body burdens of ^{90}Sr, which in the Techa River cohort, have been >100 times higher than fallout-related exposures during the same period (Shagina et al. 2000). No increase in cancer rates has been observed in the progeny of the Techa River cohort (Kossenko 1996).

As shown in numerous animal studies, oral exposure to radioactive strontium may increase the incidence of cancers of bone and bone marrow. In a small study in which young monkeys were given ^{90}Sr by gavage, one given 11.2 µCi ^{90}Sr/kg/day (0.42 MBq/kg/day) for 5 days died of leukemia, with a final skeletal dose of 4,300 rad (43 Gy) 4 years after treatment (Casarett et al. 1962). Two others exposed to an average of 18 µCi ^{90}Sr/kg/day (0.67 MBq/kg/day) for 10 days died from bone-associated cancers (chondrosarcoma, osteosarcoma) within 36 months of treatment, with estimated skeletal doses of 4,700–9,500 rad (47–95 Gy).

Acute-duration experiments using Long-Evans rats demonstrated that weanlings, with their relatively higher rate of incorporation of strontium into the skeleton, were more vulnerable than adults to the carcinogenetic effects of ^{90}Sr (Casarett et al. 1962). Weanlings (30 days old) were given 46 µCi ^{90}Sr/day (1.7 MBq/day) and adults were given 33 or 65 µCi ^{90}Sr/day (1.2 or 2.4 MBq/day) in drinking water for 10 days; on a body weight basis, the amounts given were >300 µCi/kg/day (11 MBq/kg/day) for weanlings, 64 or 135 µCi/kg/day for adult males, or 92 or 194 µCi/kg/day for adult females. After 5 months, 33 µCi (1.2 MBq) of radioisotope were detected in the skeletons of weanlings that received 460 µCi (17 MBq), but only 1 or 2 µCi (37 or 74 kBq) were detected in the skeletons of adults that received 330 or 650 µCi (12.2 or 24.1 MBq), respectively. The differences in incorporation of ^{90}Sr probably accounted for the age-related differences in the incidence of osteosarcoma; 17.5% of weanlings developed osteosarcoma compared to none of the adults. However, in the high dose adults, the overall incidence of malignancy (leukemia, squamous cell carcinoma of the skin, various other carcinomas) was more than doubled, compared to controls. At the lower dose, the overall rate of malignancies in adults was lower than in controls (6.25% compared to 16.2%). In an intermediate-duration experiment, in which male 87-day-old Long-Evans rats were given 74 µCi ^{90}Sr/kg/day (2.7 MBq/kg/day) and females were given 104 µCi ^{90}Sr/kg/day (3.8 MBq/kg/day) in drinking water for 30 days (total 790 µCi; 29.2 MBq), the incidence of osteosarcomas was 27.5% compared to none in the controls. Overall, the incidence of malignancy in the treated group was more than double that of controls; other neoplasms included 11.25% skin carcinoma (facial) and 6.25% leukemia. The 87-day-old rats treated for 30 days had a 5-month skeletal burden of about 11µCi (407 kBq), which, on a kg body weight basis, was less than one quarter that of weanlings treated for 10 days. This discrepancy reflects differences in rates of absorption and osteogenesis, which are higher in the younger rats. The older rats had a higher incidence of osteosarcoma than the weanlings because they survived beyond the latency period for the cancer. In another intermediate-duration rat study, oral exposure to ^{90}Sr for 37 days (total dose of 790 µCi; 29.2 MBq) increased the incidence of osteolysis and osteogenic sarcoma by 21% (Hopkins et al. 1966). The radiation dose to the skeleton after 150 days was 4,000 rad (40 Gy). Young rabbits (~52 days old) that

were fed an average of 6 μCi ^{90}Sr/kg/day (218 kBq/kg/day) ^{90}Sr in pellets for 224–280 days developed multiple osteogenic sarcomas in the skull and at the rapidly growing ends of the long bones within 6–8 months (Downie et al. 1959).

Relatively large studies in rats, mice, dogs, and pigs demonstrated increased tumor induction following chronic ingestion of ^{90}Sr. In the rat study, albino rats were fed between 0.05 and 2 μCi ^{90}Sr/kg/day for their post-weaning lifetime, resulting in exposures between 0.01 and 0.4 μCi/day (Zapol'skaya et al. 1974). In rats consuming 2 μCi ^{90}Sr/kg/day, the number of rats with malignant tumors was 18.7%, compared to 1.3% for controls. At 0.5 ^{90}Sr/kg/day, the tumor incidence was 3–6 times lower (not specified numerically), but the outcome at 0.05 ^{90}Sr/kg/day was not reported. The most common malignancies were lymphosarcoma (8%), osteosarcoma (6.7%), and "leukosis" (4%). The latency periods were 300–540 days for lymphosarcomas and 450–660 days for "leukosis" and osteosarcoma. The cumulative absorbed doses averaged 1,350 rad (13.5 Gy) just before the onset of lymphosarcoma, 2,200 rad (22 Gy) just before the onset of 'leukosis', and 2,400 rad (24 Gy) just before the onset of osteosarcoma.

In the mouse study, mice were exposed either as adults (beginning at age 110–250 days) or from conception to 0.05–36 μCi ^{90}Sr/kg/day (Finkel et al. 1960). There was a higher incidence of reticular tumors in blood-forming tissues, but no evidence of osteogenic sarcoma in all adult exposed groups. Possibly because of the experimental design-groups were not exposed simultaneously and were subjected to environmental differences-tumor incidence in adults did not show a clear dose-response. However, the tumor incidence was significantly elevated in mice exposed to ^{90}Sr from conception. The highest dose level resulted in the early appearance of reticular tumors, especially lymphomas; 24% of mice at this level died with reticular-tissue tumors by 525 days, compared to 6% in controls. Other tumors unique to the high-dose level included six osteogenic sarcomas, four osteolytic tumors, and two epidermoid carcinomas of the oral cavity. Radiography demonstrated that radioactive strontium was ubiquitously distributed throughout the skeleton of mice exposed from conception.

In the dog study, groups of pregnant beagles were fed between 0.002 and 3.6 μCi ^{90}Sr/kg/day (0.074 and 133.2 kBq/kg/day) from day 21 of gestation to postnatal day 42 (White et al. 1993). The pups were weaned and then fed a diet containing the same ^{90}Sr/calcium ratio as the dam until day 540. Bone sarcoma deaths occurred in dogs ingesting between 0.13 and 3.6 μCi ^{90}Sr/kg/day (4.8–133.2 kBq/kg/day) resulting in bone doses at death of 5,000–10,700 rad (50–107 Gy), but not at 0.002–0.043 μCi ^{90}Sr/kg/day (0.1–1.6 kBq/kg/day) with doses to death of 100–2,300 rad (1–23 Gy). The higher the amount of ^{90}Sr

given, the earlier the age of onset of sarcomas and the more likely they were to be osteosarcomas. Of 66 sarcomas, 75% were osteosarcomas; other types were chondrosarcoma, hemangiosarcoma, fibrosarcoma, and undifferentiated sarcoma. Multiple tumors occurred only at the two highest doses. Other cancer deaths occurred at high doses: radiation-induced myeloid leukemia (43 deaths), oral or nasal carcinoma (29 deaths), and periodontal carcinoma (16 deaths). The leukemic animals (average age at death 1,156 days) were not at risk for osteosarcoma, which had an average age of onset of 2,864 days. The mean cumulative skeletal doses at the time of onset in the four highest exposure groups for dogs with tumors were between 3,100 and 11,600 rad (31–116 Gy). The authors indicated that of the exposures that did not give rise to tumors, the lowest exposure (8 mrad/day; 0.08 mGy/day) was 25 times higher than background and the highest (146 mrad/day; 1.46 mGy/day) was 500 times higher than background. Therefore, lifetime chronic exposure to low linear energy transfer (LET) beta particle radiation up to 500 times background showed no apparent carcinogenic potential in dogs.

Stage-specific differences in carcinogenetic effects were reported in a large multigenerational study of female Pitman-Moore miniature swine that were fed between 1 and 3,100 μCi ^{90}Sr/day (0.037–114.7 MBq/day) for life (Clarke et al. 1972; Howard 1970; Howard and Clarke 1970). In the parental generation, which was started on the regimen at age 9 months of age, myeloid metaplasia was observed at nearly all levels, and lymphoid or myeloid neoplasms were observed when between 1 and 125 μCi ^{90}Sr/day were ingested. The average doses to the skeleton for the parental females were between 40 and 10,000 rad. No bone cancer occurred in the parental generation, whereas osteosarcomas occurred in F1 or F2 offspring exposed from conception to 125 or 625 μCi/day with average skeletal doses higher than 9,000 rad (90 Gy). Osteosarcoma had a longer latency period and occurred at higher exposure levels. Myeloid metaplasia and myeloid and lymphoid neoplasms developed sooner and more frequently in the F1 and F2 generations than in the parental generation.

The cancer effect levels (CELs) resulting from oral exposure to radioactive strontium in each species and duration category are recorded in Table 3-3 and plotted in Figure 3-3.

3.3.3 External Exposure

Cardiovascular, dermal, ocular, and cancer effects have been reported following acute- or intermediate-duration external exposure to beta radiation from a solid radioactive strontium source apposed to the skin or eye. In these studies, ^{90}Sr was considered to be in equilibrium with ^{90}Y; that is, following decay of ^{90}Sr, some radiation emissions could be expected from decay of its transformation product, ^{90}Y.

3.3.3.1 Death

No studies were located regarding death in humans or animals after external exposure to radioactive strontium.

3.3.3.2 Systemic Effects

No studies were located regarding respiratory, gastrointestinal, hematological, musculoskeletal, hepatic, renal, or endocrine effects in humans or animals after external exposure to radioactive strontium isotopes.

Cardiovascular Effects. Exposure to excessive ionizing radiation is known to affect the integrity of the vasculature of the skin, increasing the permeability of the vasculature to plasma protein. A study by Song et al. (1968) examined the ability of several anti-inflammatory agents to suppress this radiation-induced increase in vascular permeability. Albino male guinea pigs were exposed to 3,000 rep (Roentgen equivalent, physical) (3,230 rad; 1 rep≈0.93 rad) of particles (800 rad/min; 8.0 Gy/min) from a $^{90}Sr/^{90}Y$ source. Immediately after irradiation, ^{125}I-labeled guinea pig serum albumin was injected into the heart as a tracer. The peak increase in vascular permeability, as measured by the ratio of accumulation of labeled plasma protein in the nonirradiated control and beta-irradiated skin, was determined to occur at 18 hours. In the group receiving no anti-inflammatory drug, the irradiated epidermis and dermis exhibited approximately 3- and 1.6-fold increases in the peak accumulation of plasma protein, respectively.

The highest reliable NOAEL values and all LOAEL values for cardiovascular effects from external exposure to radioactive strontium in each species and duration category are recorded in Table 3-4.

Dermal Effects. Several studies in humans and animals have reported damage to the skin following external exposure to radioactive strontium. Beta radiation from ^{90}strontium has been used to treat hemangiomas in children and adults. One study described some delayed effects of this radiation treatment within patients in one medical practice in Belgrad, Yugoslavia (now Serbia; Bekerus 1970). The beta source was a 50 mCi ^{90}Sr plate with a diameter of 9.9 mm. Adults were treated with an initial dose of 1,600 rad (16 Gy) and subsequent doses of 1,080–1,600 rad (10.8–16 Gy) in succeeding months,

Table 3-4 Levels of Significant Exposure to Strontium - Radiation Toxicity - External Radiation

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (rad)	LOAEL Less Serious (rad)	LOAEL Serious (rad)	Reference Chemical Form
	ACUTE EXPOSURE						
	Systemic						
1	Human	once <1 min	Ocular		1700 (scleral thinning in diabetic patient)		Wesberry and Wesberry 1993 Strontium-90
2	Mouse (SAS/4)	1-60 min once	Dermal		2200 M (50% incr moist desquamation)		Hopewell et al. 1986 Strontium-90/yttrium-90
3	Mouse (ICR)	9 min once	Dermal			2700 F (acute injury, scarring)	Hoshino and Tanooka 1975 Strontium-90/yttrium-90
4	Mouse (CD-1)	once	Dermal			5000 M (late chronic fibrosis)	Randall and Coggle 1995 Strontium-90/yttrium-90
5	Mouse (CBA/ca agouti)	once	Dermal			5000 M (late chronic fibrosis)	Randall and Coggle 1995 Strontium-90/yttrium-90

Table 3-4 Levels of Significant Exposure to Strontium - Radiation Toxicity - External Radiation (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (rad)	LOAEL		Reference Chemical Form
					Less Serious (rad)	Serious (rad)	
6	Gn Pig (albino)	1.4 to 8.3 min once	Dermal		1000 M (reversible 25% loss of basal cells; erythema; hair loss)		Etoh et al. 1977 Strontium-90/yttrium-90
7	Gn Pig (albino)	4 min once	Cardio		3230 M (incr vascular permeability in dermis)		Song et al. 1968 Strontium-90/yttrium-90
8	Pig (Large White)	1-60 min once	Dermal			2000 F (late 35% dermal atrophy)	Hamlet et al. 1986 Strontium-90/yttrium-90
9	Pig Large White	once 3 to 12 min	Dermal		2340 F (moist desquamation)		Hopewell et al. 1985 Strontium-90
10	Pig (Large White)	1-60 min once	Dermal		3000 F (50% incr moist desquamation)		Hopewell et al. 1986 Strontium-90/yttrium-90

Table 3-4 Levels of Significant Exposure to Strontium - Radiation Toxicity - External Radiation (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (rad)	LOAEL Less Serious (rad)	LOAEL Serious (rad)	Reference Chemical Form
11	Pig (Large White)	1-60 min once	Dermal		3000 F (50% incr moist desquamation)		Peel et al. 1984. Strontium-90/yttrium-90
	Cancer						
12	Mouse (ICR)	1 hr once				17800 F (CEL: 1/5 fibrosarcoma of skin)	Hoshino and Tanooka 1975 Strontium-90/yttrium-90
	INTERMEDIATE EXPOSURE						
	Systemic						
13	Human	1 yr ~1 x/mo ~min/d	Dermal		220 (delayed telangiectasis, slight atrophy)		Bekerus 1970 Strontium-90

Table 3-4 Levels of Significant Exposure to Strontium - Radiation Toxicity - External Radiation (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (rad)	LOAEL Less Serious (rad)	LOAEL Serious (rad)	Reference Chemical Form
14	Human	3 wk 1 x/wk <1 min/d	Ocular		1075 (conjunctival telangiectasis, scarring; abnormal nuclei of conjunctival epithelium)		Tong et al. 1969 Strontium-90
	Cancer						
15	Mouse (ICR)	43 wks 1 x/wk 1 hr				17800 F (CEL: 1/5 reticulocyte sarcoma)	Hoshino and Tanooka 1975 Strontium-90/yttrium-90
16	Mouse (ICR)	177-300 d 3 x/wk ~min/d				150 F (CEL: fibrosarcoma; squamous cell carcinoma; basal cell carcinoma)	Ootsuyama and Tanooka 1988 Strontium-90/yttrium-90
17	Mouse (ICR)	177-300 d 3 x/wk ~min/d				150 F (CEL: osteosarcoma)	Ootsuyama and Tanooka 1989 Strontium-90/yttrium-90

[a] There is no corresponding LSE figure.

1 In these studies, a solid radioactive source was placed adjacent to the eye or skin.

~ = approximately; CEL = cancer effect level; d = day(s); Gn pig = guinea pig; hr = hour(s); incr = increased; LOAEL = lowest-observed-adverse-effect level; min = minute(s); NOAEL = no-observed-adverse-effect level

not exceeding a total of 7,530 rad (75.3 Gy). Children were treated with an initial dose of 200–300 rad (2–3 Gy) and additional treatments over 6–16 months, for a total exposure of 2,420–6,130 rad (24.2–61.3 Gy) in some cases. Eight or 10 years after treatment, about a third of the patients developed delayed reactions to radiation: achromia, excess pigmentation, slight atrophy, and telangiectasis. The author did not specify the exposure levels that resulted in these effects.

Acute dermal reactions to ^{90}Sr have been described for depilated skin in mice, guinea pigs, and pigs. In mice, skin exposed to a single 2,000–5,000 rad (20–50 Gy) dose of beta radiation from a ^{90}Sr-^{90}Y source sustained an acute reaction (Hoshino and Tanooka 1975; Randall and Coggle 1995). For example, all mice exposed once to 5,000 rad (50 Gy) from a 1 mm diameter source developed an acute skin reaction with the following characteristics (Randall and Coggle 1995). After an asymptomatic period of 3 or 4 days, the skin exhibited increasing erythema and pigmentation changes, leading to dry desquamation by day 10. Within a few days, exposed skin entered a period of moist desquamation, during which a serum scab was formed that was prevalent between days 15 and 25. Re-growth of the epithelium commenced at the edges of the irradiated field and from surviving hair follicles. By 1 month postirradiation, the epidermis was overtly normal, although histologically hyperplastic. Chronic fibrosis was a delayed skin reaction that was not apparent until 3–6 months postirradiation.

Dose-related effects were noted in guinea pig skin that was treated with a 25x25 mm square ^{90}Sr source (Etoh et al. 1977). At 1,000 rad, there was a transient 25% reduction in the number of basal epithelial cells by day 10, which approached normality by day 15. At 2,200 rad, the epithelial basal cell population dropped by about 60% at day 12, but was slightly above normal by day 20. At 3,000 and 5,000 rad, the basal epithelial cell population was reduced 75%, but hyperplasia was also detected at the margin of the field. Hyperplasia was maintained for the 50-day observation period following exposure to 2,200–5,000 rad. At 3,000 rad, erythema was noted by day 14, followed by dry desquamation and complete hair loss by day 21. A similar pattern, with ulceration at 1 month, was seen at 5,000 rad.

Within certain ranges, field-size effects for acute, localized external exposures to radioactive strontium have been demonstrated in mice and pigs. Hopewell et al. (1986) exposed young SAS/4 male mice to different levels of radiation from ^{90}Sr sources varying in diameter between 1 and 22.5 mm. The ED_{50} values for moist desquamation were 2,200–2,750 rad (22–27.5 Gy) for the 22.5-mm source and 7,500–9,000 rad for the 5-mm source. Acute tissue breakdown was only achieved in mouse skin by very high doses ($ED_{50} \geq$14,000 rad) when the smallest sources were employed ($\leq$2 mm in diameter). In a parallel study in pigs, moist desquamation occurred at 2,250–7,500 rad (22.5–75 Gy) and acute tissue necrosis

occurred at doses of ≥14,000 rad (140 Gy) (Hopewell et al. 1985, 1986). Peel et al. (1984) compared the effect on pigskin of acute exposure to ^{90}Sr sources with diameters between 1 and 40 mm. The effects of acute beta radiation included epithelial cell death within the first 16 weeks, and subsequently, dermal necrosis that was attributed to vascular damage. The rate of repair was dependent on the size of the exposed area, since repair was dependent upon the migration of healthy cells into the wound. Transient moist desquamation associated with bright red erythema was observed between 4 and 6 weeks. At 'high' doses, this intensified and the dermis became ulcerated, but healed with scarring. After doses ≥4,000 rad (22.5-mm source), 6,600 rad (11-mm source), or 12,500 rad (5-mm source), a dusky red or mauve erythema followed by dermal necrosis occurred between weeks 10 and 16. In pigs that were acutely exposed to the same range of ^{90}Sr sources at the age of 3 months, dose-dependent dermal atrophy was detected in the irradiated field 2 years later, reaching a maximal 55% reduction in dermal thickness for all doses above 4,500 rad (45 Gy; Hamlet et al. 1986). Dermal atrophy was produced by doses below the threshold required to induce moist desquamation. The threshold dose for moist desquamation following irradiation by the 22.5 mm source (2,250 rad) produced a 38% thinning of the dermis. Irradiation from the 1-mm source produced 30% dermal thinning at the threshold (7,250 rad). Irradiation from the 5-mm source (2,000 rad) reduced the thickness of the dermis by 35%. For the 11–22.5-mm sources, above doses that caused maximal thinning (in the range of 12,000–6,250 rad, respectively), the relative dermal thickness increased slightly, but remained 30–40% thinner than normal.

The highest reliable NOAEL values and all LOAEL values for dermal effects from external exposure to radioactive strontium in each species and duration category are recorded in Table 3-4.

Ocular Effects. Beta radiation has been employed medically to treat pterygium, an alteration in the conjunctival connective tissue that results in the penetration of the superficial corneal stroma by vascular connective tissue (Tong et al. 1969; Wesberry and Wesberry 1993). As an adjunct to surgical removal of the pterygium, a solid ^{90}Sr source is apposed to the site in order to reduce neovascularization. Several clinical studies reported complications resulting from this procedure. Serious effects (radiation cataracts, keratinization and telangiectasis of the conjunctiva) resulted from the high dose levels used when the technique was first employed using other beta-emitting radionuclides (Merriam 1955). Atrophy of the sclera occurred after a dose of 1,600 rad from ^{90}Sr. In a later study, 78 eyes in 62 patients were treated with 1,080 rad (10.8 Gy) of beta radiation from a ^{90}Sr source repeated at weekly intervals (total dose 3,200 rad; 32 Gy; Tong et al. 1969). Because pterygia recurred within 2–18 months, six patients were re-treated as before, two were given a single dose of 2,100 rad (21 Gy), and one of these two received a third dose of 2,100 rad (21 Gy). One eye, which had received treatments of 5,380 rad (53.8 Gy) each to two

adjacent fields, developed keratitis of the cornea. Other complications noted were telangiectasis of the conjunctiva (27%), scarring of the conjunctiva (14%), and scarring of the cornea (3%); the authors did not specify the exposure levels at which these side effects occurred. A more recent study described results for 171 eyes that had been treated with single doses of 1,700–1,800 rad (17–18 Gy) (Wesberry and Wesberry 1993). During follow-up periods lasting between 1 and 19 years, the only complications noted were one case each of corneal scarring, iritis, conjunctivitis, mild irritation, and, in a diabetic patient, scleral thinning. A complication rate of 1.8% was reported for a study of 490 eyes (399 patients) that received doses between 31 and 42 Gy (3,100–4,200 rad) in four or five fractions over 29 days (Nishimura et al. 2000). Scleral thinning, not severe enough to require treatment, was reported for four eyes in three patients 0.5, 2, and 9 years after treatment. Infectious scleral ulcer occurred within weeks of treatment in one male. Ischemic necrosis of the sclera in one male and adhesion of the eyelid and eyeball in one female occurred several years after repeat treatments for recurring pterygia; adhesive scarring of the eyelid occurred in one female 7 years after treatment.

No studies were located regarding ocular effects in animals after external exposure to radioactive strontium isotopes.

The highest reliable NOAEL values and all LOAEL values for ocular effects in humans from external exposure to radioactive strontium in each duration category are recorded in Table 3-4.

No studies were located regarding the following effects in humans or animals after external exposure to radioactive strontium isotopes:

3.3.3.3 Immunological and Lymphoreticular Effects

3.3.3.4 Neurological Effects

3.3.3.5 Reproductive Effects

3.3.3.6 Developmental Effects

3.3.3.7 Cancer

Development of skin cancers in mice following localized exposure to beta radiation from a solid ^{90}Sr-^{90}Y source depended on the dose and on strain susceptibilities (Hoshino and Tanooka 1975). In experiments

using a 40 mCi ($1.48x10^9$ Bq) ^{90}Sr-^{90}Y source that delivered doses of 290 rad/min (2.9 Gy/min) to the skin, ICR mice exposed to a single localized dose of 2,700 rad (27 Gy) developed an acute skin reaction within the first month (see Section 3.3.4.2 Dermal Effects), but did not develop skin cancer during a 23-month observation period (Hoshino and Tanooka 1975). When the exposure was repeated 7 times for a total dose of 17,800 rad (178 Gy), one fibrosarcoma of the skin appeared after 10 months among five mice. Even extending the duration of the repeated 17,800 rad treatment for 43 weeks did not increase the incidence of malignant skin tumor; a single reticulocyte sarcoma developed in one out of five mice. Mice from a different strain, Japanese ddN, exposed to single doses of up to 17,400 rad (174 Gy) did not develop skin tumors during a 1-year observation period (Hoshino and Tanooka 1975). In the acute dermal toxicity experiments described above, Randall and Coggle (1995) selected the exposure level of 5,000 rad (50 Gy) for their mouse studies since it is known to be a critical dose for carcinogenetic effects in humans exposed to ionizing radiation.

Ootsuyama and Tanooka (1988, 1989) exposed the backs of female ICR mice to beta radiation from a 40,000 µCi (1,500 MBq) source of ^{90}Sr–^{90}Y, which delivered a surface dose rate of 228 rad/minute (2.28 Gy/minute) and a 20–80% lower dose rate to the top of the vertebrae. Mice were irradiated 3 times weekly at skin entrance doses per exposure of 135–1,180 rad (1.35–11.8 Gy), and irradiation was continued until a palpable tumor appeared (up to 86 weeks). Tumors arising included squamous cell carcinomas, basal cell carcinomas, fibrosarcomas, and osteosarcomas. No skin tumors arose in mice receiving 135 rad/day (1.35 Gy/day). The total number of irradiations (and total dose) needed to induce 50% incidence of skin tumors ranged from 252 sessions for a total of 37,800 rad (378 Gy) for the 150 rad/day level and 156 sessions for a total of 192,300 rad (1,923 Gy) for the 1,180 rad/day level. Osteosarcomas were induced at lower doses, most frequently with skin surface doses of 250–350 rad (2.5–3.5 Gy) per exposure. In time, 100% of mice developed tumors in groups receiving 250–1,180 rad per exposure. Ootsuyama and Tanooka (1988) suggested that the 135 rad/day dose might represent a threshold dose, since no tumors formed. However, in their experimental design, they arbitrarily terminated exposures at this dose level on day 300, which conceivably could be shorter than the latency period for tumor development at that dose.

The CELs resulting from external exposure to radioactive strontium in each species and duration category are recorded in Table 3-4.

3.3.4 Other Routes of Exposure

This section includes injection and *in vitro* studies that provide evidence for the biological basis of toxicity of stable and radioactive strontium in humans and animals. Since these studies are not directly relevant to general population exposure conditions, no LSE tables have been created for this section.

Hematological Effects Hematological effects have been observed in several clinical studies in which ^{89}Sr, one of the shorter-lived radioactive isotopes of strontium, has been used in cancer therapy for the relief of pain by irradiating and destroying tumors that have metastasized to the bone marrow (Baziotis et al. 1998; Ben-Josef et al. 1995b; Blake et al. 1987c; Breen et al. 1992; Kan 1995; Lee et al. 1996; Piffanelli et al. 2001; Sciuto et al. 2001). Significant reductions in platelet and white blood cell counts (averaging 70 and 30%, respectively) were seen 3 months after patients were injected with a single therapeutic dose (40 μCi ^{89}Sr/kg; 1.5 MBq/kg) (Lee et al. 1996). In two patients who received two doses of 60 μCi ^{89}Sr/kg (2.2 MBq/kg) 6 months apart, platelet counts were significantly reduced (>30%) for at least 1 year. Similar effects have been observed in animals. Hypoplasia of the bone marrow has been observed in mice injected with ^{90}Sr (Ito et al. 1976; Nilsson 1970) or ^{89}Sr, the latter of which has been used intentionally to create mice with aplastic bone marrow (Bennett et al. 1976; Haller and Wigzell 1977; Levy et al. 1981; Merluzzi et al. 1978; Oghiso et al. 1988; Sawyer et al. 1982). CBA/J mice injected with fixed doses of ^{89}Sr that differed in the specific activity of the preparation, showed quantitative differences in the degree of bone marrow suppression (Shibata et al. 1985). Acute hematological symptoms (depression of hemopoiesis leading to anemia or hemorrhage) were observed in beagles beginning several weeks after injection of 64 or 98 μCi ^{90}Sr/kg (Dougherty et al. 1972). Transient neutropenia occurred at the 10.8 μCi ^{90}Sr/kg level, and prolonged (36-month) depression of all types of leukocytes was reported at 32.7–98 μCi ^{90}Sr/kg. No hematological effects were noted at levels between 0.57 and 3.46 μCi ^{90}Sr/kg.

Musculoskeletal Effects. Osteonecrosis was reported after 2 days for 2-day-old rats that were injected intraperitoneally with 2 mCi ^{90}Sr/kg of body weight (Hopkins and Casarett 1972). In weanling rabbits, injection of 600 μCi ^{90}Sr/kg resulted in increasing cell death of differentiating odontoblasts and pulp cells of immature teeth and disordered tooth structure (Rushton 1963). Mature teeth in the same animal, or teeth in adults injected at the age of 3 years or older, were not affected as severely.

Immunological and Lymphoreticular Effects. Evidence from injection studies in animals corroborates the sensitivity of the immune system to radioactive strontium. In mice that have been

injected with ^{89}Sr or ^{90}Sr to deplete bone marrow, NK cells are preferentially eliminated (Emmanuel et al. 1981; Gidlund et al. 1990; Haller and Wigzell 1977; Wiltrout et al. 1989). The loss of this cell population results in a reduced ability to defend against lymphoid tumors (Haller and Wigzell 1977; Luevano et al. 1981) or a transplanted methylcholanthrene-induced sarcoma (Scuderi and Rosse 1981b). In CBA/SU mice injected with $^{90}Sr(NO_3)_2$, the responsiveness of spleen cells to activation by B-cell mitogen lipopolysaccharide was reduced, which was attributed to the cytotoxic effect of ^{90}Sr on bone marrow, a source of precursor cells for the spleen (Bierke 1990). In mice injected with 400–800 μCi ^{90}Sr/kg to deplete bone marrow, the thymus went through two phases of weight loss and regeneration within 50 days (Järplid 1973).

Reproductive Effects. Numerous animal studies demonstrated adverse reproductive effects of injected radioactive strontium. For the first 4 weeks after male CBA mice were injected intraperitoneally with 18 μCi of ^{90}Sr and mated with untreated females, fetal deaths were 5–10% higher than controls (Lüning et al. 1963a). The increase in fetal mortality was much less (only ~2%) when the same males were mated 11–15 weeks postinjection (Lüning et al. 1963b). In a similar study using male C_3H/He mice, a single injection of 1,160 μCi $^{90}SrCl_2$/kg resulted in fetal death rates 7–8% higher than normal for matings conducted 10–40 weeks after injection (Reddi 1971). Autoradiography demonstrated that ^{90}Sr selectively accumulated in testicular stem cells.

When female CBA mice were injected with $^{90}Sr(NO_3)_2$ on the 19th day of pregnancy, a dose of ≥43 μCi $^{90}Sr(NO_3)_2$/kg (≥1,600 kBq/kg) transiently suppressed spermatocyte maturation of the male offspring, but the spermatid numbers had recovered by day 56 (De Rooij and Rönnbäck 1989). After the recovery period, the reproductive capacity (number of litters, litter size) of male offspring at the highest dose level (86 μCi $^{90}Sr(NO_3)_2$/kg; 3,200 kBq/kg) was unaffected. No testicular effects were observed at doses of 11 or 21 μCi $^{90}Sr(NO_3)_2$/kg (400 or 800 kBq/kg). Compared to the effect on male offspring, reproductive effects were more severe in female offspring of dams exposed to $^{90}Sr(NO_3)_2$ on the 19th day of pregnancy (Rönnbäck 1980). Dose-related decreases in the number of differentiating oocytes in the ovary were observed up to day 84 at all dose levels ranging from 5.5 to 43 μCi $^{90}Sr(NO_3)_2$/kg (200–1,600 kBq/kg). Injection on the 16–19th day was found to have more severe effects than injection earlier in gestation (Nilsson and Henricson 1969; Rönnbäck 1979). A longer-term study demonstrated that the radioactive-strontium-induced decrease in the number of oocytes in the ovary persisted for at least 10 months (Rönnbäck 1981b). Furthermore, the reproductive capacity (number of fertile females, number of litters, number of young per litter) of females treated *in utero* was significantly reduced at the two highest maternal dose levels (43 and 86 μCi $^{90}Sr(NO_3)_2$/kg; 1,600 and 3,200 kBq/kg). Rönnbäck (1981a) also

examined the effect of exposure via lactation using CBA mice receiving 21 μCi $^{90}Sr(NO_3)_2$/kg (800 kBq/kg). Ovarian cellularity, especially the earliest stages of oogenesis, was reduced in females exposed *in utero*, whether or not they suckled milk contaminated with ^{90}Sr. However, early stage oocyte numbers were somewhat improved by sucking uncontaminated milk. When unexposed newborn females were exposed to contaminated milk, the numbers of early stage oocytes was significantly reduced, but not as severely as in females exposed *in utero*. These studies suggest that reproductive capacity, particularly in females, may be adversely affected by gestational exposure to high levels of radioactive strontium. These levels are high compared to reported releases of ^{90}Sr from nuclear power facilities (see Table 6-1).

Developmental Effects. Injection of relatively high doses of radioactive strontium into pregnant animals resulted in severe developmental effects. A single dose of ≥764 μCi ^{90}Sr/kg into female Long-Evans rats had no effect on fetal mortality when administered on gestational day 10, but significantly increased fetal mortality when administered on gestational day 2 (Hopkins et al. 1967). In addition, there were dose-related increases in the incidence of fetuses with skeletal abnormalities (general stunting, lack of ossification, fusion of ribs, vertebral anomalies, missing tail). The incidence of micropthalmia was also significantly increased at the higher activity level (1,488 μCi ^{90}Sr/kg). The offspring of female Wistar rats injected with ≥100 μCi $^{90}Sr(NO_3)_2$ at gestational day 18 showed no gross malformations, but there was a significant increase in the incidence of meningeal and pituitary tumors (Schmahl and Kollmer 1981; Schmahl et al. 1979). This was shown to be connected with a late gestational increase in the transfer of transplacental strontium to the basioccipital and sphenoid bones of the skull. Tumor development was probably assisted by the position of the pituitary gland within the sella turcica, which resulted in the gland being irradiated from the ventral and lateral surfaces. The total radiation dose rate at that position was calculated to be between 60 and 120 rad for the lifespan of 30 months. After pregnant dogs were injected with 1 mCi of radiostrontium per kg (80–99% ^{89}Sr and 1–20% ^{90}Sr) 6 days prior to delivery, the puppies dying within 11 weeks exhibited abnormalities of the skeleton (underdevelopment of the jaws, incomplete and abnormal ossification, abnormal epiphyseal cartilage), partial atelectasis of the lungs, hyperplasia of lymph nodes and spleen, or deficient hematopoiesis (Finkel and Biskis 1969; Finkel et al. 1972). Puppies injected subcutaneously 12 days after birth showed some skull abnormalities and developed osteosarcomas. Effects on the reproductive system following *in utero* exposure to radioactive strontium are discussed in the preceding paragraphs. Cancer effects in animals exposed to radioactive strontium *in utero* are discussed in the next paragraph.

Cancer. Numerous studies in several species reported the induction of malignant tumors in response to injection of radioactive strontium (mice: Ash and Loutit 1977; Bierke and Nilsson 1990; Ito et al. 1976;

Loutit 1976; Nilsson 1971, 1972; Nilsson et al. 1980a; Reif and Triest 1982; Chinese hamsters: Benjamin et al. 1976b; Brooks et al. 1974; rabbits: Kshirsagar et al. 1965; Vaughan and Williamson 1969; mongrel dogs: Finkel and Biskis 1969; Finkel et al. 1971; beagle dogs: Lloyd et al. 1995; Taylor et al. 1966). In general, osteosarcomas and bone hemangiosarcomas developed at higher dose levels, and lymphomas and leukemias developed at lower levels. Carcinomas of soft tissues adjacent to bone also developed. The offspring of pregnant rats that were injected on gestational day 18 had a higher incidence of pituitary adenoma and meningeal sarcoma (Schmahl and Kollmer 1981; Schmahl et al. 1979). These findings were attributed to the higher incorporation of ^{90}Sr to the skull at that developmental period and to the anatomical position of the pituitary within the sella turcica, which subjected it to radiation from all but the dorsal surface. The female offspring of pregnant mice that were injected intravenously with 90Sr on gestational day 19 developed a higher incidence of tubular adenoma of the ovaries (Rönnbäck and Nilsson 1982).

3.4 GENOTOXICITY

There is little evidence for genotoxicity of stable strontium. However, radioactive strontium isotopes release ionizing radiation that, within an effective radius, is known to damage DNA (see Appendix D Section D.4.1 Radiation Effects at the Cellular Level). Summaries of *in vivo* and *in vitro* genotoxicity data are presented in Tables 3-5 and 3-6, respectively.

In Vivo Exposure

Stable Strontium. No studies were located regarding genotoxic effects in humans following exposure to stable strontium. The only *in vivo* genotoxicity study for stable strontium in animals involved acute oral exposure. Oral administration of 130 mg strontium/kg body weight as strontium chloride to Swiss albino female mice increased the incidence of chromosomal aberrations (gaps, breaks, nondisjunction, and polyploidy) in bone marrow cells 5-fold after 6 hours (Ghosh et al. 1990). Genotoxicity in male mice administered a similar dose (140 mg/kg) was only doubled, and therefore, was less severe than in females. At higher doses (440–1,400 mg/kg), the incidence of chromosomal aberrations was similar in both sexes after 6, 12, or 24 hours.

Radioactive Strontium. Human *in vivo* genotoxicity data are available from studies of the Techa River populations exposed to combined external gamma radiation and internal radiation from ^{90}Sr and ^{137}Cs between 1949 and 1956 and from studies on patients exposed to ^{89}Sr as a radiopharmaceutical. The stable

Table 3-5. Genotoxicity of Stable and Radioactive Strontium *In Vivo*

Species (test system)	End point	Results	Reference
Stable Strontium			
Strontium chloride:			
Mouse (bone marrow)	Chromosomal gaps, breaks, polyploidy, centric fusion	+	Ghosh et al. 1990
Radioactive Strontium			
^{89}Strontium chloride:			
Human (lymphocytes)	Transient increase in micronuclei	+	Watanabe et al. 1998
^{90}Strontium:			
Human (lymphocytes)	Chromosomal aberrations (rings, dicentric, tricentric)	+	Ilynskikh et al. 1999
Mouse (skin)	Unscheduled DNA synthesis	+	Ootsuyama and Tanooka 1986
Mouse (thymus, lymph nodes, bone marrow)	Aneuploidy	+	Ito et al. 1976
Chinese hamster (bone marrow)	Chromosomal breaks, exchanges, rings	+	Brooks and McClellan 1969
Miniature swine (leukocytes)	Chromosomal breaks in leukemic cells	+	Clarke et al. 1972; Howard 1970

+ = positive results; – = negative results; DNA = deoxyribonucleic acid

Table 3-6. Genotoxicity of Stable and Radioactive Strontium *In Vitro*

Species (test system)	End point	Results: With activation	Results: Without activation	Reference
Stable Strontium				
Strontium chloride:				
In vitro DNA synthesis reaction	Lack of fidelity in DNA synthesis	–	–	Loeb et al. 1977
Prokaryotic organisms:				
Bacillus subtilis Rec^-	Growth inhibition	–	–	Kanematsu et al. 1980
Eukaryotic cells:				
Chinese hamster ovary cells	Reduced cloning efficiency	–	–	Tan et al. 1984
Radioactive Strontium				
^{90}Strontium:				
Human (blood)	Chromosomal rings, dicentrics, acentrics		+	de Oliveira et al. 2001
	DNA damage in electrophoretic assay		+	
Human (lymphocytes)	Micronucleus formation		+	Mills et al. 1996
Human (lymphocytes)	Micronucleus formation		+	Hall and Wells 1988

– = negative result; + = positive result; (+) = weakly positive result; DNA = deoxyribonucleic acid

chromosomal translocation frequency in peripheral lymphocytes was evaluated in 73 radiation-exposed individuals from the Techa River area and 39 unexposed individuals from noncontaminated areas (Bauchinger et al. 1998). The mean genomic frequency of translocations per cell in the exposed group ($12.8\pm1.5x10^{-3}$) was significantly elevated compared to unexposed controls ($5.7\pm1.0x10^{-3}$). Furthermore, the translocation frequency per cell was significantly higher in the subgroup that had been exposed to radiation as teenagers ($22\pm4.3x10^{-3}$) compared to the subgroup exposed as adults ($9.7\pm2.3x10^{-3}$).

Increased skeletal incorporation of radiostrontium in teenagers, leading to higher radiation doses to the bone marrow, probably contributed to the observed increase in translocation frequency for this subgroup. In a more recent study of the Techa River populations, there was a dose relationship between the frequency of chromosomal aberrations (dicentric, ring) in T-lymphocytes (assessed in 1994–1996) and whole body ^{90}Sr activity (detected by human radiation counter in 1993) for individuals residing in the Muslyumovo settlement (Ilyinskikh et al. 1999). The frequency of chromosomal aberrations was 3.8±0.8 for a non-exposed control group (whole-body ^{90}Sr activity <100 nCi), and 8.9±0.7, 12.9±1.2, and 18.7±1.9%, respectively, for exposed individuals with ^{90}Sr activity levels of 100–500, 500–1,000, and ≥1,000 nCi. In a few cancer patients who were injected with 3 mCi (111 MBq) of $^{89}SrCl_2$ to treat severe pain from multiple bone metastases, the number of micronuclei present in the lymphocytes tripled in the week after exposure, but declined in succeeding weeks (Watanabe et al. 1998). The authors found that the percentage of micronuclei, indicative of chromosomal damage, was equivalent to the damage observed in a separate *in vitro* experiment in which cells received a dose of 53 rad (0.53 Gy) by X-irradiation.

In a long-term feeding study, chromosomal breaks were noted in leukocytes of miniature pigs that had developed leukemia as a result of exposures of 25 μCi ^{90}Sr/day (925 kBq/day) or more for >1 year (Clarke et al. 1972; Howard 1970). Unexpected ("unscheduled") DNA synthesis was detected in the skin of female ICR mice several hours after external exposure to 10,000–30,000 rad (100–300 Gy) from a ^{90}Sr-^{90}Y disk applicator (surface dose rate 228 rad/min) (Ootsuyama and Tanooka 1986). Tritiated thymidine incorporation related to DNA repair was elevated to a greater degree in epithelial cells of the irradiated epidermis than in the dermis. This difference appeared to be intrinsic to the cell type, since thymidine incorporation in hair follicle epithelium situated at the same depth as fibroblastic dermal cells, occurred at a faster rate. The authors suggested that the somewhat slower rate of DNA repair in the dermis could contribute to the higher risk of cancer in the dermis, compared to the epidermis, following exposure to ionizing radiation.

A single intraperitoneal injection of ^{90}Sr–^{90}Y into Chinese hamsters (200–5,000 μCi/kg) resulted in an increasing number of chromosomal breaks/cell over time (between 2 and 224 days), as the cumulative radiation dose to the skeleton increased (Brooks and McClellan 1969). The number of chromosomal breaks and chromatid/isochromatid deletions per bone marrow cell increased as a function of dose rate, or as the activity of radionuclide injected per body weight. The relative number of chromatid exchanges and rings and dicentrics decreased with time after exposure, whereas the number of chromosomal exchanges increased. Abnormal chromosomal numbers were detected in the thymus, lymph nodes, and bone marrow of female ICR/JCL mice as late as 90 days after interperitoneal injection with 1 mCi/kg of ^{90}Sr (Ito et al. 1976).

In Vitro Exposure

Stable Strontium. In mutagenicity assays using the Rec^- (recombination-repair-deficient) strain of *Bacillus subtilis*, strontium chloride had a negative effect *in vitro* (Kanematsu et al. 1980). Furthermore, in a survey of the effect of metal salts, strontium was found to have no adverse effect on the fidelity of DNA synthesis *in vitro*, which was thought to be consistent with its reported lack of mutagenicity and carcinogenicity (Loeb et al. 1977).

The only stable strontium compound known to be genotoxic is strontium chromate. Strontium chromate induced sister chromatid exchanges in Chinese hamster ovary cells *in vitro* (Venier et al. 1985). In the Ames test using the *Salmonella typhimurium* strain TA100, strontium chromate induced mutations in the presence, but not in the absence of S9 microsomes. The genotoxicity of strontium chromate is related to the ability of the hexavalent chromium ion to enter cells and become metabolized, forming a reactive DNA-adduct. Strontium only contributes to the solubility of the salt (Elias et al. 1989, 1991).

Radioactive Strontium. Radioactive strontium has been shown to be genotoxic to human cells *in vitro*. In lymphocytes from freshly-drawn human blood, doses of 0.2–5.0 Gy (0.002–0.05 rad) increased the frequency of chromosomal aberrations (de Oliveira et al. 2001). Acentric aberrations (acentrics and double minutes) increased at ≥0.2 Gy (0.002 rad), dicentric aberrations increased at ≥0.5 Gy (0.005 rad), and there was a slight indication that the frequency of centric rings increased at ≥3.0 Gy (0.03). In the same study, results of an electrophoretic assay (comet assay) on single exposed lymphocytes revealed that DNA damage (evaluated by visual inspection and tail moment) occurred at doses as low as 0.2 Gy (0.002 rad). The varying frequencies for the different types of chromosomal aberrations were associated with the number of DNA breaks required for their formation and whether one or more chromosomes were

involved: acentrics requiring a single break and dicentrics requiring at least two breaks on different chromosomes. Dose-related increases in micronucleus formation, predominantly derived from acentric chromosomes, were reported in human lymphocytes irradiated at doses between 0.3 and 3.0 Gy (0.003 and 0.030 rad) (Hall and Wells 1988; Mill et al. 1996).

3.5 TOXICOKINETICS

3.5.1 Absorption

3.5.1.1 Inhalation Exposure

Evidence for absorption of inhaled strontium in humans is provided by several cases of accidental exposure of workers to airborne radiostrontium (Navarro and López 1998; Petkau and Pleskach 1972; Rundo and Williams 1961). Although these cases do not provide a complete quantitative description of the absorption of inhaled strontium in humans, they demonstrate clearly that inhaled aerosols of strontium compounds (e.g., $SrCl_2$, $SrTiO_3$) can be absorbed, as indicated by the detection of radiostrontium in urine and feces.

In one case, a worker accidentally inspired an unknown quantity of $^{90}SrCl_2$ (physical form unknown) and over the subsequent 800 days, ^{90}Sr was excreted in the urine with half-times of 3.3 (52%), 17 (7%), and 347 days (18%) (Petkau and Pleskach 1972). The urinary:fecal excretion ratio was 3:1. In a second case, a worker was exposed to $^{90}SrCO_3$ (physical form unknown) with deposition within the nasal tract as well as the hands, face, and hair. The actual inhaled dose could not be determined; however, based on the excretion kinetics of ^{90}Sr over the subsequent 300 days, the reconstructed internal dose was estimated to have been approximately 300–400 nCi (11.1–14.8 kBq) (Rundo and Williams 1961). Excretion in urine occurred with half-times of 2.2 (>90%), 15, and 175 days, and the urinary:fecal excretion ratio over the first 24 days was 0.71. In a third case, two workers accidentally inhaled $^{90}SrTiO_3$ (physical form unknown), and ^{90}Sr was detected in urine over a period of 225 days (Navarro and López 1998).

Studies conducted in animals have shown that the rate of absorption depends on the chemical form of the inhaled strontium aerosol. Compounds of greater solubility are, in general, more rapidly cleared from the lung. For example, strontium is rapidly cleared from the lung after inhalation of $SrCl_2$. In dogs that received a 2–22-minute nose-only exposure to an aerosol of $^{85}SrCl_2$ (activity median aerodynamic diameter [AMAD] 1.4–2.7 μm, geometric standard deviation [GSD] 2.0), <1% of the initial lung burden remained in the lung 12 hours after the exposure; 37% of the body burden was distributed to the skeleton

within 12 hours after the exposure, and 84% was in the skeleton 4 days after the exposure (Fission Product Inhalation Project 1967a). In contrast to the relatively rapid absorption of inhaled $SrCl_2$, after exposures to strontium in particles of fused clay, absorption is much slower. In dogs that received a nose-only exposure to ^{90}Sr in fused montmorillonite clay particles (AMAD 2.2 μm, GSD 1.7), the average half-time of elimination of strontium from the lung was 490 days (Snipes et al. 1974a, 1974b). Thus, strontium compounds of lower solubility are more slowly absorbed from the lung. Support for this also comes from studies in which the rates of absorption of various compounds of strontium were compared in rats. Rats were exposed to aerosols of ^{85}Sr carbonate, phosphate, fluoride, oxide, or titanate (particle sizes and doses not specified) (Willard and Snyder 1966). Greater than 99% of the initial lung burden of ^{85}Sr was cleared from the lung 5 days after inhalation of the carbonate, phosphate, fluoride, or oxide, whereas 60% of the ^{85}Sr remained in the lung after inhalation of the more insoluble strontium titanate.

In rats exposed to airborne fly ash (sieved to have a particle diameter of distribution of 90% less than 20 μm) for 6 hours, strontium was eliminated from the lung with a half-time of 23 days (observations were made for 30 days) (Srivastava et al. 1984b). One day after the exposure, the tissue:plasma strontium concentration ratios were 0.3–0.5 in the liver, kidney, small intestine, and heart. The report of this study does not indicate whether whole-body or nose-only exposures were utilized in the study; therefore, it is not possible to know for certain how much of the absorption may have resulted from ingestion of fly ash deposited on the animals. Furthermore, given the relatively large particle size of the fly ash, it is likely that deposition in the respiratory tract was largely in the tracheobronchial and nasopharyngeal region, from which the strontium may have been cleared mechanically to the esophagus and swallowed. Nevertheless, studies in which ^{89}Sr-enriched fly ash was instilled into the trachea of rats indicate that strontium in this form was partly absorbed and appeared in plasma and other tissues within days of the exposure (Srivastava et al. 1984a).

Although intratracheal instillation does not precisely replicate inhalation exposure, these studies provide additional evidence that strontium compounds of greater solubility are absorbed more rapidly from the lung. Strontium was cleared relatively rapidly from the lungs of rats that received an intratracheal dose of $SrCl_2$ (half-times <1 day) and was eliminated from the body in the urine (4–6% of the initial body burden) and in the feces (10–18%) (Naményi et al. 1986). By contrast, in rats that received an intratracheal dose of 360–760 μg Sr as $SrTiO_3$, strontium was eliminated from the lung with half-times of 0.4 days (85%) and 130 days (15%); the long retention phase reflects the slow absorption of the insoluble $SrTiO_3$ deposited in the lung, whereas the rapid phase reflects the mechanical clearance from the tracheobronchial region (Anderson et al. 1999b).

Strontium has been shown to be absorbed from the nasopharyngeal region of the respiratory tract. In hamsters administered $^{85}SrCl_2$ (in saline solution) directly into the nasal tract, 67% of the ^{85}Sr was absorbed in 4 hours and 63% was estimated to have been absorbed directly from the nasopharynx region of the respiratory tract (Cuddihy and Ozog 1973).

3.5.1.2 Oral Exposure

The fractional absorption of ingested strontium has been estimated in healthy human subjects or hospital patients who received an oral dose of strontium chloride ($SrCl_2$) or ingested strontium in the diet (Table 3-7). Absorption was quantified in these studies from measurements of plasma strontium concentration-time profiles for ingested and intravenously injected strontium (bioavailability), or from measurements of the difference between the amount ingested and excreted in feces (balance). Collectively, the results of these studies indicate that approximately 20% (range, 11–28%) of ingested strontium is absorbed from the gastrointestinal tract. Balance measurements can be expected to yield underestimates of absorption as a result of excretion of absorbed strontium in the feces (see Section 3.5.4); nevertheless, the two methods have yielded similar estimates of absorption.

Vezzoli et al. (1998) compared the area under the plasma strontium concentration-time curves in adult males and females and found no significant difference (males, 10.6±0.6 mmol/L-minute; females, 9.3±0.6 mmol/L-minute). The subjects included groups of healthy age-matched men and women (15 males, 12 females) and groups of normocalcuric patients (29 males, 18 females) who had calcium-oxalate urinary tract stones. Although the fraction absorbed could not be estimated in this study because the area under the curve for an intravenous dose was not measured, the results suggest that there were no substantive differences in absorption between males and females. This conclusion may not be valid for physiologic states in which there is an increased demand for calcium such as pregnancy and lactation. Calcium absorption is higher in these states, and studies in animals suggest that strontium absorption may also be higher (Kostial et al. 1969b). In general, strontium absorption appears to be a good indicator of calcium absorption in adult humans as both elements appear to share common mechanisms of absorption (Bianchi et al. 1999; Blumsohn et al. 1994; Milsom et al. 1987; Reid et al. 1986; Sips et al. 1994) (see Section 3.6.1).

Studies conducted in infants and children indicate that approximately 15–30% of dietary strontium is absorbed, similar to estimates in adults (Alexander et al. 1974; Harrison et al. 1965; Kahn et al. 1969a;

Table 3-7. Summary of Estimates of Absorption of Ingested Strontium in Humans

Dose and media[a]	Subjects (N)[b]	Absorption (% of dose)[c]	Comment	Reference
Tracer	Adults (9M)	28±3	Healthy adults. Absorption estimate based on whole body retention (R): R_{oral}/R_{iv}.	Likhtarev et al. 1975
44 mg, $SrCl_2$	Adults (8M)	25±7	Healthy, fasted subjects adults. Absorption estimate based on plasma AUC_{oral}/AUC_{iv}.[d]	Sips et al. 1995
44 mg, $SrCl_2$	Adults (8M)	25±6	Healthy fasted subjects. Absorption estimate based on plasma AUC_{oral}/AUC_{i}.	Sips et al. 1996
88 mg, $SrCl_2$	Adults (8M)	19±5	Healthy subjects. Dose administered with meal. Absorption estimate based on plasma AUC_{oral}/AUC_{iv}.	Sips et al. 1996
219 mg, $SrCl_2$	Adults (6M, 11F)	20	Patients with osteoporosis or chronic renal failure. Dose administered with meal. Absorption estimate based on plasma AUC_{oral}/AUC_{iv}.	Blumsohn et al. 1994
Tracer	Adults (3M)	21 (18–24)	Patients with osteoporosis. Dose administered with meal. Absorption estimate based on plasma AUC_{oral}/AUC_{iv}.	Hart and Spencer 1967
1.45 mg/kg, $SrCl_2$	Adults (6M, 4F)	22±2	Healthy fasted subjects. Absorption estimate based on fraction of dose in plasma at 3 hours.	Bianchi et al. 1999
Tracer	Adults (12)	17 (8–34)	Healthy subjects without a pre-dosing fast. Absorption estimate based on whole body counting.	LeRoy et al. 1966
44 mg, $SrCl_2$	Adults (43M, 20F)	13	Fasted patients with growth hormone deficiency, osteoporosis, hypothyroidism or hypercalcuric urinary tract stones. Absorption estimate based on fraction of dose in plasma at 4 hours.	Sips et al. 1994
219 mg, $SrCl_2$	Adults (6M)	20	Healthy fasted subjects. Absorption estimated from cumulative urinary excretion.	Leeuwenkamp et al. 1990
Tracer in milk	Adults (5)	11	Healthy subjects. Dose administered in milk, daily for 21–32 days. Absorption estimated from whole body retention kinetics.	Rundo and Lilligraven 1966
Tracer	Adults (4F)	42 (25–59)	Two health subjects, two patients with osteoporosis. Absorption estimated from intake minus 20-day fecal excretion, corrected for fecal excretion after an intravenous dose.	Uchiyama et al. 1973
0.8 mg/day diet	Adults (11M)	18 (-17–42)	Patients with various disorders, including osteoporosis. Absorption estimate based on	Warren and Spencer 1976

Table 3-7. Summary of Estimates of Absorption of Ingested Strontium in Humans

Dose and media[a]	Subjects (N)[b]	Absorption (% of dose)[c]	Comment	Reference
			6-day balance; dietary intake minus fecal excretion[e].	
Tracer	Adults (11M)	18 (-17–42)	Patients with various disorders, including osteoporosis. Absorption estimate based on estimated from 6-day balance; dietary intake minus fecal excretion[e].	Warren and Spencer 1976
1,500 mg/day	Adults (5F, 1M)	22 (20–28)	Patients with various illnesses. Absorption estimated from dietary intake minus fecal excretion minus fecal excretion after and I.V. dose (endogenous fecal excretion).	Spencer et al. 1960
Diet	Adults (9)	12 (0–48)	Patients with various illnesses. Absorption estimate based on estimated from 6-day balance; dietary intake minus fecal excretion.[e]	Spencer et al. 1972a
5–100 mg, $SrCl_2$	Children (5) 4–14 years	22	Patients with various illnesses. Dose administered for 24–28 days. Absorption estimated from dose minus 14-day fecal excretion.	Sutton et al. 1971b
100 µg breast milk	Infants 6–8 days (12)	15 (-47–59)	Healthy breast-feeding subjects. Absorption estimate based on estimated from 3-day balance intake minus fecal excretion.[e]	Harrison et al. 1965
600 µg diet	Infants 20 days–1 year (21)	28 (12–43)	Healthy subjects. Absorption estimate based on estimated from seven sequential 28-day balances; dietary intake minus fecal excretion.[e]	Kahn et al. 1969a

[a]Doses are in mass of strontium.
[b]Number of males (M) or females (F) is presented if reported.
[c]Values are reported means ± standard deviation; values in parentheses are reported ranges.
[d]AUC refers to the area under the plasma strontium concentration-time curve.
[e]Calculated from reported individual subject data.

Sutton et al. 1971a). Although age-related changes in strontium absorption cannot be discerned from the studies in humans, age-related changes in absorption of strontium have been observed in rats, suggesting the possibility of increased absorption of strontium during the neonatal period in humans. Adult male rats that received a single oral dose of 1.4 mg Sr as $SrCl_2$ absorbed 19% (±5 standard deviation [SD]) of the dose (Sips et al. 1997); this value is similar to that reported for humans (Sips et al. 1995, 1996).

However, when absorption was estimated at various ages, absorption was found to decrease from 85% of the dose at 15 days of age to 8% of the dose at ages older than 89 days (Forbes and Reina 1972). The differences between the adult estimates in these two studies may reflect the different methodologies; in the Sips et al. (1997) study, absorption was estimated from the area under the plasma strontium concentration-time curve for orally and intravenously administered strontium, whereas in the Forbes and Reina (1972) study, the absorption estimate was based on the measurements of 8-hour body burdens of strontium minus strontium in the gastrointestinal tract.

The fractional absorption of strontium appears to increase in rats during lactation. Rats that received a tracer dose of ^{85}Sr as $SrCl_2$ in drinking water between 14 and 16 days after the start of lactation absorbed twice as much strontium as control rats that were not lactating and received the same oral dose of strontium; 11% of the dose was absorbed in lactating rats compared to 5% in controls (Kostial et al. 1969b). Absorption was estimated in this study as the fraction of the dose in the skeleton, urine, and pups 3 days after the start of exposure.

The exact site of absorption of strontium in the gastrointestinal tract is not known; however, studies in hamsters suggest the possibility of absorption in both the stomach and small intestine. In hamsters that received a gavage tracer dose of $^{85}SrCl_2$, 37% was absorbed, whereas 20% was absorbed when the dose was administered to hamsters that had their pyloric sphincter ligated (Cuddihy and Ozog 1973). Studies in preparations of *in vitro* and *in situ* isolated intestine of the rat provide direct evidence for strontium absorption in the small intestine (see Section 3.6.1).

3.5.1.3 Dermal Exposure

There is little evidence for systemic toxicity following dermal exposure to strontium compounds, which would suggest that they are not readily absorbed across the skin of humans. Ilyin et al. (1975) estimated absorption rates for solutions of strontium chloride across intact or abraded skin of human subjects. Three groups of three male volunteers received topical applications of ^{85}Sr as strontium chloride in

aqueous solution (pH 7.0) without a carrier. In the first group, intact forearm skin (average area 8 cm^2) was exposed for 6 hours. In the second and third groups, the skin of the forearm was abraded with a metal grater just before the solution was applied; exposures were 6.1 cm^2 for 30 minutes and 6.9 cm^2 for 6 hours, respectively. For comparison, a fourth group received an intravenous injection of $^{85}SrCl_2$. After exposure and decontamination of the skin, radioactivity measurements were taken over 40 days of the ^{85}Sr present in the whole body, the patella, the right unexposed forearm, and, during the first 20 days, in daily urine samples. Absorption of strontium was estimated from whole body or partial body ^{85}Sr burdens, or urinary excretion of ^{85}Sr in comparison to the same end points after an intravenous dose of $^{85}SrCl_2$. The absorption of radiostrontium through intact skin over 6 hours was estimated to be 0.26% (range, 0.14–0.37%) of the applied dose, indicating that undamaged skin is a relatively effective barrier to penetration by strontium. Strontium absorption was greater through scratched and abraded skin. An average of 38% (range, 25.5–45.8%) of the applied dose was absorbed after 30 minutes and an average of 57.4% (range of coefficients, 55.7–65.3%) was absorbed after 6 hours. No other studies were located regarding dermal absorption of strontium compounds in humans.

An *in vitro* study evaluated penetration of ^{90}Sr through abdominal skin removed from 5- or 9-day-old Wistar rats and arranged in vertical penetration cells (Bauerová et al. 2001). The radionuclide in a chloride carrier solution (0.01–1.0% strontium chloride w/v) was applied to the epidermal surface; radioactivity of the permeated ^{90}Sr in the receptor chamber solution was measured by liquid scintillation spectrometry. Penetration was inversely related to concentration of the carrier solution. Penetration of the radiostrontium through the hairless skin of 5-day-old rats over 24 hours was 4 times lower than through the hairy skin of 9-day-old rats: at a carrier concentration of 0.1%, penetration was 0.5% for hairless skin of 5-day old rats compared to 2% for 9-day old rats. The authors attributed this difference to the barrier provided by the intact stratum corneum in 5-day skin, indicating that hair follicles in skin of 9-day-old rats increase the permeability of skin to strontium. In experiments in which epidermal layers were stripped (by the 20x repeated application of adhesive tape) or entirely removed from skin of 5-day-old rats, penetration was approximately 25% over 24 hours.

3.5.2 Distribution

3.5.2.1 Inhalation Exposure

Information on the distribution of inhaled strontium in humans is not available; however, it is reasonable to assume that the distribution of strontium absorbed into the systemic circulation after deposition in the respiratory tract would be similar to that absorbed after ingestion (see Section 3.5.2.2).

Studies in animals have shown that strontium that is absorbed after an initial deposition in the respiratory tract ultimately distributes primarily to the skeleton. In dogs that received a 2–22-minute nose-only exposure to aerosols of $^{85}SrCl_2$ (AMAD 1.4–2.7 μm, GSD 2.0), 37% of the body burden was distributed to the skeleton within 12 hours after the exposure and 84% was in the skeleton 4 days after the exposure (Fission Product Inhalation Project 1967a). Four to 6 days after a 30-minute inhalation exposure of rats to aerosols of ^{85}Sr carbonate, phosphate, fluoride, or oxide (particle sizes and doses not specified), >99% of the body burden of ^{85}Sr was in the skeleton (Willard and Snyder 1966). Two days after rats received a 10-minute head-only exposure to tracer levels of ^{85}Sr or a mixture of ^{85}Sr and ^{90}Sr aerosols (AMAD 1.8–2.8), at which time radioactive strontium could no longer be detected in the lung, the concentration in bone was 100–2,000 times that in soft tissues (Fission Product Inhalation Project 1967b). The rank order of soft tissue concentrations (highest to lowest) was muscle > skin > liver > kidney. In rats exposed to airborne fly ash (sieved to have a particle diameter of distribution of 90% less than 20 μm) for 6 hours, strontium was detected in various tissues; 1 day after the exposure, the tissue:plasma strontium concentration ratios were 0.3–0.5 in the liver, kidney, small intestine, and heart (Srivastava et al. 1984b).

Information on the distribution of strontium absorbed after deposition in the respiratory tract can be derived from studies in which strontium compounds were instilled directly into the trachea. Although intratracheal instillation does not precisely replicate inhalation exposure, the distribution of the absorbed strontium is likely to be similar to that which would be absorbed after inhalation. In rats that received an intratracheal dose of ^{89}Sr-enriched fly ash (sieved to have a particle diameter of distribution of 90% less than 20 μm), radioactivity was eliminated from the lung and appeared in plasma and other tissues within days of the exposure; tissue:plasma concentration ratios were >1 (1.5–2) in the liver, kidney, stomach, and small intestine, and <1 (0.7–0.9) in the spleen, heart, and brain (Srivastava et al. 1984a). The relatively high concentrations of strontium in the gastrointestinal tract may reflect the mechanical clearance of strontium from the airways to the esophagus.

Although placental transfer of strontium has been demonstrated in humans and animals exposed to strontium by other routes of exposure (see Section 3.5.2.2), only one study has examined placental transfer after a dose to the respiratory tract. Pregnant rats received an intratracheal dose of ^{89}Sr-enriched fly ash (sieved to have a particle diameter of distribution of 90% less than 20 μm) on days 14–18 of gestation. The concentrations of strontium in whole fetus, liver, lung, heart, and kidney were not significantly different from controls that received an instillation of saline (Srivastava et al. 1990).

3.5.2.2 Oral Exposure

The distribution of absorbed strontium in the human body is similar to that of calcium, with approximately 99% of the total body burden in the skeleton (ICRP 1993). The skeletal burden of stable strontium has been estimated from analyses of bone samples from human autopsies (Herring and Keefer 1971a; O'Connor et al. 1980; Papworth and Vennart 1984; Tanaka et al. 1981). Skeletal burden was estimated in Japanese adult males to be approximately 440 mg compared to 850 g of calcium (Tanaka et al. 1981).

Papworth and Vennart (1984) analyzed published data on ^{90}Sr and calcium concentrations in human bone tissues and diets of people in the United Kingdom during the period from 1955 to 1970 and concluded that approximately 4.75% of the dietary intake of ^{90}Sr was taken up by the adult skeleton. Approximately 7.5% of the cortical bone ^{90}Sr burden was eliminated from bone each year (equivalent to elimination half-times of approximately 9.2 years). The rate of elimination from trabecular bone was approximately 4 times this value. The same analysis yielded estimates of skeletal uptakes of strontium that varied with age, being highest, approximately 10%, in infants and during adolescence, ages in which bone growth rates are high relative to other ages.

Strontium distributes relatively uniformly within the bone volume where it exchanges with calcium in hydroxyapatite (see Section 3.6.1), although small differences in the calcium and strontium distributions within bone have been reported. The Sr:Ca concentration ratio in bone increases with age from approximately 0.3 mg strontium/g Ca at birth to a value of 0.5 in adults (Papworth and Vannart 1984; Tanaka et al. 1981). The Sr:Ca ratio in bone also has been shown to vary with the bone type; ratios in cortical bone were approximately 10–20% higher than in trabecular bone (Tanaka et al. 1981).

Information on the distribution of strontium in soft tissue is extremely limited. In rats that were exposed to 3.4 mg strontium/L (as $SrCl_2$) in drinking water for 3 months, the serum concentration of strontium was

8.7 mg/L and tissue:serum strontium concentration ratios (based on the latter mean serum concentration) were as follows: liver, 0.7; heart, 1.2; muscle, 1.1; adrenal, 1.3; brain, 1.2; and bone, 1,300 (Skoryna 1981b). Strontium:calcium ratios in these tissues were approximately 0.05–0.1. Tissue:plasma strontium concentration ratios in rats 1–5 hours after they received an intraperitoneal injection of strontium revealed ratios <1 in the fat, spleen, liver, ovary, testis, skeletal muscle, and heart; and values of 1.2–1.7 in the lung, small intestine, salivary gland, kidney, and skin (Brues et al. 1969). Tissue:plasma concentration ratios of seminal vesicles in mice increased to values exceeding 2 several days after an intraperitoneal dose of strontium (Brues et al. 1967).

Information on the subcellular location of strontium in soft tissues is also extremely limited. In rats that were exposed to 1.9 mg strontium/L (as $SrCl_2$) in drinking water for 3 months, the strontium concentrations (per mg protein) in the mitochondrial, lysosomal, and microsomal fractions of liver were approximately 5 times that of cytosol (Skoryna 1981b). A major fraction of the strontium in tissues, possibly as much as 50–80% appears to be bound to protein (Kshirsagar 1977).

The partitioning of strontium in blood has not been extensively explored. The concentrations of strontium in the erythrocyte and plasma fractions of human blood obtained from blood banks were 7.2 µg/L in the erythrocyte fraction and 44 µg/L in the plasma fraction, suggesting that most of the strontium in blood resides in the plasma (Olehy et al. 1966). The strontium concentration in serum from 100 human subjects (health status not reported) was 53 µg/L, similar to the value reported for blood bank serum (Skoryna 1981b). Strontium binds to proteins in human serum; however, the specific proteins to which strontium binds have not been characterized. Alda and Escanero (1985) found that 45% of the strontium incubated with human serum at a concentration of 10 mg/L was ultrafilterable. Harrison et al. (1955) reported a value of 60% for the ultrafilterable fraction of plasma at a plasma concentration of 3.5 mg/L in two subjects who received an intravenous dose of 20 or 100 mg strontium chlorides. Note that this concentration is 300–1,000 times that reported for serum concentrations in subjects that were not receiving strontium supplements (Olehy et al. 1966; Skoryna 1981b); at lower concentrations, a larger fraction of the serum strontium may be bound, as binding appears to be saturable (Alda and Escanero 1985; Berg et al. 1973). Values of 40–60% bound to protein have been reported for guinea pig and rabbit plasma or serum, respectively (Lloyd 1968; Twardock et al. 1971).

Strontium in the maternal skeleton can be transferred to the fetus during pregnancy. Studies of residents of the Techa River who were exposed to strontium as result of releases from a plutonium production plant provide evidence for fetal transfer of strontium (Tolstykh et al. 1998, 2001). The fetal:maternal transfer

coefficient—the ratio of ^{90}Sr concentrations in the fetal and maternal skeletons (expressed in becquerels per gram of calcium)—was determined for six subjects who were exposed prior to pregnancy and their seven stillborn infants (Tolstykh et al. 1998). The transfer coefficients varied from 0.012 to 0.24, with the higher values associated with maternal exposures that occurred during adulthood and lower values associated with maternal exposures during childhood or adolescence. The difference was not related to the maternal strontium burden at pregnancy and may reflect a lower availability of strontium deposited in cortical bone during periods of active bone growth.

Studies in animals provide additional evidence for transfer of strontium through the placenta to the fetus. The fetus begins to accumulate strontium as the fetal skeleton develops. In mice, ossification of the fetal skeleton begins on approximately the 14th day of gestation, at which point, the fetal strontium burden begins to increase (Olsen and Jonsen 1979). In pregnant mice that received an injection of strontium at different stages of pregnancy, fetal strontium burden was 4.5% of the maternal dose administered on the 18th day of pregnancy compared to 0.7% of the maternal dose administered on the 14th day of pregnancy (Rönnbäck 1986). Thus, fetal transfer was highest when the maternal dose occurred at the time of greatest skeletal growth. A similar observation has been made in rats; uptake of strontium by the fetus is highest (1–2% of an injected maternal dose) if the maternal dose is given on or after the 16th day of gestation when ossification of the fetal skeleton begins (Hartsook and Hershberger 1973; Wykoff 1971). The distribution of strontium in the fetus at the end of gestation is similar to that of the mother with most of the strontium burden in the skeleton. In mice, the skeletal (long bones):soft tissue concentration ratio was approximately 40 in both the fetuses and dams (Jacobsen et al. 1978).

Strontium enters mammary milk in humans and can be transferred to newborns during breast feeding (Harrison et al. 1965). The concentration of strontium in breast milk of 12 healthy women was estimated to be 74 µg/L (range, 39–93) and the Sr:Ca concentration ratio was 0.24 µg strontium/mg Ca (Harrison et al. 1965). In a study of the transport of trace elements, the concentration of strontium in colostrum samples collected from 29 healthy women during the first 3 days after delivery was found to be comparable to that in serum from venous blood samples taken 20 minutes before delivery (Rossipal et al. 2000). In contrast, the concentration of calcium in colostrum was significantly increased over the level in maternal serum, which was indicative of active transport. The authors concluded that the transfer of strontium was based primarily on a concentration gradient mode of action. Numerous studies in animals provide additional evidence for transfer of strontium from breast milk to newborns during lactation (Hopkins 1967; Jacobsen et al. 1978; Kostial et al. 1969b; Rönnbäck et al. 1968). In lactating rats that received an oral exposure to tracer concentrations ^{85}Sr in drinking water during the 14th through 16th days

of lactation, approximately 5% of the ingested dose was recovered in the nursing pups 24 hours after the end of the 2-day exposure (Kostial et al. 1969b). In a study in which lactating mice received an intraperitoneal injection of radioactive strontium, strontium levels of the nursing pups was approximately 20% of that of the dams (Rönnbäck et al. 1968). These results are consistent with the oral exposure study (Kostial et al. 1969b), if one assumes that approximately 25% of the oral dose was absorbed by the dam. The tissue distribution of strontium in lactating mice and their offspring was found to be similar after an intraperitoneal dose to the dams during lactation; concentrations in bone were approximately 1,000 times higher than liver and kidney (Jacobsen et al. 1978). The strontium concentration in calvaria of the lactating pups, after 5 days of lactation, was approximately 3 times that of the dams, whereas the concentration in long bones of pups and dams were similar (Jacobsen et al. 1978). The difference in the bone concentrations in the dams and pups may reflect the relatively higher rate of bone formation in the pups and associated incorporation of strontium into the new bone.

3.5.2.3 Dermal Exposure

In volunteers who were exposed to dermally applied $^{85}SrCl_2$ in the left forearm, ^{85}Sr was detected by external counting of the patella and right forearm 3 and 6 hours after the exposure was initiated, suggesting that the absorbed strontium had been taken up by bone (Ilyin et al. 1975). Although no other studies were located regarding the distribution of dermally absorbed strontium, it is likely that the distribution would be similar to that absorbed from the oral route, with the most of the body burden in the skeleton (see Section 3.5.2.2).

3.5.3 Metabolism

The metabolism of strontium consists of binding interactions with proteins and, based on its similarity to calcium, probably complex formation with various inorganic anions such as carbonate and phosphate, and carboxylic acids such as citrate and lactate (Alda and Escanero 1985; Inoue et al. 1988; Kshirsagar 1977; Lloyd 1968; Twardock et al. 1971). These types of interactions would be expected for all routes of exposure. These types of interactions would be expected for all routes of exposure including the following:

3.5.3.1 Inhalation Exposure

3.5.3.2 Oral Exposure

3.5.3.3 Dermal Exposure

3.5.4 Elimination and Excretion

3.5.4.1 Inhalation Exposure

Whole body elimination times have been measured in dogs and rats that received inhalation exposures to $SrCl_2$. In dogs that were exposed to aerosols of $^{85}SrCl_2$ (AMAD 1.4–2.7 μm, GSD 2.0), elimination half-times were 0.6 (59%), 9 (12%), and 300 days (29%) (Fission Product Inhalation Project 1967a). The rapid early phase of elimination reflects the mechanical clearance of strontium deposited in the tracheobronchial region of the respiratory tract and transfer to the gastrointestinal tract and feces, whereas the slower elimination component reflects the elimination from the skeleton. A similar pattern of elimination has been observed in rats. In rats that were exposed to tracer levels of ^{85}Sr or a mixture of ^{85}Sr and ^{90}Sr aerosols (AMAD 1.8–2.8), the long-term whole-body elimination half-time, measured 5–230 days after exposure, was 330 days (Fission Product Inhalation Project 1967b).

Strontium that is absorbed after an initial deposition in the respiratory tract is excreted in feces and urine. Evidence for this comes from accidental exposures to radioactive strontium. In one case, a worker accidentally inspired an unknown quantity of $^{90}SrCl_2$ (physical form unknown) and, over the subsequent 800 days, the urinary:fecal excretion ratio was 3:1 (Petkau and Pleskach 1972). The urinary:fecal excretion ratio of 3 is consistent with observations of long-term urinary:fecal excretion ratios observed in people who ingested radioactive strontium or short-term ratios in people who received an intravenous dose of radioactive strontium (see Section 3.5.4.2). In a second case, a worker was exposed to $^{90}SrCO_3$ with deposition within the nasal tract as well as the hands, face, and hair and the urinary:fecal excretion ratio over the first 24 days was 0.71 (Rundo and Williams 1961). The lower ratio in this case probably reflects the fecal contribution of strontium that was mechanically cleared from the respiratory tract over the shorter observation period (24 days compared to 800 days). Similar observations have been made in animals. In dogs that received a 2–22-minute nose-only exposure to aerosols of $^{85}SrCl_2$ (AMAD 1.4–2.7 μm, GSD 2.0), an initially large fecal component of excretion was followed by urinary:fecal excretion ratios of 1.0–1.4 (Fission Product Inhalation Project 1967a). An increase over time in the

urinary:fecal excretion ratios from values <1 to 2–4 has also been observed after intratracheal instillation of $SrCl_2$ in rats (Fission Product Inhalation Project 1967b; Namenyi et al. 1986).

3.5.4.2 Oral Exposure

The long-term (decades) elimination of strontium has been studied in people who were exposed to strontium in the Techa River area of Russia after fission products from a plutonium production process were released in the area. Whole-body elimination half-times were estimated in a study population of 361 males and 356 females to be 28 years in males and 16 years in females (Tolstykh et al. 1997). Most of the difference in the elimination rate estimated for males and females resulted from a pronounced increase in the elimination rate in females after age 50 years. The increase most likely reflects the increase in bone resorption that tends to occur in females after menopause. Müller et al. (1966) estimated a similar value, 25 years, for the long-term elimination half-time of strontium in 56 radium dial painters. In two dial painters, long-term elimination half-times were estimated to be 9 years (Wenger and Soucas 1975). Estimates of the long-term elimination half-times of strontium reflect primarily the storage and release of strontium in bone. Over shorter time periods after exposure, faster elimination rates are observed that reflect soft-tissue elimination as well as elimination from a more rapidly exchangeable pool of strontium in bone. When whole-body elimination of a tracer dose of ^{85}Sr was measured for periods of 42–108 days in nine subjects, the mean elimination half-time was 91 days (±32, SD) (Likhtarev et al. 1975). In three healthy subjects that received a single oral dose of $SrCl_2$, the estimated average whole-body elimination half-times, estimated over 13 days, were 2 (30%) and 59 days (70%) (Uchiyama et al. 1973). Similar short-term rates of elimination have been observed within days to a few weeks after an intravenous injection of $SrCl_2$ (MacDonald et al. 1965; Newton et al. 1990).

Strontium that has been absorbed from the gastrointestinal tract is excreted primarily in urine and feces. In two dial painters, rates of urinary and fecal excretion of radium approximately 10 years after the exposure were approximately 0.03 and 0.01% of the body burden per 24 hours, respectively (Wenger and Soucas 1975). The urine:fecal excretion ratio of 3 that was observed in the radium dial workers is consistent with ratios of 2–6 observed several days to weeks after subjects received an intravenous injection of $SrCl_2$ (Bishop et al. 1960; Blake et al. 1989a, 1989b; Likhtarev et al. 1975; Newton et al. 1990; Samachson 1966; Snyder et al. 1964; Uchiyama et al. 1973). Thus, urine appears to be the major route of excretion of absorbed strontium. The observation of fecal excretion of radioactive strontium weeks to decades after an oral exposure or over shorter time periods after an intravenous exposure suggests the existence of a mechanism for transfer of absorbed strontium into gastrointestinal tract, either

from the bile or directly from the plasma. Evidence for direct secretion of strontium from the plasma into the intestine is provided by studies in animals (see Section 3.5.1). The available information does not address the extent to which biliary excretion may also contribute to fecal excretion of strontium.

As discussed in Section 3.5.2.2, absorbed strontium is eliminated in breast milk during lactation. The concentration of strontium in breast milk of 12 healthy women was estimated to be 74 µg/L (range, 39–93) and the Sr:Ca concentration ratio was 0.24 µg strontium/mg Ca (Harrison et al. 1965).

Strontium has been detected in human saliva and seminal fluid. In healthy subjects who received a single intravenous injection of $SrCl_2$, the saliva:plasma concentration ratio was 0.9 and the semen:plasma ratio was 0.6 (Harrison et al. 1967a).

3.5.4.3 Dermal Exposure

In volunteers who were exposed to dermally applied $^{85}SrCl_2$ in the left forearm, ^{85}Sr was excreted in urine (fecal excretion was not measured in this study) (Ilyin et al. 1975). Although no other studies were located regarding the excretion of dermally absorbed strontium, it is likely that the excretion would be similar to that absorbed from the oral route, with urinary excretion being approximately 2–3 times greater than fecal excretion (see Section 3.5.4.2).

3.5.5 Physiologically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Models

Physiologically based pharmacokinetic (PBPK) models use mathematical descriptions of the uptake and disposition of chemical substances to quantitatively describe the relationships among critical biological processes (Krishnan et al. 1994). PBPK models are also called biologically based tissue dosimetry models. PBPK models are increasingly used in risk assessments, primarily to predict the concentration of potentially toxic moieties of a chemical that will be delivered to any given target tissue following various combinations of route, dose level, and test species (Clewell and Andersen 1985). Physiologically based pharmacodynamic (PBPD) models use mathematical descriptions of the dose-response function to quantitatively describe the relationship between target tissue dose and toxic end points.

PBPK/PD models refine our understanding of complex quantitative dose behaviors by helping to delineate and characterize the relationships between: (1) the external/exposure concentration and target

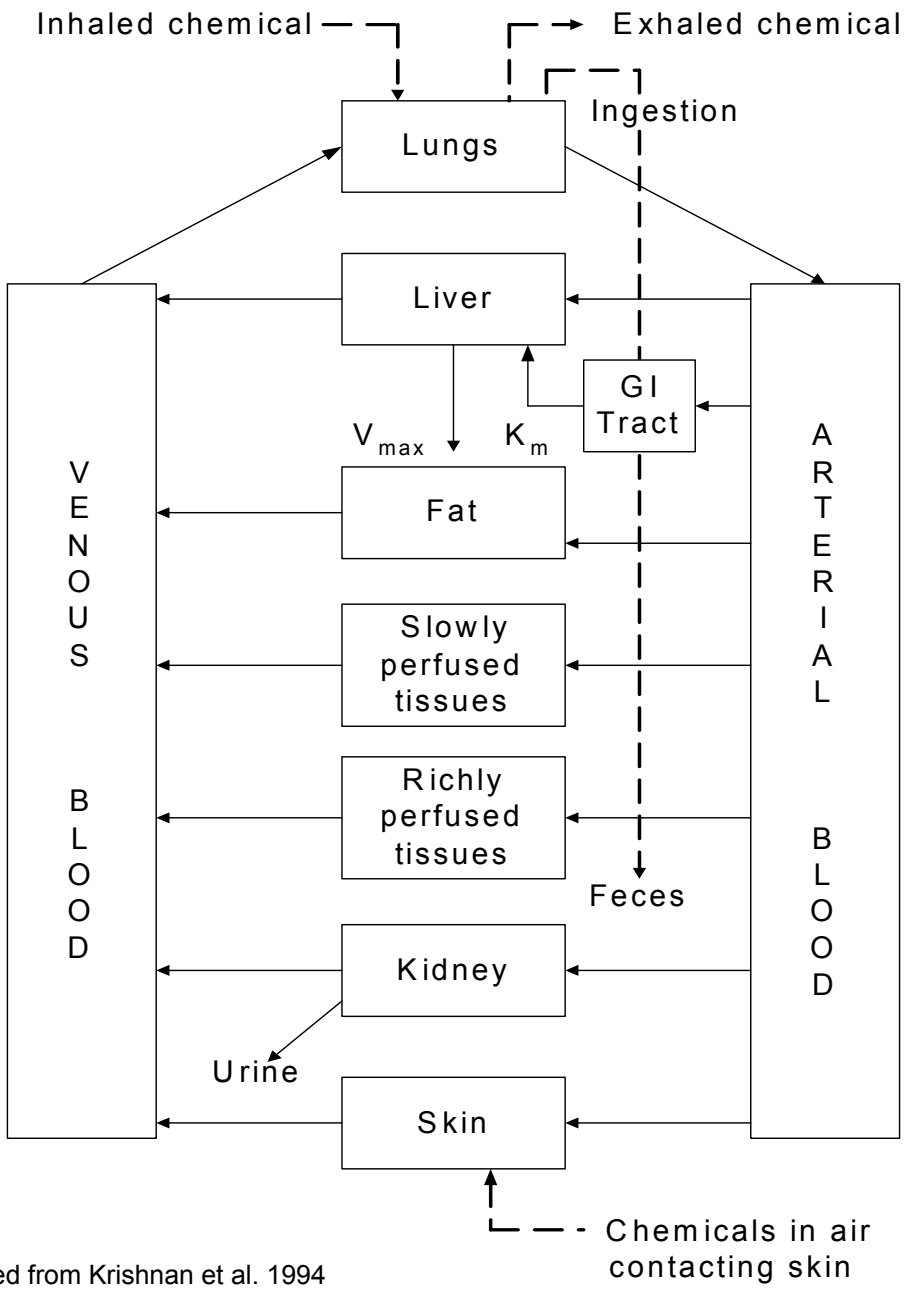
tissue dose of the toxic moiety, and (2) the target tissue dose and observed responses (Andersen et al. 1987; Andersen and Krishnan 1994). These models are biologically and mechanistically based and can be used to extrapolate the pharmacokinetic behavior of chemical substances from high to low dose, from route to route, between species, and between subpopulations within a species. The biological basis of PBPK models results in more meaningful extrapolations than those generated with the more conventional use of uncertainty factors.

The PBPK model for a chemical substance is developed in four interconnected steps: (1) model representation, (2) model parametrization, (3) model simulation, and (4) model validation (Krishnan and Andersen 1994). In the early 1990s, validated PBPK models were developed for a number of toxicologically important chemical substances, both volatile and nonvolatile (Krishnan and Andersen 1994; Leung 1993). PBPK models for a particular substance require estimates of the chemical substance-specific physicochemical parameters, and species-specific physiological and biological parameters. The numerical estimates of these model parameters are incorporated within a set of differential and algebraic equations that describe the pharmacokinetic processes. Solving these differential and algebraic equations provides the predictions of tissue dose. Computers then provide process simulations based on these solutions.

The structure and mathematical expressions used in PBPK models significantly simplify the true complexities of biological systems. If the uptake and disposition of the chemical substance(s) is adequately described, however, this simplification is desirable because data are often unavailable for many biological processes. A simplified scheme reduces the magnitude of cumulative uncertainty. The adequacy of the model is, therefore, of great importance, and model validation is essential to the use of PBPK models in risk assessment.

PBPK models improve the pharmacokinetic extrapolations used in risk assessments that identify the maximal (i.e., the safe) levels for human exposure to chemical substances (Andersen and Krishnan 1994). Similar models have been developed for radionuclides. These PBPK models provide a scientifically sound means to predict the target tissue dose of chemicals in humans who are exposed to environmental levels (for example, levels that might occur at hazardous waste sites) based on the results of studies where doses were higher or were administered in different species. Figure 3-4 shows a conceptualized representation of a PBPK model. Figures 3-5 through 3-8 show models for radionuclides in general or specifically for strontium.

Figure 3-4. Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a Hypothetical Chemical Substance



Source: adapted from Krishnan et al. 1994

Note: This is a conceptual representation of a physiologically based pharmacokinetic (PBPK) model for a hypothetical chemical substance. The chemical substance is shown to be absorbed via the skin, by inhalation, or by ingestion, metabolized in the liver, and excreted in the urine or by exhalation.

Human Respiratory Tract Model for Radiological Protection (ICRP 1994a).

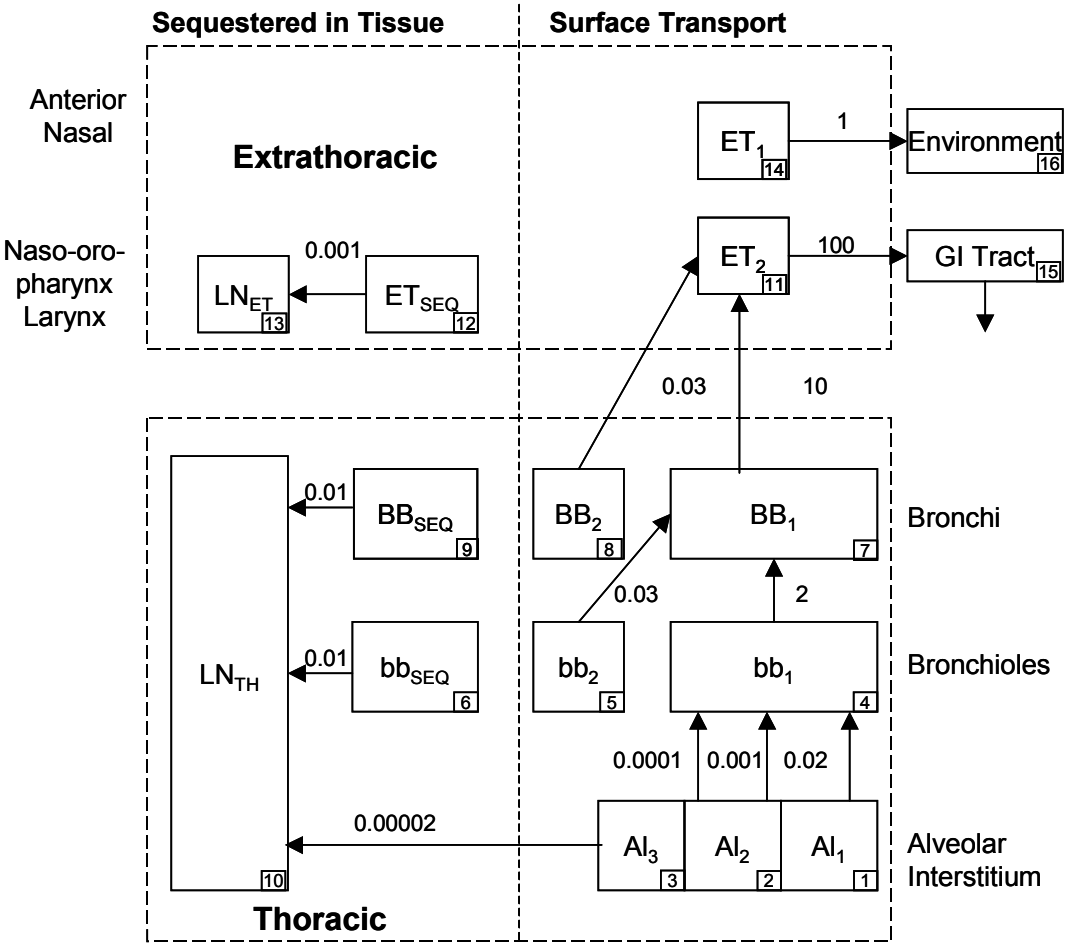
Deposition. The ICRP (1994a) has developed a deposition model for behavior of aerosols and vapors in the respiratory tract. It was developed to estimate the fractions of radioactivity in breathing air that are deposited in each anatomical region of the respiratory tract. ICRP (1994a) provides inhalation dose coefficients that can be used to estimate the committed equivalent and effective doses to organs and tissues throughout the body based on a unit intake of radioactive material. The model applies to three levels of particle solubility and a wide range of particle sizes (approximately 0.0005–100 μm in diameter), and parameter values, which can be adjusted for various segments of the population (e.g., sex, age, level of physical exertion). This model also allows one to evaluate the bounds of uncertainty in deposition estimates. Uncertainties arise from natural biological variability among individuals and the need to interpret some experimental evidence that remains inconclusive. It is applicable to particulate aerosols containing strontium, but was developed for a wide variety of radionuclides and their chemical forms.

The ICRP deposition model estimates the amount of inhaled material that initially enters each compartment (see Figure 3-5). The model was developed with the following 5 compartments: (1) the anterior nasal passages (ET_1); (2) all other extrathoracic airways (ET_2) (posterior nasal passages, the naso- and oropharynx, and the larynx); (3) the bronchi (BB); (4) the bronchioles (bb); and (5) the alveolar interstitium (AI). Particles deposited in each of the regions may be removed from each region and redistributed either upward into the respiratory tree or to the lymphatic system and blood by different particle removal mechanisms.

For extrathoracic deposition of particles, the model uses experimental data, where deposition is related to particle size and airflow parameters, and scales deposition for women and children from adult male data. Similarly, to the extrathoracic region, experimental data served as the basis for lung (bronchi, bronchioles, and alveoli) aerosol transport and deposition. A theoretical model of gas transport and particle deposition was used to interpret data and to predict deposition for compartments and subpopulations other than adult males. Table 3-8 provides reference respiratory values for the general Caucasian population under several levels of activity.

Deposition of inhaled gases and vapors is modeled as a partitioning process which depends on the physiological parameters noted above as well as the solubility and reactivity of compound in the

Figure 3-5. Compartment Model to Represent Particle Deposition and Time-Dependent Particle Transport in the Respiratory Tract*



*Compartment numbers shown in lower right corners are used to define clearance pathways. The clearance rates, half-lives, and fractions by compartment, as well as the compartment abbreviations are presented in Table 3-9.

Source: ICRP 1994a

Table 3-8. Reference Respiratory Values for a General Caucasian Population at Different Levels of Activity

Activity:		Resting (sleeping)			Sitting awake			Light exercise			Heavy exercise		
Maximal workload:		8%			12%			32%			64%		
Breathing parameters:		V_T (L)	B (m^3h^{-1})	f_R (min^{-1})	V_T (L)	B (m^3h^{-1})	f_R (min^{-1})	V_T (L)	B (m^3h^{-1})	f_R (min^{-1})	V_T (L)	B (m^3h^{-1})	f_R (min^{-1})
Age	Sex												
3 months		0.04	0.09	38	N/A	N/A	N/A	0.07	0.19	48	N/A	N/A	N/A
1 year		0.07	0.15	34	0.1	0.22	36	0.13	0.35	46	N/A	N/A	N/A
5 years		0.17	0.24	23	0.21	0.32	25	0.24	0.57	39	N/A	N/A	N/A
10 years	Male:										0.841	2.22	44
	Both:										0.667	1.84	46
	Female:	0.3	0.31	17	0.33	0.38	19	0.58	1.12	32			
15 years	Male:	0.500	0.42	14	0.533	0.48	15	1.0	1.38	23	1.352	2.92	36
	Female:	0.417	0.35	14	0.417	0.40	16	0.903	1.30	24	1.127	2.57	38
Adult	Male:	0.625	0.45	12	0.750	0.54	12	1.25	1.5	20	1.923	3.0	26
	Female:	0.444	0.32	12	0.464	0.39	14	0.992	1.25	21	1.364	2.7	33

[a]See Annex B (ICRP 1994a) for data from which these reference values were derived.

B = ventilation rate; f_R = respiration frequency; h = hour; min = minute; N/A = not applicable; V_T = tidal volume

respiratory tract (Figure 3-6). The ICRP (1994a) model defines three categories of solubility and reactivity: SR-0, SR-1, and SR-2:

- Type SR-0 compounds include insoluble and nonreactive gases (e.g., inert gases such as H_2, He). These compounds do not significantly interact with the respiratory tract tissues and essentially all of the compound that is inhaled is exhaled. Radiation doses from inhalation of SR-0 compounds are assumed to result from the irradiation of the respiratory tract from the air spaces.

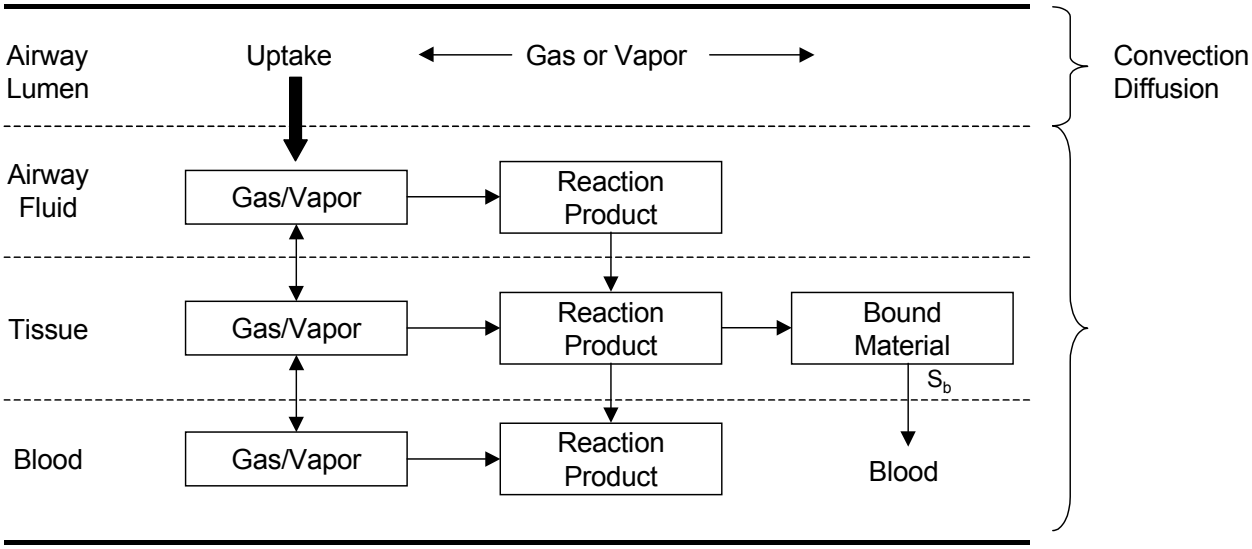
- Type SR-1 compounds include soluble or reactive gases and vapors that are expected to be taken up by the respiratory tract tissues and may deposit in any or all of the regions of the respiratory tract, depending on the dynamics of the airways and properties of the surface mucous and airway tissues, as well as the solubility and reactivity of the compound.

- Type SR-2 compounds include soluble and reactive gases and vapors that are completely retained in the extrathoracic regions of the respiratory tract. SR-2 compounds include sulfur dioxide (SO2) and hydrogen fluoride (HF).

Mechanical Clearance from the Respiratory Tract. This portion of the model identifies the principal clearance pathways within the respiratory tract. The model was developed to predict the retention of various radioactive materials. Figure 3-7 presents the compartmental model and is linked to the deposition model (Figure 3-5) and to reference values presented in Table 3-9. Table 3-9 provides clearance rates and deposition fractions for each compartment for insoluble particles. The table provides rates of insoluble particle transport for each of the compartments, expressed as a fraction per day and also half-time. ICRP (1994a) also developed modifying factors for some of the parameters, such as age, smoking, and disease status. Parameters of the clearance model are based on human evidence for the most part, although particle retention in airway walls is based on experimental data from animal experiments.

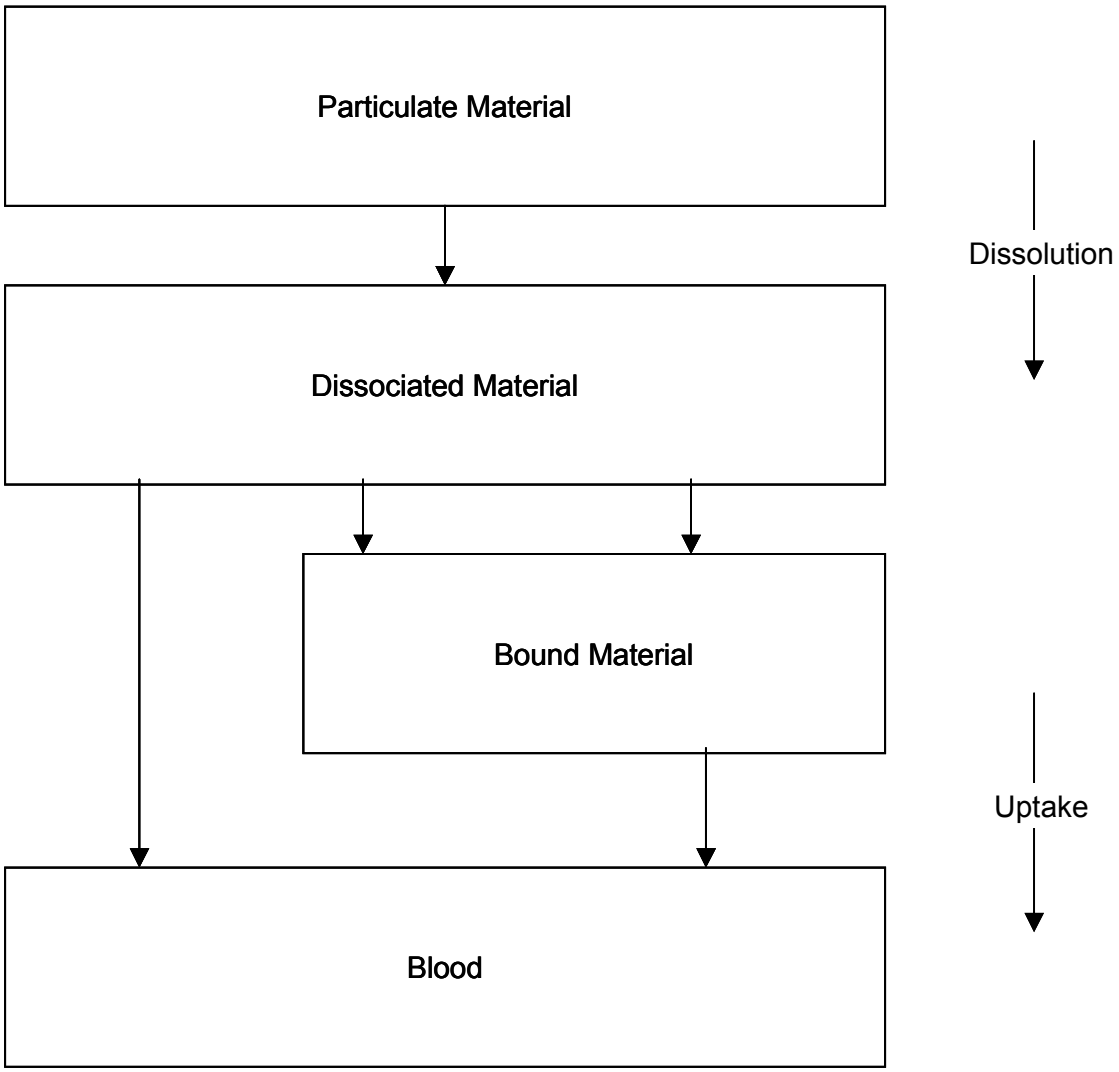
The clearance of particles from the respiratory tract is a dynamic process. The rate of clearance generally changes with time from each region and by each route. Following deposition of large numbers of particles (acute exposure), transport rates change as particles are cleared from the various regions. Physical and chemical properties of deposited material determine the rate of dissolution and as particles dissolve, absorption rates tend to change over time. By creating a model with compartments of different clearance rates within each region (e.g., BB_1, BB_2, BB_{seq}), the ICRP model overcomes problems associated with time-dependent functions. Each compartment clears to other compartments by constant rates for each pathway.

Figure 3-6. Reaction of Gases or Vapors at Various Levels of the Gas-Blood Interface



From ICRP 1994a

Figure 3-7. The Human Respiratory Tract Model: Absorption into Blood



Source: ICRP 1994a

Table 3-9. Reference Values of Parameters for the Compartment Model to Represent Time-dependent Particle Transport from the Human Respiratory Tract

Part A

	Clearance rates for insoluble particles			
Pathway	From	To	Rate (d^{-1})	Half-time[a]
$m_{1,4}$	AI_1	bb_1	0.02	35 days
$m_{2,4}$	AI_2	bb_1	0.001	700 days
$m_{3,4}$	AI_3	bb_1	0.0001	7,000 days
$m_{3,10}$	AI_3	LN_{TH}	0.00002	No data
$m_{4,7}$	bb_1	BB_1	2	8 hours
$m_{5,7}$	bb_2	BB_1	0.03	23 days
$m_{6,10}$	bb_{seq}	LN_{TH}	0.01	70 days
$m_{7,11}$	BB_1	ET_2	10	100 minutes
$m_{8,11}$	BB_2	ET_2	0.03	23 days
$m_{9,10}$	BB_{seq}	LN_{TH}	0.01	70 days
$m_{11,15}$	ET_2	GI tract	100	10 minutes
$m_{12,13}$	ET_{seq}	LN_{ET}	0.001	700 days
$m_{14,16}$	ET_1	Environment	1	17 hours

Table 3-9. Reference Values of Parameters for the Compartment Model to Represent Time-dependent Particle Transport from the Human Respiratory Tract

Part B

Partition of deposit in each region between compartments[b]		
Region or deposition site	Compartment	Fraction of deposit in region assigned to compartment[c]
ET_2	ET_2	0.9995
	ET_{seq}	0.0005
BB	BB_1	0.993-f_s
	BB_2	f_s
	BB_{seq}	0.007
bb	bb_1	0.993-f_s
	bb_2	f_s
	bb_{seq}	0.007
AI	AI_1	0.3
	AI_2	0.6
	AI_3	0.1

[a]The half-times are approximate since the reference values are specified for the particle transport rates and are rounded in units of d^{-1}. A half-time is not given for the transport rate from AI_3 to LN_{TH}, since this rate was chosen to direct the required amount of material to the lymph nodes. The clearance half-time of compartment AI_3 is determined by the sum of the clearance rates from it.
[b]See paragraph 181, Chapter 5 (ICRP 1994a) for default values used for relating f_s to d_{ae}.
[c]It is assumed that the slow-cleared fraction f_s is size-dependent. For modeling purposes f_s is taken to be:

$$f_s = 0.5 \; for \; d_{ae} \le 2.5\sqrt{\rho / \chi} \; \mu m \; and$$
$$f_s = 0.5e^{0.63(d_{ae}\sqrt{\rho/\chi} - 2.5)} \; for \; d_{ae} > 2.5\sqrt{\rho / \chi} \; \mu m$$

AI = alveolar-interstitial region; BB = bronchial region; bb = bronchiolar region; BB_{seq} = compartment representing prolonged retention in airway walls of small fraction of particles deposited in the bronchial region; bb_{seq} = compartment representing prolonged retention in airway walls of small fraction of particles deposited in the bronchiolar region; d = day(s); ET = extrathoracic region; ET_{seq} = compartment representing prolonged retention in airway tissue of small fraction of particles deposited in the nasal passages; GI = gastrointestinal; LN_{ET} = lymphatics and lymph nodes that drain the extrathoracic region; LN_{TH} = lymphatics and lymph nodes that drain the thoracic region

Source: ICRP 1994a

Particle transport from all regions is toward both the lymph nodes and the pharynx, and a majority of deposited particles end up being swallowed. In the front part of the nasal passages (ET_1), nose blowing, sneezing, and wiping remove most of the deposited particles. Particles remain here for about a day. For particles with AMADs a few micrometers or greater, the ET_1 compartment is probably the largest deposition site. A majority of particles deposited at the back of the nasal passages and in the larynx (ET_2) are removed quickly by the fluids that cover the airways. In this region, particle clearance is completed within 15 minutes.

Ciliary action removes deposited particles from both the bronchi and bronchioles. Though it is generally thought that mucocilliary action rapidly transports most particles deposited here toward the pharynx, a fraction of these particles are cleared more slowly. Evidence for this is found in human studies. For humans, retention of particles deposited in the lungs (BB and bb) is apparently biphasic. The "slow" action of the cilia may remove as many as half of the bronchi- and bronchiole-deposited particles. In human bronchi and bronchiole regions, mucus moves more slowly the closer it is to the alveoli. For the faster compartment, it has been estimated that it takes about 2 days for particles to travel from the bronchioles to the bronchi and 10 days from the bronchi to the pharynx. The second (slower) compartment is assumed to have approximately equal fractions deposited between BB_2 and bb_2, and both with clearance half-times estimated at 20 days. Particle size is a primary determinant of the fraction deposited in this slow thoracic compartment. A small fraction of particles deposited in the BB and bb regions is retained in the airway wall for even longer periods (BB_{seq} and bb_{seq}).

If particles reach and become deposited in the alveoli, they tend to stay imbedded in the fluid on the alveolar surface or move into the lymph nodes. The one mechanism by which particles are physically resuspended and removed from the AI region is coughing. For modeling purposes, the AI region is divided into three subcompartments to represent different clearance rates, all of which are slow.

Particle clearance from the alveolar-interstitial region has been measured in human subjects. The ICRP model uses two half-times to represent clearance: about 30% of the particles have a 30-day half-time, and the remaining 70% are given a half-time of several hundred days. Over time, AI particle transport falls, and some compounds have been found in lungs 10–50 years after exposure.

Absorption into Blood. The ICRP model assumes that absorption into blood occurs at equivalent rates in all parts of the respiratory tract, except in the anterior nasal passages (ET_1), where no absorption occurs. Absorption is essentially a 2-stage process, as shown in Figure 3-7. First, there is a dissociation

(dissolution) of particles; then, the dissolved molecules or ions diffuse across capillary walls and are taken up by the blood. Immediately following dissolution, rapid absorption is observed. For some elements, rapid absorption does not occur because of binding to respiratory-tract components. In the absence of specific data for specific compounds, the model uses the following default absorption rate values for those specific compounds that are classified as Types F (fast), M (medium), S (slow), and V (instantaneous):

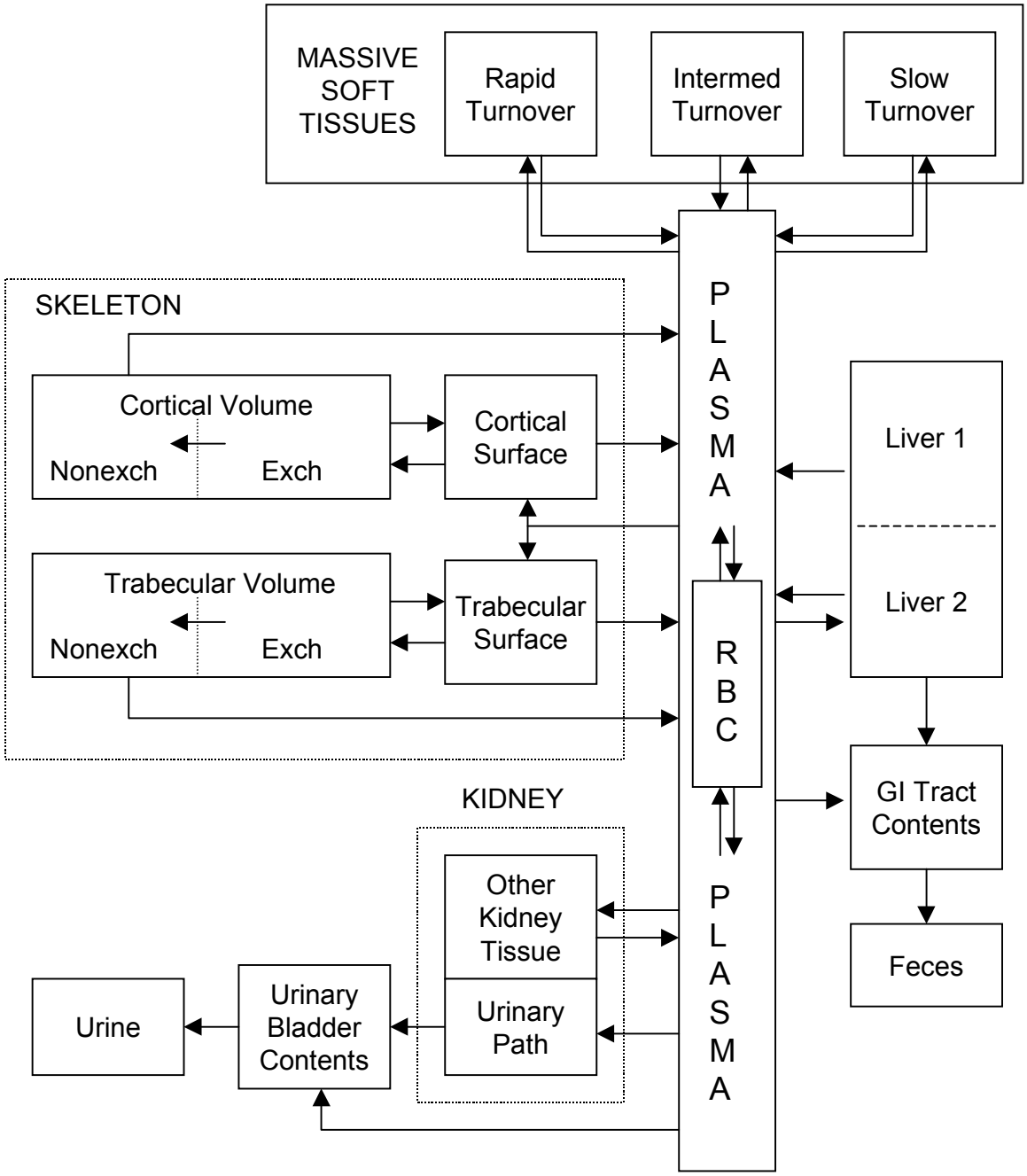
- For Type F, there is rapid 100% absorption within 10 minutes of the material deposited in the BB, bb, and AI regions, and 50% of material deposited in ET_2. Thus, for nose breathing, there is rapid absorption of approximately 25% of the deposit in ET and 50% for mouth breathing.
- For Type M, about 70% of the deposit in AI reaches the blood eventually. There is rapid absorption of about 10% of the deposit in BB and bb, and 5% of material deposited in ET_2. Thus, there is rapid absorption of approximately 2.5% of the deposit in ET for nose breathing, and 5% for mouth breathing.
- For Type S, 0.1% is absorbed within 10 minutes and 99.9% is absorbed within 7,000 days, so there is little absorption from ET, BB, or bb, and about 10% of the deposit in AI reaches the blood eventually.
- For Type V, complete absorption (100%) is considered to occur instantaneously.

ICRP (1995) considers the experimental data on strontium carbonate, and chloride, and sulfate to support classification of these compounds as Type F. Data on strontium particulates released from irradiated fuel support their classification as either Type F or M. Data on strontium in fused aluminosilicate particles support a classification as Type S. ICRP (1995) recommends assigning all strontium aerosols to Type M in the absence of specific information supporting an alternative classification.

ICRP (1993) Strontium Biokinetics Model

Description of the model. ICRP (1993) developed a compartmental model of the kinetics of alkaline earth elements, including strontium, in humans that is applicable to infants, children, adolescents, and adults. The model is based on a nearly identical model developed by Leggett (1992). The fraction of ingested strontium that is absorbed (uptake to blood) is assumed to vary with age and have values of 0.6 in infants up to 12 months of age, 0.4 from 12 months of age through 15 years, and 0.3 from age 15 years through adulthood. Absorbed strontium that enters the blood plasma is assumed to distribute to the skeleton, liver, and other tissues (Figure 3-8). Excretion pathways included in the model are plasma to urine, plasma to feces, and liver to feces. Transfer rate coefficients between compartments are age-specific and, depending on the specific coefficient, values can change at ages 3 months, 1 year, 5 years, 10 years, 15 years, and adult (>15 years). The model assumes that 99% of the strontium that enters the

Figure 3-8. ICRP (1993) Model of Strontium Biokinetics



body and is not excreted is ultimately transferred to the skeleton and 1% is in soft tissues. Skeletal deposition is assumed to distribute initially to the bone surface of either cortical or trabecular bone, from which it can exchange relatively rapidly with calcium in plasma or more slowly with calcium in the bone volume. Two pools are assumed to exist within the bone volume, an exchangeable pool that communicates with surface bone, and a nonexchangeable pool from which strontium can be returned to plasma as a result of bone resorption. Approximately 55% of the transfer from plasma to bone in adults is to the trabecular bone surface and 45% to the cortical bone surface.

Validation of the model. The extent to which the ICRP model has been validated is not described in ICRP (1993).

Risk assessment. The model has been used to establish radiation dose equivalents (Sv/Bq) of ingested ^{89}Sr and ^{90}Sr for ages 3 months to 70 years (ICRP 1993). The model has also been applied by the ICRP to calculate limits on inhalation for ^{89}Sr and ^{90}Sr (ICRP 1995) and limits on inhalation or ingestion for ^{80}Sr, ^{81}Sr, ^{82}Sr, ^{83}Sr, ^{85}Sr, ^{85m}Sr, ^{87m}Sr, ^{91}Sr, and ^{92}Sr (ICRP 1994b). It was used in the U.S. Federal Guidance Report No. 13 (EPA 2000e) to calculate inhalation risk coefficients and ingestion risk coefficients (separately for food and water) for the following radionuclides: ^{80}Sr, ^{81}Sr, ^{82}Sr, ^{83}Sr, ^{85}Sr, ^{85m}Sr, ^{87m}Sr, ^{89}Sr, ^{90}Sr, ^{91}Sr, and ^{92}Sr.

Target tissues. The model is designed to calculate ^{89}Sr and ^{90}Sr intake limits, based on radiation dose to all major organs, including the bone surfaces, bone marrow, and liver, to which the highest doses would be expected.

Species extrapolation. The model is designed for applications to human dosimetry and cannot be applied to other species without modification.

Interroute extrapolation. The model is intended for application to strontium reaching blood by absorption from lungs, gastrointestinal tract, or wound, or by injection.

3.6 MECHANISMS OF ACTION

3.6.1 Pharmacokinetic Mechanisms

Absorption. Airborne particulate aerosols of strontium can be deposited in the respiratory tract when the aerosols are inhaled. Amounts and patterns of deposition of particulates in the respiratory tract are affected by the size of the inhaled particles, age-related factors that determine breathing patterns (e.g., nose breathing vs mouth breathing), airway geometry, and airstream velocity within the respiratory tract (Gehr 1994; James et al. 1994; Roy et al. 1994). In general, large particles (>2.5 μm) deposit in the nasopharyngeal tract where high airstream velocities and airway geometry facilitate inertial impaction (Chan and Lippman 1980; James et al. 1994). In the tracheobronchial and alveolar regions, where airstream velocities are lower, processes such as sedimentation and interception become important for deposition of smaller particles (<2.4 μm). Breathing patterns, airflow velocity, and airway geometry change with age, giving rise to age-related differences in particle deposition (James 1978; James et al. 1994; Phalen et al. 1985). Deposition in the various regions of the respiratory tract in children may be higher or lower than in adults depending on particle size; for submicron particles, fractional deposition in 2-year-old children has been estimated to be 1.5 times greater than in adults (Xu and Yu 1986). Absorption of insoluble strontium is influenced by particle size and solubility as well as the pattern of regional deposition within the respiratory tract. Larger particles (>2.5 μm) that are deposited in the ciliated airways (nasopharyngeal and tracheobronchial regions) can be transferred by mucociliary transport into the esophagus and swallowed. Particles deposited in the alveolar region can be absorbed after extracellular dissolution or ingestion by phagocytic cells. Strontium-bearing pulmonary alveolar macrophages (PAMs) can migrate either to the airways where mucocilliary transport to the esophagus can occur or to tracheobronchial lymph nodes. The relative contributions of these two pathways to strontium absorption have not been quantified.

The exact site of absorption of strontium in the gastrointestinal tract is not known; however, studies in hamsters suggest the possibility of absorption in both the stomach and small intestine. In hamsters that received a gavage tracer dose of $^{85}SrCl_2$, 37% was absorbed, whereas 20% was absorbed when the dose was administered to hamsters that had their pyloric sphincter ligated (Cuddihy and Ozog 1973). In isolated, everted segments of small intestine of the rat, transfer from the mucosal (lumen) to the serosal (blood) side of the duodenum, jejunum, and ileum was observed. The serosal:mucosal strontium concentrations were approximately 0.2–0.4, whereas the ratio for calcium in preparations of duodenum was 1.98 (Stantic and Gruden 1974). Ratios >1 would be indicative of an active transport process; therefore, this study did not detect an active component of strontium transfer across the small intestine.

Measurements of the rate of uptake of strontium into slices of rat small intestine when incubated with increasing concentrations of strontium suggested the existence of a saturable uptake mechanism in the intestinal epithelium (Papworth and Patrick 1970). The fractional absorption of a gavage dose of strontium appears to be a relatively constant ratio to that of calcium. In rats, the strontium:calcium absorption ratio was 0.75 over a fairly wide range of absorbed fractions of calcium (Marcus and Wasserman 1965). This suggests that strontium and calcium may be absorbed by similar mechanisms. Strontium has been shown to be a substrate for a Ca^{2+}-ATPase on the basolateral membrane of the renal proximal tubule in the rat, which is thought to play an important role in the tubule reabsorption of calcium (Sugihira et al. 1992).

Active vitamin D (calcitriol or $1,25(OH)_2D_3$) has an indirect, delayed effect on the gastrointestinal absorption of strontium or calcium by inducing the synthesis of calcium-binding proteins in both humans and animals (Bianchi et al. 1999). A calcitriol-inducible Ca^{2+}-ATPase has been shown to be important in the absorption of calcium in the rat intestine, and may provide a common mechanism for absorption of calcium and strontium (Bronner et al. 1986). Other possible common mechanisms may involve binding of calcium and strontium to an intracellular calcium-binding protein, calbindin-D, which is a $1,25(OH)_2D_3$-inducible calcium binding protein that is thought to play an important role in calcium absorption (Gross and Kumar 1990). In a group of 18 66-year-old women who received calcitriol at a daily dose of 0.5 μg of calcitriol for two years, the intestinal absorption of strontium was 13.7% compared to 10.4% for the untreated controls (Sairanen et al. 2000); the basal absorption percentages before treatment were 8.7 and 9.2%, respectively. Age-related decreases in the gastrointestinal absorption of strontium in men (ages 20–79) were found to be positively correlated with serum levels of insulin-like growth factor I (IGF-I) (Fatayerji et al. 2000). These authors proposed that IGF-I increases strontium absorption by maintaining the structural integrity of the intestine and the sensitivity of the intestine to $1,25(OH)_2D$ and increasing the synthesis of calcium-binding protein in that tissue. IGF-I also acts by stimulating the synthesis of $1,25(OH)_2D$ in the kidney (Audi et al. 1999; Fatayerji et al. 2000).

Distribution. The close similarity in the distribution of strontium and calcium derives from the ability of strontium to interact with ligands that normally bind calcium (Skoryna 1981b). These include hydroxyapatite, the main component of mineralized bone (Harrison et al. 1959; Schoenberg 1963) and a variety of calcium binding and transport proteins that are important in the physiological disposition of calcium in cells, including Ca^{2+}-ATPases (Berman and King 1990; Mermier and Hasselbach 1976; Pfleger and Wolf 1975; Sugihira et al. 1992; Yu and Inesi 1995), Na^{+}-Ca^{+}-antiport (McCormack and

Osbaldeston 1990; Niggli 1989; Richard et al. 1989), and Ca^{2+} channels (Fukushi et al. 1995a, 1995b; Gregoire et al. 1993).

Metabolism. As noted in Section 3.5.3, the metabolism of strontium consists of binding interactions with proteins and probably complex formation with various inorganic anions such as carbonate and phosphate, and carboxylic acids such as citrate and lactate.

Excretion. The renal clearance of strontium has been measured in human subjects who received an intravenous injection of a dose of $SrCl_2$ and is approximately 4–10 L/day and 2–3 times greater than renal calcium clearance (Blake et al. 1986, 1989a, 1989b; Harrison et al. 1955, 1966a; Newton et al. 1990; Samachson 1966). Based on these estimates, the renal clearance of strontium is substantially less than the product of the glomerular filtration rate in humans (approximately 180–200 L/day) and the estimated rate of filtration of strontium, assuming that approximately 50% of the strontium in plasma is ultrafilterable (Harrison et al. 1955). Thus, strontium appears to undergo net tubular reabsorption in the human kidney. The mechanism by which strontium is reabsorbed in the renal tubule has not been determined, although it is likely that it may share common transport mechanisms with calcium, possibly including the Na^{+}-Ca^{2+}-antiport, Ca^{2+}-ATPase and membrane Ca^{2+} channels, all of which are thought to play a role in the reabsorption of calcium (Friedman and Gesek 1995). Direct evidence for this comes from *in vitro* studies of basolateral membranes isolated form the rat renal cortex (primarily proximal tubule). In this preparation, strontium has been shown to be a substrate for a Ca^{2+}-ATPase, which transports calcium from the proximal tubular cells into the plasma (Sugihira et al. 1992).

The observation of fecal excretion of radioactive strontium for weeks to decades after an oral exposure or over shorter time periods after an intravenous exposure suggests the existence of a mechanism for transfer of absorbed strontium into gastrointestinal tract, either from the bile or directly from the plasma. Evidence for direct secretion of strontium from the plasma into the intestine is provided by studies conducted with the *in situ* lumen-perfused rat intestine. When the lumen of either the small or large intestine was perfused (below the entrance of the bile duct) *in situ*, and radioactive strontium was injected intravenously, radioactive strontium was detected in the lumen, indicating that strontium was secreted from blood into the intestine (Palmer and Thompson 1961). The amount of strontium secreted into the small intestine was approximately 4–8 times that in the large intestine; however, the strontium:calcium secretion ratio was approximately 1 in the small intestine and 1.3 in the large intestine. The mechanism by which strontium is secreted into the intestine has not been determined. Transfer of strontium from the serosal (blood) side of the intestinal epithelium to the mucosal (lumen) side of the epithelium has been

demonstrated in *in vitro* preparations of isolated rat colon mucosa. Serosal-to-mucosal transfer was observed to be completely dependent on the transepithelial electrochemical potential for strontium, completely insensitive to calcium concentration of the serosal bathing medium, and unaffected by prior treatment of the rats with 1,2,-dihydroxyvitamin D_3, which stimulated calcium transport in the same preparation (Karbach and Rummel 1987). Based on these observations, transfer of strontium into the lumen of the colon in this preparation appeared to be explainable as a passive process.

3.6.2 Mechanisms of Toxicity

The fact that strontium is chemically similar to calcium allows it to exchange for calcium in bone and other cellular compartments that are enriched in calcium. Many enzymes that are calcium-dependent will function when strontium is substituted, but changes in kinetic parameters may occur. As discussed in Section 3.6.1, strontium can interact with secondary cell messenger systems and transporter systems that normally use calcium. Furthermore, as described in Section 3.2.4 (Neurological Effects), synaptic transmission may be variably affected by strontium. Consequently, at high concentrations, differences in the chemical characteristics between strontium and calcium may be the basis for neurotoxic and neuromuscular perturbations associated with strontium intoxication.

Effect of Metabolism on Toxicity. Variations in the rate of absorption of soluble strontium compounds will affect the severity of their effects following oral exposure. One report identified polymorphisms in three alleles for the vitamin D receptor that imparted a 40% difference in efficiency in intestinal strontium absorption in humans (Gennari et al. 1997). The significance of this finding is unresolved, since other studies have found no link between vitamin D receptor genotypes and enteral absorption rates for calcium or strontium (Vezzoli et al. 2002; Wolf et al. 2000). Furthermore, no association was found between vitamin D receptor polymorphisms and bone mineral density when other parameters are taken into consideration (Poggi et al. 1999). However, daily administration of 0.5 μg of activated vitamin D to 66-year-old women over 2 years increased both the rate of strontium absorption and the bone mineral density at the femoral neck and the lumbar spine (Sairanen et al. 2000). The rate of strontium incorporation into bone may be influenced by other factors thought to affect bone mineralization, such as parathyroid hormone receptor, estrogen receptor 1, and others (Audi et al. 1999; Duncan et al. 1999). However, the effects of these factors on strontium utilization have not been established definitively. Genetic variants of the parathyroid hormone receptor 1 result in either increased or decreased bone mineralization (Duncan et al. 1999). There is a potential physiological link between the estrogen receptor and vitamin D in osteoblasts, although the relationship to bone mineralization has not been established

(Audi et al. 1999); vitamin D regulates the expression of P450 aromatase, an enzyme expressed in osteoblasts that modulates the availability of estrogen to its receptor. The cytokine interleukin-6 is associated with osteoclast differentiation, and therefore, could potentially be involved with the removal of strontium from bone (Audi et al. 1999; Duncan et al. 1999). Persons with chronic kidney failure may be more susceptible to effects of excess strontium because of a reduced ability to excrete strontium (Apostolidis et al. 1998; see Section 3.12); in this study, plasma levels of strontium were 60% higher in afflicted patients compared to controls. A study in rats demonstrated that protein deficiency, especially in combination with ethanol consumption, may increase strontium incorporation into bone while reducing fecal and urinary excretion of strontium (Gonzales-Reimers et al. 1999; see Section 3.12).

Differences in bone physiology suggest that adult rats may have a higher susceptibility to stable or radioactive strontium effects than adult humans. Unlike most mammals (including humans), the epiphyseal growth plate of the long bones of rats never entirely transforms into bone after sexual maturity, so that bone growth continues throughout life (although reduced after the age of 12 months) (Leininger and Riley 1990). Thus, incorporation of strontium into the skeleton is likely to be relatively higher in adult rats compared to other mammals.

Stable Strontium. The toxicity of excess stable strontium is related to its interference in biological processes that normally involve calcium, most notably, skeletal development.

Calcium Absorption. In animals, excess strontium indirectly suppresses the activation of vitamin D_3 in the kidney, which severely reduces the expression of calbindin D mRNA and the translation of calbindin D protein in the duodenum (Armbrecht et al. 1979, 1998; Omdahl and DeLuca 1972). As a result, duodenal absorption of calcium is reduced. The reported inverse correlation between the amount of strontium that is absorbed and the levels of parathyroid hormone (Vezzoli et al. 1998) suggest that changes in parathyroid hormone levels mediate this effect. While there are no data on strontium-binding to the calcium receptor of the parathyroid gland, it is likely that strontium binds in place of calcium, mimicking calcium and thereby suppressing parathyroid hormone levels. A reduction in parathyroid hormone levels will decrease the level of 1-hydroxylase available to activate vitamin D_3.

Bone Toxicity. In addition to its effect on calcium absorption, excess absorbed strontium adversely affects bone development in several ways, leading to the development of rickets in young laboratory animals and possibly in children under special circumstances (Özgür et al. 1996). Strontium binds directly to hydroxyapatite crystals, which may interfere with the normal crystalline structure of bone

(Storey 1961). In addition, excess strontium may prevent the normal maturation of chondrocytes in the epiphyseal plates of long bones (Matsumoto 1976). Excess strontium apparently interferes with the mineralization of complexed acidic phospholipids that is thought to help initiate the formation of hydroxyapatite crystals in developing bone (Neufeld and Boskey 1994). As a result, affected bone contains an excess of complexed acidic phospholipid and a significantly lower ash weight. Insufficient mineralization reduces the strength of bones, so that the inability to resist compression from increasing body weight results in bone distortion (bowing).

Anaphylactic Response After Inhalation Exposure. There was one case of anaphylaxis reported in a paramedic who inhaled strontium-containing smoke in an enclosed space (Federman and Sachter 1997; see Section 3.2.1.2). Although other irritants in the smoke may have contributed to the incident, there is supporting evidence that large concentrations of stable strontium can stimulate the release of histamine from mast cells (Alm and Bloom 1981a, 1981b; Atkinson et al. 1979; Foreman 1977; Foreman and Mongar 1972a, 1972b; Foreman et al. 1977). Stable strontium stimulates degranulation in several cell types (see Section 3.2.5 Hematological Effects) and it has been suggested that it acts by mimicking the receptor-linked rise in calcium that is the usual trigger for such events (Best et al. 1981). It is conceivable that the conditions of the paramedic's exposure were such to result in locally high concentrations of strontium in the respiratory tract, thereby eliciting histamine release and contraction of smooth muscle.

Radioactive Strontium. The adverse health effects of radioactive strontium are related to its sequestration in bone, the high energy of its beta emissions, and, in the case of ^{90}Sr, its long half-life and the radiation from the decay product, ^{90}Y, produced in the body after intake of ^{90}Sr. An extensive discussion of ionizing radiation and its health effects is found in the Appendix D of this document and in the Toxicological Profile for Ionizing Radiation (Agency for Toxic Substances and Disease Registry 1999). There is some evidence that body size or skeletal density may affect the outcome of exposures to radioactive strontium. It was suggested that two cows that survived large oral doses of ^{90}Sr owed their survival to their breed characteristics (Cragle et al. 1969). The massive skeletons of Holsteins have wide bone marrow cavities so that tissue in the center of the bone marrow is not within range of the 1 cm beta emissions from radiostrontium (and radioyttrium) bound to bone. Conversely, mice and rats are more vulnerable than large animals to radioactive strontium because all bone marrow tissues are within striking range. This renders rats and mice less useful than larger mammals as models for human exposure to radioactive strontium. In addition, adult rats are less satisfactory models than adults of other species because of the persistence of the epiphyseal cartilaginous plate, which will result in the incorporation of larger amounts of radioactive strontium into bone.

Bone Toxicity. Beta emissions from radiostrontium bound to bone resulted in various bone lesions (trabecular osteoporosis, sclerosis, osteolytic lesions), particularly in animals that were exposed chronically (Book et al. 1982; Clarke et al. 1972; Momeni et al. 1976). In young rats and rabbits exposed orally to ^{90}Sr, necrotic effects on the vasculature of developing bone secondarily disrupted the process of osteogenesis (Casarett et al. 1962; Downie et al. 1959). Disruption in the metaphyseal microvasculature disorganized the transformation of cartilage into bone, so that chondrocytes inappropriately resumed active proliferation.

Pancytopenia. The severe reduction in hematopoetic tissue results from irradiation of the bone marrow by radiostrontium incorporated into bone. At high exposure levels, thrombocytopenia may lead to platelet loss severe enough to cause hemorrhaging and the resulting anemia will be exacerbated by destruction of erythropoietic tissue. Impaired immune function results from the genetic damage to lymphocytes.

Carcinogenicity. Radioactive strontium is a genotoxic carcinogen. Following exposure *in vivo*, cytogenetic analysis has revealed aneuploidy, chromosomal breaks, gaps, rings, and exchanges (see Table 3-5), which are manifestations of unrepairable changes in DNA. It is generally understood that radiation-induced damage to genes that regulate cell growth is a major factor in the development of cancer in affected cells, and the observation of chromosomal breaks in leukemic cells of miniature swine following chronic oral exposure to $^{90}SrCl_2$ is consistent with this idea (Clarke et al. 1972; Howard 1970). However, the specific genes involved in radiostrontium-induced malignancies have not been identified. Because of strontium's chemical properties, which determine its distribution in the body, exposure to sufficient radiostrontium results in an increased risk of malignancy for particular tissues. In dogs, acute inhalation of insoluble ^{90}Sr particles that lodged in the lungs resulted in chronic radiation exposure to the lungs, leading to pulmonary hemangiomas and carcinomas of pulmonary epithelia (Snipes et al. 1979). Other tissues were subsequently affected as the radioactive particles were cleared from the lungs. Following acute inhalation of soluble $^{90}SrCl_2$ aerosols, some dogs developed carcinomas of nasal airway tissues, probably resulting from irradiation of these tissues from the ^{90}Sr bound to the underlying bone (Gillett et al. 1987b). Following oral or inhalation exposures, absorbed ^{90}Sr was distributed to bone, from which it irradiated the surrounding tissues and induced various kinds of osteosarcomas, as well as malignancies of hematopoietic tissues in bone marrow (see Section 3.3.2.7).

Induction of Delayed Fibrosis Following External Exposure. A single high-dose external exposure to beta radiation can elicit acute epidermal reactions, late connective tissue damage, and carcinogenesis in

murine skin, as was demonstrated in experiments that used ^{90}Sr as a convenient beta source (Randall and Coggle 1996; see Section 3.3.3.7). A biochemical change that is associated with both acute and late effects is the enhanced expression of mRNA and protein for transforming growth factor beta 1 (TGF-beta l, Randall and Coggle 1995, 1996). Following an acute exposure to beta radiation from a ^{90}Sr source that is sufficient to generate moist desquamation, CBA/ca mouse skin exhibited two separate peaks of TGF-beta l expression (Randall and Coggle 1996). The first, occurring within the first few weeks after exposure, coincided with a period of epithelial hyperplasia that occurred during and after the phase of re-epithelialization. TGF-beta l expression declined to a low at 3 months postexposure, but then rose to another peak at about 9 months. Expression was especially high in the fibrotic dermis, which was also the site of skin tumors that appeared at about 9 months. TGF-beta l expression in tumors was elevated by 1.8 to 87 times the level in unirradiated control skin from the same animal. The implication of this study is that sustained high expression of transforming growth factor-betal may drive the progressive fibrosis and, possibly, contribute to malignancy following radiation damage. Another study from this laboratory indicates that there may be genetic differences in the control of TGF-beta l expression, and therefore, susceptibility to long-term effects of radiation damage (Randall and Coggle 1995).

3.6.3 Animal-to-Human Extrapolations

The toxic effects of stable and radioactive strontium have been similar in all species studied. However, as mentioned in Section 3.6.2, adult rats are not an optimal model for bone effects in adult humans because of the lack of a Haversian (bone remodeling) system in the rat and because of the persistence of the epiphyseal cartilaginous plate into adulthood (Leininger and Riley 1990). Because the epiphyseal cartilage persists, the long bones of rats continue to lengthen during adulthood, and therefore, the rates of incorporation of strontium will be proportionally higher. This will make adult rats more susceptible to adverse effects of both stable and radioactive strontium. This caveat does not apply to young rats, which are comparable to the young of other species. In general, rodents are not optimal models for radiostrontium effects because their small size ensures that most of their tissues will be within the effective range of beta emissions from radiostrontium bound to bone. Larger laboratory animals, such as dogs or non-human primates, avoid the problems of both radiation scatter to adjacent tissues and closure of the epiphysis as they become adults.

3.7 TOXICITIES MEDIATED THROUGH THE NEUROENDOCRINE AXIS

Recently, attention has focused on the potential hazardous effects of certain chemicals on the endocrine system because of the ability of these chemicals to mimic or block endogenous hormones. Chemicals with this type of activity are most commonly referred to as *endocrine disruptors*. However, appropriate terminology to describe such effects remains controversial. The terminology *endocrine disruptors*, initially used by Colborn and Clement (1992), was also used in 1996 when Congress mandated the Environmental Protection Agency (EPA) to develop a screening program for "...certain substances [which] may have an effect produced by a naturally occurring estrogen, or other such endocrine effect[s]...". To meet this mandate, EPA convened a panel called the Endocrine Disruptors Screening and Testing Advisory Committee (EDSTAC), which in 1998 completed its deliberations and made recommendations to EPA concerning *endocrine disruptors.* In 1999, the National Academy of Sciences released a report that referred to these same types of chemicals as *hormonally active agents*. The terminology *endocrine modulators* has also been used to convey the fact that effects caused by such chemicals may not necessarily be adverse. Many scientists agree that chemicals with the ability to disrupt or modulate the endocrine system are a potential threat to the health of humans, aquatic animals, and wildlife. However, others think that endocrine-active chemicals do not pose a significant health risk, particularly in view of the fact that hormone mimics exist in the natural environment. Examples of natural hormone mimics are the isoflavinoid phytoestrogens (Adlercreutz 1995; Livingston 1978; Mayr et al. 1992). These chemicals are derived from plants and are similar in structure and action to endogenous estrogen. Although the public health significance and descriptive terminology of substances capable of affecting the endocrine system remains controversial, scientists agree that these chemicals may affect the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body responsible for maintaining homeostasis, reproduction, development, and/or behavior (EPA 1997c). Stated differently, such compounds may cause toxicities that are mediated through the neuroendocrine axis. As a result, these chemicals may play a role in altering, for example, metabolic, sexual, immune, and neurobehavioral function. Such chemicals are also thought to be involved in inducing breast, testicular, and prostate cancers, as well as endometriosis (Berger 1994; Giwercman et al. 1993; Hoel et al. 1992).

No studies were located regarding endocrine disruptive effects in humans resulting from inhalation, oral, or dermal exposure to stable or radioactive strontium. Stable strontium, as an analog to calcium, is unlikely to cause endocrine disruption at normal levels of exposure. Endocrine glands, such as the pituitary, that are in close association with bone could potentially be damaged by irradiation from radioactive strontium incorporated into bone. For example, increases in tumors of the pituitary and

ovaries were observed in rats following gestational exposure to injected ^{90}Sr (Rönnbäck and Nilssen 1982; Schmahl and Kollmer 1981; Schmahl et al. 1979; Section 3.4.5.7). However, endocrine function was not tested in these studies. Ingested radioactive strontium had no effect on reproductive function in animals, suggesting that it did not affect reproductive hormones to an obvious degree (Clarke et al. 1972; Finkel et al. 1960). However, no study has specifically investigated the endocrine system.

3.8 CHILDREN'S SUSCEPTIBILITY

This section discusses potential health effects from exposures during the period from conception to maturity at 18 years of age in humans, when all biological systems will have fully developed. Potential effects on offspring resulting from exposures of parental germ cells are considered, as well as any indirect effects on the fetus and neonate resulting from maternal exposure during gestation and lactation. Relevant animal and *in vitro* models are also discussed.

Children are not small adults. They differ from adults in their exposures and may differ in their susceptibility to hazardous chemicals. Children's unique physiology and behavior can influence the extent of their exposure. Exposures of children are discussed in Section 6.6 Exposures of Children.

Children sometimes differ from adults in their susceptibility to hazardous chemicals, but whether there is a difference depends on the chemical (Guzelian et al. 1992; NRC 1993). Children may be more or less susceptible than adults to health effects, and the relationship may change with developmental age (Guzelian et al. 1992; NRC 1993). Vulnerability often depends on developmental stage. There are critical periods of structural and functional development during both prenatal and postnatal life and a particular structure or function will be most sensitive to disruption during its critical period(s). Damage may not be evident until a later stage of development. There are often differences in pharmacokinetics and metabolism between children and adults. For example, absorption may be different in neonates because of the immaturity of their gastrointestinal tract and their larger skin surface area in proportion to body weight (Morselli et al. 1980; NRC 1993); the gastrointestinal absorption of lead is greatest in infants and young children (Ziegler et al. 1978). Distribution of xenobiotics may be different; for example, infants have a larger proportion of their bodies as extracellular water and their brains and livers are proportionately larger (Altman and Dittmer 1974; Fomon 1966; Fomon et al. 1982; Owen and Brozek 1966; Widdowson and Dickerson 1964). The infant also has an immature blood-brain barrier (Adinolfi 1985; Johanson 1980) and probably an immature blood-testis barrier (Setchell and Waites 1975). Many xenobiotic metabolizing enzymes have distinctive developmental patterns. At various stages of growth

and development, levels of particular enzymes may be higher or lower than those of adults, and sometimes unique enzymes may exist at particular developmental stages (Komori et al. 1990; Leeder and Kearns 1997; NRC 1993; Vieira et al. 1996). Whether differences in xenobiotic metabolism make the child more or less susceptible also depends on whether the relevant enzymes are involved in activation of the parent compound to its toxic form or in detoxification. There may also be differences in excretion, particularly in newborns who all have a low glomerular filtration rate and have not developed efficient tubular secretion and resorption capacities (Altman and Dittmer 1974; NRC 1993; West et al. 1948). Children and adults may differ in their capacity to repair damage from chemical insults. Children also have a longer remaining lifetime in which to express damage from chemicals; this potential is particularly relevant to cancer.

Certain characteristics of the developing human may increase exposure or susceptibility, whereas others may decrease susceptibility to the same chemical. For example, although infants breathe more air per kilogram of body weight than adults breathe, this difference might be somewhat counterbalanced by their alveoli being less developed, which results in a disproportionately smaller surface area for alveolar absorption (NRC 1993).

The ubiquitous nature of stable strontium in soils and water supplies, and the chemical similarity of strontium to calcium, ensure that strontium will unavoidably be incorporated into the human body to some degree. Because of the requirement for high calcium intake during the period of bone development, the absorption and retention of strontium is higher in children than in adults; an ICRP (1993) model postulates that the fractional gastrointestinal absorption of strontium by infants (up to 12 months) is double that of adults (see Sections 3.5.1.2 and 3.5.5). Consequently, children are more at risk than adults from exposures to excess stable strontium or radioactive strontium.

Stable Strontium. A Turkish epidemiological study indicated that children with probable deficient vitamin D status (from insufficient exposure to sunlight) and diets low in calcium and animal protein were more likely to develop rickets as a result of exposure to excess dietary strontium (Özgür et al. 1996). The rachitic signs of craniotabes, rachitic rosary, bulging at the wrist, genu valgus, genu varus, and delayed closure of the fontanelles represented biomarkers of effect in children exposed to excess strontium. This study is consistent with numerous animal studies that demonstrated abnormal skeletal development (i.e., rickets) in young animals exposed to sufficiently high levels of dietary strontium (Kshirsagar 1976; Matsumoto 1976; Morohashi et al. 1994; Reinholt et al. 1985; Storey 1961, 1962; Svensson et al. 1985,

1987). Young rats may be sensitive to levels of ingested strontium that have no effect on adults (Storey 1961).

Children or young animals are likely to be more sensitive than adults to excess strontium, in part, because the rates of intestinal strontium absorption may be higher, although this has not been consistently demonstrated in humans (see Section 3.5.1.2 and Table 3-7). The ICRP (1993) biokinetic model for strontium assumes that the fraction of ingested strontium that is absorbed decreases from 0.6 in infancy to 0.3 in adulthood (see Section 3.5.5); some models assume the absorbed dose may be 8 times higher in infants compared to adults (NCRP 1991). These estimates are consistent with rat studies in which rates of strontium absorption were much higher (4–8 times) in weanlings compared to adults (Forbes and Reina 1972; Harrison et al. 1966b). This age-dependent difference in absorption may be partly explained by the duodenal level of vitamin-D-dependent calbindin D protein (a calcium-binding protein involved in absorption), which is much lower in old rats than in young rats (Armbrecht et al. 1979). Armbrecht et al. (1998) have demonstrated that the translation of calbindin D-9k mRNA into protein declines in the rat duodenum with age and this would be expected to reduce the rates of intestinal absorption of calcium and strontium in older animals.

Children are particularly vulnerable to excess strontium because the immature skeleton has a high rate of bone remodeling, and strontium adversely affects bone development in several ways, as demonstrated in animal studies. In chickens and rats, excess strontium suppresses the activation of vitamin D_3 in the kidney, which severely reduces the expression of calbindin D mRNA and the translation of calbindin D protein in the duodenum (Armbrecht et al. 1979, 1998; Omdahl and DeLuca 1972). As a result, duodenal absorption of calcium is reduced. Strontium also binds directly to hydroxyapatite crystals, which may interfere with the normal crystalline structure of bone in rats (Storey 1961). In addition, excess strontium may prevent the normal maturation of chondrocytes in the epiphyseal plates of long bones of rats (Matsumoto 1976). Excess strontium apparently interferes with the mineralization of complexed acidic phospholipids that is thought to help initiate the formation of hydroxyapatite crystals in developing bone (Neufeld and Boskey 1994). As a result, affected bone contains an excess of complexed acidic phospholipid and a significantly lower ash weight. This finding is consistent with the reduced rate of matrix vesicle degradation observed by Reinholt et al. (1984) in rachitic cartilage in strontium-treated rats.

The placenta does not accumulate strontium nor does it prevent transfer of strontium to the fetus following maternal exposure (see Section 3.5.2.2). However, no studies were located that addressed

developmental effects following maternal exposure to stable strontium in humans or animals. Stable strontium is also transferred to nursing infants through breast milk of exposed mothers at a ratio of approximately 0.24 µg strontium/mg Ca (Harrison et al. 1965). These levels are unlikely to be sufficiently high to perturb bone development in the fetus. Strontium stored in maternal bone because of prior exposure can be mobilized during pregnancy or lactation, resulting in fetal or infant exposure (Tolstykh et al. 1998).

Alginates, carbohydrates rich in guluronic acid, have been found to reduce peak exposure to strontium (see Section 3.12.1). Sutton et al. (1971a) showed that gastrointestinal absorption of stable ^{84}Sr was reduced 4-fold in children who were simultaneously given 10% sodium alginate-97% guluronic acid. Exposure to sunlight to enhance vitamin D status and diets with adequate calcium, phosphorus and protein may be considered to some degree protective against the effects of stable strontium (see Section 3.12).

Radioactive Strontium. During the period of above-ground nuclear weapons testing, the possible effects in children resulting from exposure to ^{90}Sr in radioactive fallout was a matter of concern. However, no studies have been able to identify unequivocally any increase in infant mortality, childhood cancers, or genetic damage in humans that could be attributed to oral or inhalation exposure to ^{90}Sr in fallout (NCRP 1991; Shaw and Smith 1970). In the Techa River populations that received higher oral doses of radiation, including radiostrontium, individuals who were exposed as teenagers exhibited a significantly higher frequency of stable chromosomal translocations compared to individuals who were exposed as adults (Bauchinger et al. 1998). Adverse pregnancy outcomes (mortality from developmental anomalies, chromosomal anomalies, labor complications, and other unspecified perinatal conditions) were elevated in the progeny of exposed individuals from the Techa River cohort, 60% of whom were exposed to radiation as teenagers (Kossenko et al. 1994). However, Kossenko et al. (1994) calculated that relatively high radiation doses (20–480 rem or 0.2–4.8 Sv) to the parental gonad would be required to double the incidences of stillbirths, miscarriages, early neonatal mortality, or lethal developmental effects. (Note that the gonadal radiation doses may have primarily been caused by exposure to external gamma radiation [Akleyev et al. 1995]). No increase in cancer incidence was observed among the progeny of the exposed Techa River population (Kossenko 1996). Dermal effects (slight dermal atrophy, telangectiasis, and pigmentation changes) were reported as delayed reactions to superficial ^{90}Sr treatments for facial hemangiomas in adults and children (Bekerus 1970). However, this study did not compare the relative sensitivity of children and adults.

It would not be expected that the immediate consequences of radioactive strontium exposure would differ in children and adults at the cellular level; that is, the initial damage to proteins and nucleic acids caused by ionizing radiation would be the same. Thus, children and adults might be expected to have similar effects following exposure to solid radiostrontium sources apposed to the skin or to insoluble particles of radiostrontium lodged in the lungs. However, as discussed in Appendix Section D.4.1, ionizing radiation is more damaging to actively mitotic cells than to differentiated postmitotic cells, largely because genetic lesions become permanent when cell division occurs before repair can occur. Since children have proportionally more mitotic cells than adults, the biological effect of radiation exposure in children would be expected to be proportionally more severe. Other developmental aspects contribute to the higher potential vulnerability of children to radiation effects. One is the higher rate of gastrointestinal absorption in children, as discussed for Stable Strontium, above. In addition, animal studies indicate that the young are more vulnerable than adults to inhalation or oral exposures to radioactive strontium in soluble form, because of higher rates of retention in the developing skeleton (see Stable Strontium section above). Thus, a given absorbed dose of soluble radiostrontium will have a longer biological half-life in young animals compared to adults, leading to higher cumulative radiation doses to bone and surrounding soft tissues and more severe adverse effects (see Section 3.3). Examples of this age-related difference in severity are discussed under Section 3.2.2.2 Musculoskeletal Effects (especially Storey 1961, the basis for the intermediate oral MRL) and Section 3.3.2.2 Hematological Effects (Cragle et al. 1969), and Section 3.3.2.6 Reproductive Effects (Clarke et al. 1970). Young animals exhibit the same types of effects as adults (e.g., malignancies), in addition to other effects specific to their developmental stage. For example, radioactive strontium disturbed osteogenesis of long bones in young rats by damaging the epiphyseal cartilaginous discs, and the vasculature that supports resorption (Casarett et al. 1962). In weanling rats, irradiation of the marrow prevented its invasion of metaphyseal cartilage, thereby causing cartilage to resume active proliferation, rather than undergo transformation into bone. Because of disruption of these processes, cartilage and fibrous marrow were sometimes incorporated into cortical bone, resulting in weakness or fracture. For all species studied, a long-term effect of ^{90}Sr incorporation in young animals or *in utero* was a higher incidence of bone-associated cancers compared to animals exposed as adults (Clarke et al. 1972; Finkel et al. 1960; White et al. 1993). Size differences may contribute to the possible higher vulnerability of children to bone marrow effects from retained radiostrontium. Since bone marrow cavities in children have smaller diameters, a larger proportion of the hemopoietic bone marrow is within the approximate centimeter range of beta radiation emitted from radiostrontium bound to the endochondral surface.

There are two theoretical ways in which the fetus might be exposed to radiation from the decay of radioactive strontium: from transfer of strontium across the placenta or from proximity to radiation emitted from the maternal body. Placental transfer of radioactive strontium to the fetus has been demonstrated in humans (Sikov et al. 1991, Stather et al. 1992) and animals (rodent: Onyskowova and Josifko 1985, Taylor and Bligh 1992; pig: Palmer et al. 1969). Studies of residents of the Techa River who were exposed to strontium as a result of an accident at a plutonium production plant provide evidence that fetal exposures can result from previous maternal exposures. The fetal:maternal strontium concentration ratio in four subjects who were exposed prior to pregnancy varied from 0.012 to 0.24, with the higher values associated with maternal exposures that occurred during adulthood and lower values associated with maternal exposures during childhood or adolescence (Tolstykh et al. 1998). A dosimetry study in minipigs determined that exposure of the fetal thymus (ages 55–110 days of gestation) to radiostrontium (^{90}Sr–^{90}Y) is related to the amount that is incorporated by the fetus after placental transfer; no appreciable radiation reached the thymus from radiostrontium in the maternal uterine wall (Palmer et al. 1969). Palmer et al. (1969) indicated that results might vary for other organs, for younger fetuses (which may be relatively closer to the maternal uterine wall or pelvic bone), or for single fetuses compared to multiple fetuses (as in the pig). As discussed in Section 4.2, strontium isotopes and their transformation product isotopes differ with respect to their emission energies; this factor is another variable that will determine whether the fetus is subject to radiation from the maternal body.

Animal studies demonstrate that the developmental consequences of injecting pregnant females with radioactive strontium are qualitatively different depending on the gestational day of administration (Finkel and Biskis 1969; Finkel et al. 1972; Hopkins et al. 1967). This is partly related to temporal differences in the onset of osteogenic activity and calcification in different parts of the skeleton. For example, the increase in calcification of the basioccipital and sphenoid bones of the skull occurring by gestational day 18 of the rat probably contributed to the development of pituitary gland tumors after an injection of ^{90}Sr was administered that day (Schmahl and Kollmer 1981; Schmahl et al. 1979). A single injection administered to pregnant mice late in gestation transiently affected fertility of male offspring by suppressing spermatocyte maturation, but severely depressed oocyte maturation of the female offspring (De Rooij and Rönnbäck 1989; Nilsson and Henricson 1969; Rönnbäck 1979, 1980, 1981a, 1981b).

Radioactive strontium, like stable strontium, can be transferred to infants through breast milk of exposed mothers (Harrison et al. 1965). Rönnbäck (1981a) demonstrated that the numbers of oocytes (all stages) in the ovary was reduced in neonatal mice that were exposed to radioactive strontium in the milk of surrogate females that had been given high doses by injection.

Various methods for reducing the body burden and toxic effect of radioactive strontium have been investigated (see Section 3.12). Only the administration of alginates high in guluronic acid, described in the previous section, has been validated in children (Sutton et al. 1971a). A single oral dose of aluminum phosphate antacid gel taken soon after exposure is a recommended treatment for reducing absorption of ingested strontium (Ellenhorn et al. 1997; Haddad et al. 1998). This would be a suitable treatment for children as long as the dosage recommendations were followed, since excess ingestion of aluminum phosphate can cause rickets (Chines and Pacifici 1990; Pivnick et al. 1995). A diet high in calcium would tend to reduce the incorporation of radioactive strontium into bone (Steinbach 1968).

3.9 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).

Due to a nascent understanding of the use and interpretation of biomarkers, implementation of biomarkers as tools of exposure in the general population is very limited. 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 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 strontium are discussed in Section 3.9.1.

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 not often substance specific. They also may not be directly adverse, but can indicate potential health impairment (e.g., DNA adducts). Biomarkers of effects caused by strontium are discussed in Section 3.9.2.

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, a decrease in the biologically effective dose, or a target tissue response. If biomarkers of susceptibility exist, they are discussed in Section 3.11 "Populations That Are Unusually Susceptible".

3.9.1 Biomarkers Used to Identify or Quantify Exposure to Strontium

The biomarkers to quantify exposure to stable or radioactive strontium are similar in children and adults.

Stable strontium is ubiquitous in the diet and can be measured in urine, blood and feces by a number of methods outlined in Section 7.1. After exposure, approximately 99% of the absorbed strontium that is retained is found in bone and connective tissues (Schroeder et al. 1972). Normal background levels of strontium were measured by emission spectrography in cadaver tissue from 168 American subjects (Tipton 1981; Tipton and Cook 1963). Average strontium levels in human tissues expressed as ppm ash were as follows: rib bone 110 ppm, vertebra 100 ppm, aorta 33 ppm, ileum 25 ppm, duodenum 11 ppm, lung 8.2 ppm, kidney 5.2, heart 2.6 ppm, and liver 1.6 ppm. In a small group of adult males, the mean strontium concentration in plasma was 29 μg/L (Sutton et al. 1971b).

Soluble radioactive strontium can be detected in urine, blood, or feces by liquid scintillation counting. Whole body counters (or chest counters for inhalation exposures) can measure internal radioactive strontium deposited in bone following high level exposures (see Section 7.1.1). Children tend to incorporate strontium more homogenously throughout bone than is the case for adults.

3.9.2 Biomarkers Used to Characterize Effects Caused by Strontium

Deformities of bone in response to excess strontium can be detected by radiography. Exposure to excess stable strontium may cause specific abnormalities in bone calcification that can lead to obvious bone deformities, particularly in the young. Such 'rachitic' signs in children include craniotabes, rachitic rosary, conspicuous bulging at the wrist, genu valgus, genu varus, and delayed closure of the fontanelles (Özgür et al. 1996). However, excess exposure to other metals, such as aluminum (Bhattacharyya et al. 1995; Carmichael et al. 1984; Chines and Pacifici 1990; Pivnick et al. 1995; Woodson 1998) or deficiencies in calcium, vitamin D, and/or phosphate can generate the same effects. Thus, this is not a specific biomarker for strontium, but can be confirmatory. Although bone biopsies can measure strontium chemically, these tests are not warranted because of the relatively high risk/benefit ratio.

Exposure to radioactive strontium may result in lowered blood cell counts, which can be detected using standard clinical laboratory methods. However, exposure to other sources of ionizing radiation has similar effects. Sufficiently high exposures to radioactive strontium can result in genetic damage to tissues adjacent to bone. Recently, Sutherland et al. (2000a, 2000b) developed a molecular biological strategy to identify clustered lesions in DNA resulting from *in vitro* cellular exposure to gamma radiation. It is possible that this technique might be adapted to evaluate genetic damage in blood cells following exposure to radioactive strontium, although, again, it would not be specific for radiostrontium, but rather for ionizing radiation. It is uncertain whether the technique would be applicable for the chronic exposures characteristic of absorbed radiostrontium compared to the acute high-dose exposures for which it was designed.

3.10 INTERACTIONS WITH OTHER CHEMICALS

Several agents reduce the absorption or retention of strontium, reducing its toxic effects (see Section 3.12).

Calcium. Strontium has chemical properties similar to calcium, but is less efficient than calcium in most biological processes. Calcium and strontium appear to compete for the same transporter elements in the intestine (Bianchi et al. 1999; Blumsohn et al. 1994; Milsom et al. 1987; Reid et al. 1986; Sips et al. 1994), but calcium is preferentially absorbed. Co-administration strontium and calcium reduces the

uptake of strontium and also reduces skeletal retention of strontium (Palmer et al. 1958; Roushdy et al. 1980, 1981; Steinbach 1968).

Anions. Oral administration of phosphate, as aluminum phosphate antacid gel, reduces the gastrointestinal absorption of strontium by increasing its excretion in feces (Carr and Nolan 1968; Keslev et al. 1972; Spencer et al. 1969a, 1969b). Oral administration of sulfates at the same time as strontium reduces its retention in the skeleton (Volf 1964). These agents are discussed in Section 3.12.1.

3.11 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

A susceptible population will exhibit a different or enhanced response to strontium than will most persons exposed to the same level of strontium in the environment. Reasons may include genetic makeup, age, health and nutritional status, and exposure to other toxic substances (e.g., cigarette smoke). These parameters result in reduced detoxification or excretion of strontium, or compromised function of organs affected by strontium. Populations who are at greater risk due to their unusually high exposure to strontium are discussed in Section 6.7, Populations With Potentially High Exposures.

In general, children, who are in the stage of active bone synthesis and growth, are more vulnerable to adverse effects of strontium. A more detailed discussion of children's susceptibility can be found in Section 3.8. The following discussion is limited to other individual variations or health conditions that may modify the usual effects of strontium.

Protein Deficiency and Ethanol Consumption. Protein-deficient diets may increase the adverse effects of exposure to excess stable strontium or to radioactive strontium, by reducing clearance and increasing incorporation into bone. A metabolic experiment in adult male Wistar rats showed that consumption of a protein-deficient diet increased the intestinal absorption of dietary strontium and its incorporation into bone, while reducing fecal and urinary excretion of strontium (Gonzales-Reimers et al. 1999). When rats were given ethanol in addition to the protein-deficient diet, incorporation of strontium into bone was significantly enhanced, although ethanol given with a protein-normal diet tended to reduce strontium incorporation through its diuretic effects.

Renal Disorders. Patients with chronic kidney failure may be more susceptible to excess strontium than the general population, because of a reduced ability to excrete strontium and retain calcium (Apostolidis et al. 1998). In such patients, plasma levels of strontium were found to be 60% higher compared to

controls. In a variety of studies, uremic patients on dialysis were found to have significantly higher levels of strontium in serum, muscle, and brain tissue compared to normal undialized controls (Alfrey et al. 1975; Couttenye et al. 1999; D'Haese and De Broe 1996; D'Haese et al. 1999, 2000; Krachler et al. 2000; Schrooten et al. 1999). Although the high level of strontium in serum in uremic patients was correlated with the high level of strontium in the local tap water, it is also possible that uremic patients may have reduced rates of strontium excretion.

Paget's Disease (osteitis deformans). Patients with Paget's disease (osteitis deformans) had a higher than normal retention rate following administration of ^{85}Sr (Tothill et al. 1983). Part-body retention measurements demonstrated that diseased bone had relatively higher uptakes of strontium compared to undiseased bone. Pagetic bone contains a higher proportion of small mineral crystals with greater surface area, which accounts for its increased ability to accumulate strontium. Reflecting the high degree of osteoclast activity in Paget's disease, diseased bone had an increased turnover of ^{85}Sr, compared to undiseased bone in the same patient. Since bone metabolism is locally accelerated in persons with this disease, they are likely to develop higher body burdens of radioactive strontium than healthy adults.

Rheumatoid Arthritis or Seronegative Spondarthritis. Patients with active rheumatoid arthritis or seronegative spondarthritis were found to have significantly higher levels of strontium and calcium in their granulocytes (Hällgren et al. 1984). The strontium overload was thought to be linked to the degree of inflammation and was positively related to serum levels of the acute-phase protein haptoglobin; corticosteroid therapy differentially reduced the strontium content of granulocytes compared to calcium. It is not known whether granulocytes in persons with active disease would take up relatively more radiostrontium from plasma, and therefore incur more damage, than would be the case for otherwise healthy individuals under an identical exposure scenario.

Diabetes. Persons with diabetes may be more vulnerable to adverse effects from dermally-applied radioactive strontium. Thinning of the sclera developed in a diabetic patient who had been treated for pterygium with a single dose (1,700–1,800 rad; 17–18 Gy) of ^{90}Sr (Wesberry and Wesberry 1993; see Section 3.3.3.2). This reaction was not observed in 170 other eyes treated at that dose level; however, the authors did not state whether other diabetics were in the group that was unaffected. Conversely, in rats made diabetic by injection of streptozotocin, the absorption of strontium in the duodenum was significantly reduced, which would appear to be protective (Miller and Schedl 1976).

Genetic Polymorphisms. Polymorphisms in genes that may affect rates of strontium (calcium) absorption and bone mineralization are currently under investigation. In a study of postmenopausal women with osteoporosis, polymorphisms of vitamin D receptor genes apparently caused a 40% variation in the rate of strontium absorption (Gennari et al. 1997); however, another study found no association between vitamin D receptor polymorphisms and bone mineral density in osteoporotic women (Poggi et al. 1999). Similarly, 3'-end region polymorphisms of the vitamin D receptor were found to have no effect on enteral strontium absorption or bone mineral density in patients with calcium kidney stone disease (Vezzoli et al. 2002). Insulin-like growth factor (IGF-I) is correlated with age-related changes in strontium absorption in men (Fatayerji et al. 2000), but polymorphisms have not been evaluated. Other candidate genes that may affect bone mineralization include the parathyroid hormone receptor 1, the estradiol receptor, collagen type I alpha 1, transforming growth factor-beta 1, interleukin-6, calcitonin receptor, alpha2-HS-glycoprotein, osteocalcin, calcium-sensing receptor, interleukin-1 receptor antagonist, beta-3-adrenergic receptor, apolipoprotein E, glucocorticoid receptor, and epidermal growth factor (Audi et al. 1999; Duncan et al. 1999). The relative contribution of these factors on bone mineralization has yet to be clarified and whether any polymorphisms increase susceptibility to adverse effects of strontium remains to be determined.

3.12 METHODS FOR REDUCING TOXIC EFFECTS

This section will describe clinical practice and research concerning methods for reducing toxic effects of exposure to strontium. 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 strontium. When specific exposures have occurred, poison control centers and medical toxicologists should be consulted for medical advice. The following texts provide specific information about treatment following exposures to strontium:

Ellenhorn MJ, Schonwald S, Ordog G, et al., eds. 1997. Medical toxicology: Diagnosis and treatment of human poisoning. 2nd ed. Baltimore, MD: Williams & Wilkins, 1682–1723.

Haddad LM, Shannon MW, Winchester JF, eds. 1998. Clinical management of poisoning and drug overdose. 3rd ed. Philadelphia, PA: W.B. Saunders, 413–425.

Viccellio P, ed. 1998. Emergency toxicology. 2nd ed. Philadelphia, PA: Lippincott-Raven, 991–996.

3.12.1 Reducing Peak Absorption Following Exposure

Human exposure to strontium and its compounds occurs primarily by inhalation and ingestion, since absorption is poor following dermal contact. Current suggestions for reducing absorption of radiostrontium include ingestion of antacids containing aluminum phosphate (Ellenhorn et al. 1997; Haddad et al. 1998). Treatment is most effective when it is initiated within 2 hours of exposure.

The threat of nuclear fallout from atomic weapons testing was the impetus for a large number of studies that investigated methods to prevent absorption of radiostrontium, while not adversely affecting the absorption of calcium. Reasonably effective strategies have included alginates, aluminum phosphate, and sulfates. Less effective or less practical strategies have included cold, diet, dietary fiber, flavones, and stable strontium.

Alginates. Alginates are carbohydrates derived from seaweed that have been found to reduce the absorption of strontium in humans and animals, without significantly affecting the absorption of calcium. When 10% sodium alginate-97% guluronic acid was given orally along with the stable marker $^{84}SrCl_2$ to children (ages 2.5–10 years), plasma ^{84}Sr was reduced by 75% and urinary excretion of the tracer was reduced 72% (Sutton et al. 1971a). The authors concluded that absorption was reduced 4-fold. In adults, sodium alginate extracts administered as a liquid or in bread, reduced strontium absorption by 50% in humans and 3-fold in rats (Gong et al. 1991). Alginates with a high guluronic acid/mannuronic acid ratio were found to be more effective in humans and rats (Carr and Nolan 1968; Gong et al. 1991). Sodium alginate administered orally to rats effectively reduced the whole body retention of ^{85}strontium that had been administered intratracheally (Naményi et al. 1986). Calcium alginate added to the diet of female goats reduced the transfer of ^{85}strontium to milk, which was attributed to a reduction in strontium absorption (Beresford et al. 1999). In rats given ^{89}Sr and ^{45}Ca by gavage, alginate treatment, particularly in combination with stable calcium, differentially increased the fecal excretion of ^{89}Sr and reduced the skeletal retention of ^{89}Sr (Light et al. 1970a).

Aluminum Phosphate Antacid Gel. Aluminum phosphate antacid gels, administered just prior to or shortly after oral strontium exposure, have been shown to reduce absorption of strontium by increasing its excretion in feces in humans (Spencer et al. 1969a, 1969b), rats (Carr and Nolan 1968), and mice (Keslev et al. 1972). A practical advantage of this treatment is that the gels are readily available as over-the-counter pharmaceuticals. In elderly men who had been maintained on a low calcium diet for several weeks, oral administration of an antacid gel just prior to oral $^{85}Sr/^{45}Ca$ exposure reduced plasma

radiostrontium levels by 88%, but reduced radiocalcium levels by only 38% (Spencer et al. 1969a). In the same study group, antacid treatment reduced strontium absorption by 57% when given 0.5 hours after exposure, but by only 43%, 1 hour after exposure (Spencer et al. 1969b). In similar studies on rats fed antacid for several days prior to exposure, the absorption of strontium was reduced by 83%, whereas there was no effect on the absorption of calcium (Carr and Nolan 1968). In mice, an aluminum phosphate gel reduced the absorption of strontium by about 13-fold and of calcium by about 3-fold (Keslev et al. 1972).

Sulfates. In rats orally exposed to radiostrontium and monitored on day 2, oral administration of barium sulfate in combination with sodium sulfate or magnesium sulfate reduced radiostrontium retention in the femur by nearly 80% (Volf 1964). Treatment was effective if given within 10 minutes of exposure, but not if delayed more than 80 minutes. Strontium sulfate was less effective, reducing radiostrontium retention by only 30%. Volf (1964) did not determine whether the effectiveness of the barium sulfate combination therapy was a result of increased diuresis or decreased bioavailability by means of adsorption to radiostrontium in the intestine.

The following treatments have been shown to be less effective or less practical.

Diet or Dietary Fiber. A pulverized solid diet administered to rat sucklings over 8 hours resulted in 10–20% less whole body retention of ^{85}Sr (reduced absorption) than cow milk (Kostial et al. 1981b, 1984). Supplementing cow milk with trace elements did not improve its effectiveness, ruling out the possibility that trace elements in the food competitively inhibited intracellular transport of ingested strontium. Rather, the authors suggested that the solid diet contained ligands for strontium that reduced the amount of strontium available for transport. Another study demonstrated that the inclusion of cellulose fiber into the diet of suckling rats decreased the retention of simultaneously administered $^{85}Sr/^{45}Ca$ by 20% (Momčilovič and Gruden 1981). However, cellulose fiber was less satisfactory than alginates, both in effectiveness and in the lack of discrimination between strontium and calcium.

Flavones. In rats given doses of flavone (Ipriflavone, 7-isopropyl-isoflavone, or Morin, 2',2,4',5,7-pentahydroxy-flavone) for 3 weeks prior to acute oral exposure to radiostrontium, the whole body retention of radiostrontium was reduced by 50 and 30%, respectively, after 1 month (Gachályi et al. 1988). Similar experiments on pregnant rats demonstrated that both flavones reduced fetal uptake of radiostrontium administered to dams on gestational days 17/18 and 19/20. No studies were located that demonstrated the usefulness of flavones for emergency situations, rather than as pretreatments.

Stable Strontium. In weanling rats previously given varying amounts of strontium lactate in the diet, 4 or 6% strontium lowered the retention of injected radiostrontium to a greater extent than the retention of injected radiocalcium (Teree et al. 1965). The disadvantage of this treatment is the adverse effect on bone development caused by excess stable strontium.

3.12.2 Reducing Body Burden

Absorption of strontium can vary with the chemical form of the compound and its solubility. Those strontium compounds that are readily absorbed following inhalation or oral exposure are rapidly distributed throughout the body (see Section 3.5). Because of its similarity to calcium, strontium entering the circulation preferentially accumulates in bone. Methods for reducing the body burden of radiostrontium that have been tested in animals include calcium, chelators (with variable results), hemodialysis, and magnesium sulfate. Exposure to cold temperatures, use of the few pharmacological agents that have been tested, and use of stable strontium are less satisfactory treatments.

Calcium. In human patients with osteoporosis who were injected with tracer doses of $^{85}SrCl_2$, intravenous infusions of calcium gluconate significantly increased urinary excretion of strontium, but had no effect on fecal excretion (Spencer et al. 1967d). This effect was attributed to the decreased renal tubular reabsorption of calcium under these conditions. Calcium gluconate was more effective than magnesium chloride tested in the same study. A 10-day series of injections with a combination of calcium and calciferol reduced the retention of ^{90}Sr in rabbits by 70%, if the treatments started as soon as 24 hours after exposure (George et al. 1979). If treatments were delayed 96 hours, the removal of strontium was reduced by 50%. Slightly less effective treatments included calcium alone, sodium citrate, or a combination of calcium and magnesium, which reduced strontium retention by 40, 30, and 20%, respectively. A 3-week diet high in calcium and low in phosphorus, initiated 24 hours after injection of ^{90}Sr into rats, significantly reduced the incorporation of the isotope into bone (Steinbach 1968). In rats, pretreatment with diets rich or adequate in calcium tend to result in lower accumulations of radiostrontium in bone following exposure than diets poor in calcium (Palmer et al. 1958; Roushdy et al. 1980, 1981). However, administration of a high-calcium diet to rats following a month-long parenteral exposure to radiostrontium, only slightly reduced the strontium content of the femur after 65 days (Ray et al. 1956).

Chelators. Chelators are not effective once strontium has become incorporated into hydroxyapatite. A variety of chelators have been tested in rodents, with variable results. In general, chelators did not

successfully increase the excretion of radiostrontium, if administered 6 or 24 hours after exposure (e.g., Llobet et al. 1991a, 1991b, 1992a). In tests on rats, the cryptator hexaoxa-diamine macrobicycle was effective when given simultaneously with radiostrontium (Müller 1970). The aza crown ether 2NaCa Kryptofix 22 was effective in tests on mice and rats when administered intravenously or intratracheally within 1 hour of exposure to radiostrontium (Varga et al. 1994). Other aza crown ethers and other chelators have been tested on mice following parenteral exposure to strontium, but their effectiveness has been so variable and no consistent conclusions can be drawn (Colomina et al. 1991; Llobet et al. 1992b; Ortega et al. 1989). For example, Na_2Ca EGTA (Na_2Ca ethylenglycol-bis-(β-amino-ethyl-ether)-N,N'-tetraacetic acid) increased fecal excretion of subcutaneously administered strontium (nitrate), but decreased urinary excretion to the same degree, and thus, there was no net change (Colomina et al. 1991).

Chelators that were not at all effective in rodent studies include monosodium glutamate, Tiron (4,5-dihydroxy-1,3-benzene-disulfonic acid), DMSA (2,3-dimercaptosuccinic acid), succinic acid, malic acid, $CaNa_2CTDA$ (cyclohexanediaminetetraacetic acid), and THPC, a cyclic derivative of EDTA (Kostial et al. 1979; Llobet et al. 1992b; Ortega et al. 1989).

The chelating agent, zirconium citrate, administered intraperitoneally in several injections soon after parenteral exposure to ^{90}Sr, significantly reduced the number of mice with bone tumors, reduced the multiplicity of tumors, and delayed the onset of tumors (Zander-Principati and Kuzma 1964). Measurements of external brehmsstrahlung emissions 10–12 months later demonstrated that mice treated with zirconium citrate had a reduced body burden of radiostrontium, which is the likely cause of the reduced tumor rate. One source of uncertainty regarding this study, despite the claims of low toxicity for zirconium citrate, is the unexplained reduction in lifespan in all the groups treated with the chelator.

Cold. In mice exposed to low temperature (9 °C), the rate of urinary excretion of a radiostrontium tracer was increased (Wedin 1972; Wedin et al. 1972). This was attributed to a specific effect of cold on the rate of diuresis. However, since the rate of calcium excretion was not measured in this study, but is also known to be increased by cold, the usefulness of this finding is not clear. Urinary excretion rates of radioactive strontium in mice intraperitoneally injected with ^{85}Sr were increased about 10% by transfer to 4 °C (Nilsson and Rönnbäck 1988).

Hemodialysis. Hemodialysis is only effective if administered soon after exposure to strontium. In 100-day-old calves injected with ^{85}Sr, a 12-hour hemodialysis session administered 4, 14, or 24 hours

later resulted in removal of only 14, 4, and 2.5% of the administered dose, respectively (Downey et al. 1964).

Magnesium. In human patients with osteoporosis who were injected with tracer doses of $^{85}SrCl_2$, intravenous infusions of magnesium chloride significantly increased urinary excretion of strontium, but had no effect on fecal excretion (Spencer et al. 1967a). Magnesium chloride was not as effective as calcium gluconate tested in the same study. Magnesium sulfate injected 10 minutes after $^{85}SrCl_2$ significantly reduced the body burden of strontium in rats, irrespective of the dietary calcium or vitamin D status (Roushdy et al. 1980, 1981).

Pharmacological Agents. Tests of the effectiveness of hormones or drugs in reducing the body burden of strontium have been disappointing. In rats, progesterone had no significant effect on radiostrontium retention, whereas estrogen actually increased the amount of ^{90}Sr in the femur (Steinbach 1968). In rabbits, the steroid prednislone, thyroxine, and the diuretic furosemide removed only about 30, 15, and 10%, respectively, of the administered dose of ^{90}Sr (George et al. 1979).

Phosphorus-reduced Diet. A diet low in phosphorus (0.017%, Ca/P ratio of 21.5) was most effective in mobilizing radiostrontium from the rat skeleton (Ray et al. 1956). Nearly 85% of the strontium incorporated into the femur was removed by the 50th day; only 0.24% of the injected dose remained in the femur. However, this diet caused serious adverse effects: minimal increase in body weight, delayed growth and narrowing of epiphyseal discs in the tibia, reduced ash weight of the femur, and poor health necessitating termination of the experiment. Consumption for 64 days of a diet 'subminimal' in phosphorus (0.21%, Ca/P ratio of 2.19) removed nearly 64% of the radiostrontium incorporated into the femur. Rats exhibited normal body weight gain and ash weight of the femur, but there were histopathological changes in the epiphyseal discs and trabeculae of the tibia. Although the low and 'subminimal' phosphorus diets were relatively effective in reducing the body burden of radiostrontium, the potential for adverse health effects from inadequate phosphorus intake reduces the value of this strategy.

Strontium-free Diet. In young rats maintained on a diet high in strontium for 28 days, returning to a normal diet low in strontium noticeably reversed the adverse effect on bone mineralization (Johnson et al. 1968). The reduced percentage of ash in bone began to show improvement after 2 weeks and was nearly normal after 5 weeks. In addition, the abnormal deposition of osteoid in vertebrae was repaired.

3.12.3 Interfering with the Mechanism of Action for Toxic Effects

Hyperbaric oxygen therapy was successfully used to treat a case of scleral necrosis resulting from ^{90}Sr therapy following pterygiectomy (Green and Brannen 1995). Repeated hyperoxygenation enhanced neovascularization and regrowth of the scleral tissue that had become avascular and abnormally thin as a result of exposure to beta radiation.

In tests on irradiated skin of guinea pigs, anti-inflammatory compounds reduced the permeability of the dermal vasculature to plasma proteins by up to 30% (Song et al. 1968). However, since drug treatment was administered both before and after irradiation, this study is not definitive proof of the efficacy of these compounds.

3.13 ADEQUACY OF THE DATABASE

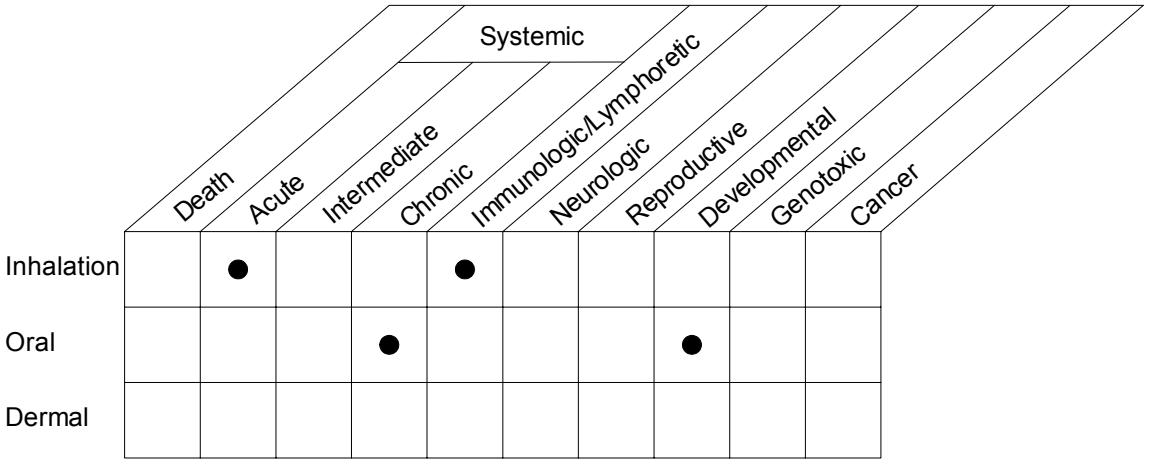
Section 104(i)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of strontium is available. Where adequate information is not 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 strontium.

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 the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

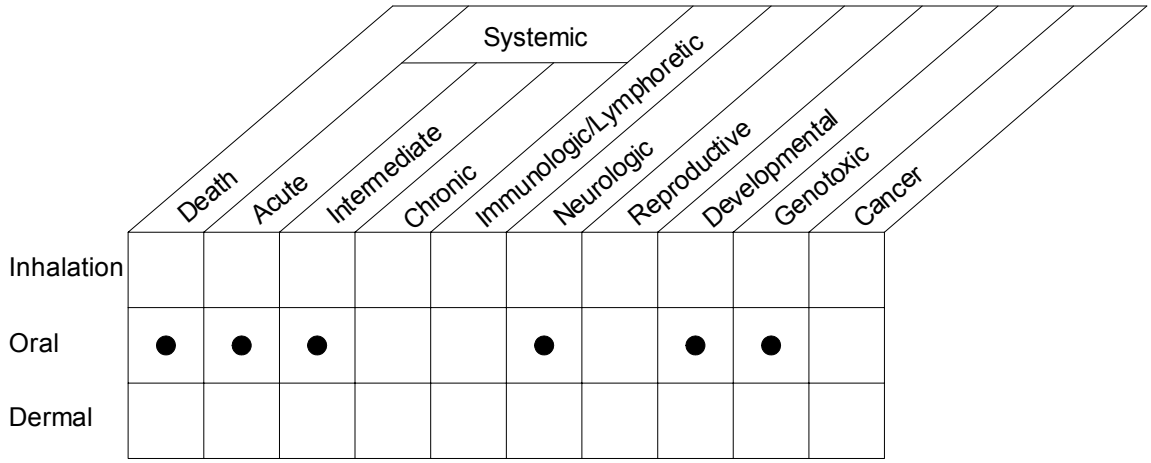
3.13.1 Existing Information on Health Effects of Strontium

The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals are summarized in Figure 3-9 for stable strontium and in Figure 3-10 for radioactive strontium. The purpose of these figures is to illustrate the existing information concerning the health effects of strontium. Each dot in the figure indicates that one or more studies provide information associated with that particular

Figure 3-9. Existing Information on Health Effects of Stable Strontium



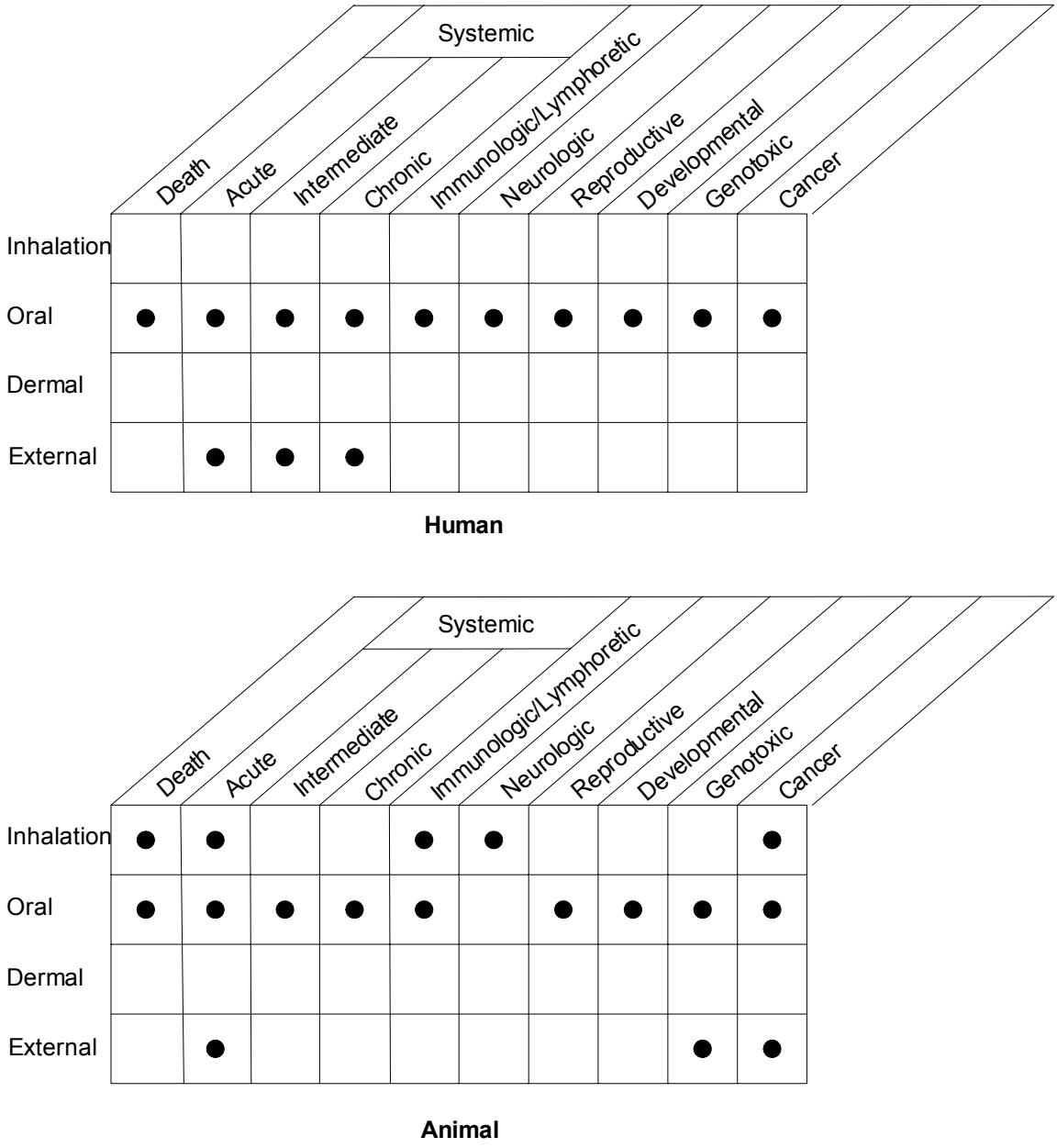
Human



Animal

● Existing Studies

Figure 3-10. Existing Information on Health Effects of Radioactive Strontium



effect. The dot does not necessarily imply anything about the quality of the study or studies, nor should missing information in this figure be interpreted as a "data need". A data need, as defined in ATSDR's *Decision Guide for Identifying Substance-Specific Data Needs Related to Toxicological Profiles* (Agency for Toxic Substances and Disease Registry 1989), is substance-specific information necessary to conduct comprehensive public health assessments. Generally, ATSDR defines a data gap more broadly as any substance-specific information missing from the scientific literature.

3.13.2 Identification of Data Needs

In the following discussion, the toxicity (carcinogenicity) of inhaled strontium chromate is omitted, since its adverse effects are attributed to hexavalent chromium (see Section 3.2.1.7). Unless otherwise stated, the proposed investigations refer to studies of health effects in animals.

Acute-Duration Exposure.

Stable Strontium. Information from injection and kinetic studies in humans and oral, inhalation, and injection studies in animals indicates that bone is the primary target tissue of absorbed stable strontium. The acute database is inadequate for deriving MRLs. A data need for an acute inhalation study is discussed under Data Needs for Immunotoxicity. Animal studies have shown that stable strontium is not toxic at low doses (Kroes et al. 1977). On the other hand, high oral doses of stable strontium can severely depress the serum levels of 1,25-dihydroxyvitamin D in rats within a week, which has an adverse effect on calcium absorption (Armbrecht et al. 1979, 1998). Of the two available acute oral toxicity studies, one employed ineffective doses, and the other used a single high dose (Kroes et al. 1977; Kshirsagar 1976).

Thus, there is a need for an acute-duration oral study that would enable an analysis of dose-response relationships with regard to strontium ingestion and skeletal effects. Consideration should be given to comparing the relative effects of different forms of strontium (e.g., strontium chloride, strontium carbonate, strontium phosphate), and different modes of delivery (in food, in water), since these factors probably affect the bioavailability of ingested strontium. In addition, such a study could provide a basis for investigating possible biomarkers of effect (by monitoring changes in the serum levels of vitamin D, 1,25-dihydroxyvitamin D, calcium, phosphorus, phosphatases, and other biomarkers) that could be used to characterize the early systemic response to strontium.

Radioactive Strontium. Acute-duration inhalation or oral administration of radioactive strontium caused adverse effects. No dermal studies were conducted. Rather, external studies used solid strontium apposed to the skin, which did not provide an opportunity for dermal absorption (Hoshino and Tanooka 1975; Randall and Coggle 1995; Song et al. 1968). In dogs, inhalation of relatively insoluble particles of radiostrontium resulted in prominent damage to pulmonary tissues (Benjamin et al. 1975, 1976c; Snipes et al. 1979). Inhalation or ingestion of soluble radiostrontium resulted in radiostrontium incorporation into bone and subsequent chronic radiation exposure of the surrounding tissues (inhalation: Gillett et al. 1987a, 1987b; oral: Casarett et al. 1962; Cragle et al. 1969). No inhalation or oral MRLs could be derived because the effects of exposure, even at the lowest levels, were serious. There is a need for an inhalation study using soluble strontium aerosols that would test a lower range of exposure levels than had previously been employed, primarily to assess the effects on the lymphocyte population; existing studies found chronic depression of lymphocyte numbers even at the lowest concentrations. Existing acute-duration oral studies are inadequate because either the study size was small and/or a single dose was used. There is a need for an acute oral multi-dose study, in particular, one comparing effects in young and adult animals, primarily for the purpose of relating genotoxicity to dosage. Dermal studies using strontium applied to the skin should be conducted to evaluate systemic effects that might occur following the kind of exposure that might occur in the vicinity of a hazardous waste site.

Intermediate-Duration Exposure.

Stable Strontium. An intermediate oral MRL was derived on the basis of a study that showed young rats were more susceptible to adverse skeletal effects (rickets) than adults (Storey 1961). A considerable number of studies support this finding (see Section 3.2.2.2 Musculoskeletal Effects). No intermediate inhalation study was located. The necessity for an intermediate inhalation study should be evaluated once the data from the proposed acute inhalation study are assessed. No intermediate dermal study was located, but given the low cytotoxicity of stable strontium, such a study does not seem necessary.

Radioactive Strontium. No intermediate-duration inhalation, oral, or dermal studies were located. There is a need for intermediate-duration inhalation and oral studies, using low levels of exposure, to help define the risk associated with longer-term exposures, such as may occur from radiostrontium releases at nuclear fuel reprocessing facilities or nuclear power plants into air, into drinking water, or settling onto croplands. The primary focus of these studies should be hematological and immunological effects. Some information is available in intermediate external studies, but in these, radiostrontium was not applied to the skin in a form that could be absorbed. Dermal studies need to be conducted to assess the systemic risks that children might incur by playing in the open after radiostrontium has settled on the ground.

Chronic-Duration Exposure and Cancer.

Stable Strontium. There were no adequate chronic-duration studies of stable strontium effects in humans or animals. In a review paper, Skoryna (1981a) briefly mentioned that oral administration of low doses of strontium had no adverse effect in rats over a 3-year period or over several generations, but provided no experimental details. A chronic-duration oral study would be useful for evaluating the long-term health effects of strontium ingestion. Some consideration should be given to comparing the effects of compounds having different chemical properties (e.g., strontium chloride, strontium carbonate, and strontium phosphate).

Although there are no chronic studies of stable strontium exposure, the rest of the database provides no evidence to suspect that stable strontium might be carcinogenic. It does not appear that a long-term carcinogenesis study would prove useful.

Radioactive Strontium. There is no chronic inhalation study for radioactive strontium. Such a study should be considered after an intermediate inhalation study is conducted, as a means of evaluating long-term exposure to low levels of radioactivity on the immune system. The Techa River cohort represents the major source of information regarding the health effects of chronic exposure to radiostrontium: suppression of hematopoiesis and immune function (Akleyev et al. 1995). Chronic oral administration of radioactive strontium has been shown to suppress hematopoiesis and lymphocyte function in animals (Dungworth et al. 1969; Howard 1970). Since these effects were observed at the lowest exposure levels, chronic oral studies using even lower exposure levels are needed to evaluate potential adverse effects on the immune system. A single clinical study reported late-developing changes in the skin following chronic application of solid strontium (external exposure) to treat hemangioma (Bekerus 1970). It is not clear that the database needs a chronic dermal study of radiostrontium applied to the skin in a form that might be absorbed, since significant dermal absorption of strontium only occurs through abraded skin (see Section 3.5.1.3).

An increase in the incidence of leukemia has been reported in the Techa River cohort, which received doses of 10 rem (0.1 Sv) or more from radioactive strontium (Kossenko 1996; Kossenko et al. 2000). Chronic oral administration of radioactive strontium was shown to increase the incidence of bone-associated cancer in animals (Book et al. 1982; Clarke et al. 1972; Finkel et al. 1960; White et al. 1993; Zapol'skaya et al. 1974). No chronic inhalation or dermal studies were located. Since the dynamics of strontium uptake into bone are known, estimations of the risk of cancer in humans following inhalation

exposure can be derived using dose-response data from the Techa River cohort and the beagle inhalation studies. There is no realistic scenario for chronic dermal exposure at damaging levels.

Genotoxicity.

Stable Strontium. *In vitro* studies listed in Table 3-6 demonstrate a lack of adverse effects from treatment with stable strontium. A single gavage study in mice is the only evidence for genotoxicity of stable strontium (at doses of 140–1,400 mg/kg), but it seems likely that the bolus delivery may have influenced the outcome (Ghosh et al. 1990). None of the intermediate-duration studies (no chronic study is available) presented any evidence of effects that could be attributed to genotoxicity. Additional genotoxicity studies on stable strontium appear to be unnecessary.

Radioactive Strontium. The genotoxicity of radioactive strontium is well-documented. In the Techa River cohort, an elevated frequency of stable chromosomal translocations was observed (Bauchinger et al. 1998). Other evidence includes *in vitro* cytogenetic studies (see Table 3–6), and, by implication, the increased cancer rates that were observed in most investigations (see Data Needs for Cancer). However, the mechanism of radiostrontium genotoxicity (i.e., the specific DNA alterations that occur following exposure) has yet to be characterized. Recently, Sutherland et al. (2000a, 2000b) developed molecular biological assays for characterizing clustered DNA lesions caused by exposure to gamma radiation. If such a technique were to be developed for radiostrontium-exposed cells, it might provide a means of recording molecular damage.

Reproductive Toxicity.

Stable Strontium. There is no evidence regarding the effect of stable strontium on reproduction, but levels of exposure possible by inhalation or dermal routes are not likely to be harmful. Stable strontium was found to have beneficial effects when it was used in solutions designed for testing the functional capacity of human spermatozoa *in vitro* (Mortimer 1986; Mortimer et al. 1986). The possible consequences of excess strontium ingestion on reproduction need to be explored. Such experiments should compare the relative toxicity of stable strontium compounds that have different properties and may have different rates of absorption (e.g., strontium chloride, strontium carbonate and strontium phosphate).

Radioactive Strontium. In the Techa River cohort, average radiation doses to the gonads of up to 74 rem (0.74 Sv) had no effect on birth rate, fertility, or the incidence of spontaneous abortions (Kossenko et al. 1994). However, the contribution of radiostrontium to the gonadal radiation dose is likely to have been

negligible compared to that of external gamma radiation. Multigenerational oral studies in animals demonstrated a dose-dependent effect of radioactive strontium on reproduction. In pigs, only the highest doses affected fetal survival, and in those treated as adults, there was no effect on litter size, percentage of stillborn, or birth weight (Clarke et al. 1970, 1972; McClellan et al. 1963). Injection studies have reported a higher incidence of adverse reproductive effects, perhaps because of the higher dose levels. Injection of male mice prior to mating increase the rate of fetal death, and there is some evidence that radioactive strontium selectively accumulates in the testis (Reddi 1971). Injection of pregnant female mice reduced the reproductive capacity of female offspring, reducing the numbers of oocytes of all stages in the ovary (Rönnbäck 1981a, 1981b). Thus, the fetal reproductive system appears to be vulnerable to radioactive strontium. Further studies to evaluate the dose-response of gonadal effects, including cytogenetic aspects, would appear to be warranted.

Developmental Toxicity.

Stable Strontium. The main developmental effect of stable strontium is impaired bone development (rickets) following oral exposure at high doses (Johnson et al. 1968; Kshirsagar 1976; Marie and Hott 1986; Neufeld and Boskey 1994; Ögzur et al. 1996; Reinholt et al. 1984; Storey et al. 1961, 1962). Inhalation and dermal exposures are unlikely to be high enough to have an adverse effect. The oral developmental toxicity studies have concentrated on the initiation of rickets in young children or young animals during the postnatal or juvenile periods, but none have addressed the effect of maternal exposures on the fetus during gestation or on the neonate during lactation. The relative effectiveness of strontium compounds that have different properties (e.g., strontium chloride, strontium carbonate, and strontium phosphate) needs to be evaluated with regard to maternal absorption, placental transfer, fetal toxicity, and postnatal toxicity during lactation. In addition, behavioral testing should be conducted on the young animals to determine whether there are any neurological consequences of fetal exposure to excess stable strontium.

Radioactive Strontium. In the Techa River cohort, individuals who were exposed to high levels of radiostrontium as teenagers had a higher frequency of stable transformations than those who were adults at the time (Bauchinger et al. 1998); the differences were attributed to increased skeletal incorporation of radiostrontium in the young. The progeny of the exposed cohort showed an elevated incidence of adverse pregnancy outcomes (mortality from developmental anomalies, chromosomal anomalies, labor complications, and other unspecified perinatal conditions), but no increase in the incidence of cancer (Kossenko et al. 1994). Multigenerational oral studies in animals showed no teratogenic effect of radioactive strontium administered from the time of conception, but showed reduced survival of the F1

generation because of an increased incidence of bone-associated cancer (Clarke et al. 1970; Finkel et al. 1960; McClellan et al. 1963). Injection of high doses of radioactive strontium during gestation had teratogenic effects on the fetus, primarily skeletal abnormalities (Hopkins et al. 1967; Finkel and Biskis 1969). Injections had qualitatively different effects depending on the day of gestation, because of regional differences in rates of bone mineralization during gestation. More information is needed regarding the effect of the timing of maternal exposure relative to developmental stages. In addition, developmental studies that evaluate neurological effects in the offspring are needed.

Immunotoxicity.

Stable Strontium. There is no evidence that oral or dermal exposures to stable strontium affect the immune system. However, one case report described an anaphylactic reaction to inhalation of smoke that contained ~30% strontium among other irritants (Federman and Sachter 1997). Strontium's possible involvement is supported by reports that excess strontium elicits degranulation of mast cells *in vitro*, causing histamine release (Alm and Bloom 1981a, 1981b; Atkinson et al. 1979; Foreman 1977; Foreman and Mongar 1972a, 1972b; Foreman et al. 1977). For this reason, a short-term inhalation study would help to determine whether strontium by itself can elicit anaphylaxis and, if so, identify the effective concentration levels.

Radioactive Strontium. There is evidence that immunosuppression, resulting from irradiation of bone marrow, may occur in humans and animals following absorption of radioactive strontium. Immunological effects were noted in the Techa River cohort, which received relatively high radiation doses to bone marrow following ingestion of food and water contaminated with radiostrontium (Akleyev et al. 1995). In animal studies, the lowest applied inhalation or oral doses were reported to result in lymphopenia lasting as long as 2 years (Benjamin et al. 1976c; Howard 1970; Jones et al. 1976). There appears to be a need for studies that examine the effect of a lower range of exposures on immune function. Another reason for such studies comes from the reports demonstrating that NK cells may be preferentially eliminated following injection of ^{89}Sr or ^{90}Sr (Emmanuel et al. 1981; Gidlund et al. 1990; Haller and Wigzell 1977; Wiltrout et al. 1989), with the result that the organism's ability to defend against lymphoid tumors is impaired (Haller and Wigzell 1977; Luevano et al. 1981). The implication is that reduced cellular defenses may compound the effect of genotoxicity, increasing the risk of cancer. However, it is not known whether NK cells are equally vulnerable at lower exposure levels.

Neurotoxicity.

Stable Strontium. The only evidence for neurotoxicity of stable strontium is a report of hindlimb paralysis following intermediate-duration ingestion of excess strontium (Johnson et al. 1968). Given the absence of any other evidence for neurotoxicity, it is possible that, in this case, the paralysis may have resulted from compression of the hypertrophic epiphyseal cartilage, which was insufficiently mineralized to support the weight of the body. Additional neurotoxicity studies in adult animals for stable strontium do not appear to be necessary.

Radioactive Strontium. Neurological effects were reported in the Techa River population that was exposed to radiostrontium from water and food contaminated from releases at a plutonium processing plant between 1949 and 1956 (Akleyev et al. 1995). However, external gamma radiation, also released at this time, undoubtedly contributed to these effects. A single instance of epilepsy in a dog exposed by inhalation to a high concentration represents the only evidence for neurotoxicity of radioactive strontium in animals (Gillett et al. 1987b). The authors concluded that epilepsy was not related to treatment. However, no studies have specifically measured behavioral or neurological deficits in exposed animals. The database needs studies that measure neurological effects in offspring following exposure *in utero* and/or during lactation.

Epidemiological and Human Dosimetry Studies.

Stable Strontium. Strontium is ubiquitous in the environment, so everyone is exposed to it to some degree. Children who exhibit pica behavior or persons living in areas with high levels of strontium in the drinking water may have higher exposures than the general population. A Turkish epidemiological study demonstrated a higher incidence of rickets among children living in rural communities whose diet was based on grain crops grown in local soil containing high levels of strontium (Özgür et al. 1996). This study did not attempt to measure strontium levels in the affected children. In addition, this study may not be directly applicable to conditions in the United States, given the different diet and the availability of foods from a wider geographic range. One epidemiological study found that relatively high levels of strontium in the drinking water had no adverse effect on cardiovascular health, and, in fact appeared to have a beneficial effect on the rate of mortality from hypertension with heart disease (Dawson et al. 1978). Information regarding the higher levels in drinking water could be used to design animal experiments for evaluating chronic exposure effects, which are currently lacking in the database. In one case-control study that tried to account for the higher incidence of liver cancer in 1984 on Chongming

Island in China, no association was found with the levels of stable strontium detected in hair (Wang et al. 1990).

Radioactive Strontium. Dosimetry data are available for approximately 16,000 members of the Techa River population that was exposed to radiostrontium because of releases from a plutonium processing plant between 1949 and 1956 (Kossenko et al. 1997). Since exposure levels in this population were 30–100 times higher than the maximum exposure from global fallout, this cohort represents the largest group of subjects available for examining health effects of chronic radiation exposure. Subpopulations living in certain regions within the Techa River area received different levels of exposure, so that dose relationships are being established for health effects. In addition, investigators have been able to examine the effect of developmental age at the time of exposure on health outcomes. Although individuals were exposed to multiple sources of radiation during the first years (including ^{137}Cs bound in soft tissues), in recent decades, their radiation exposure was primarily from ^{90}Sr incorporated into bone. The health effects have been similar to those observed for animals exposed chronically to radiostrontium, and have included suppression of hematopoeisis and leukemia (Akleyev et al. 1995; Kossenko 1996; Kossenko et al. 1997, 2000).

A Danish epidemiological study found no association between the incidence of thyroid cancer in Denmark between 1943 and 1988 and the levels of skeletal incorporation of ^{90}Sr from fallout (Sala and Olsen 1993). However, the reason for this study is uncertain since strontium is not taken up preferentially in the thyroid, unlike iodine, which is incorporated into thyroid hormones (T_3 and T_4). A Scottish epidemiological study found no evidence for increased risks of total cancers, leukemia and non-Hodgkin's lymphoma, or acute myeloid leukemia for cohorts of children born during the period of highest fallout (radiostrontium) exposure (Hole et al. 1993). The few cases of bone tumors showed a nonsignificant increase for children born during the 'high risk' period. The reduction in fallout from above-ground nuclear weapons testing has reduced the exposure of the general population to radioactive strontium. Currently, populations working at or living in the vicinity of nuclear power plants or reprocessing facilities might have higher than background exposures. Workers at the facilities may have less exposure because protective equipment and safety procedures are in use. Environmental levels of radiostrontium that are measured near these facilities could be used to guide exposure levels in the toxicity experiments proposed above.

Biomarkers of Exposure and Effect.

Exposure.

Stable Strontium. Levels of stable strontium can be measured in blood or urine to determine exposures of any duration. Within a few days, most of the retained strontium is found in bone, but because of bone remodeling, strontium will be released over time and be detectable in blood and urine. Inductively coupled plasma mass spectroscopy (ICP-MS) was able to detect strontium in amniotic fluid and maternal plasma at levels of 0.03 and 0.06 ppb, respectively, in untreated humans (Silberstein et al. 2001). The sensitivity of this method is adequate to detect unusual accumulations of strontium. No additional biomarkers of exposure to stable strontium appear to be needed.

Radioactive Strontium. Exposures to radioactive strontium can be determined readily by measuring levels of radioactivity in blood or urine by liquid scintillation counting techniques. In addition, whole body counters can determine the level of radiostrontium retained in the skeleton. There appears to be no need for additional biomarkers of exposure to radioactive strontium.

Effect.

Stable Strontium. The typical signs of rickets (craniotabes, rachitic rosary, bulging at the wrist, genu valgus, genu varus, and delayed closure of the fontanelles) represent biomarkers of exposure to excess stable strontium in children (Özgür et al. 1996). Excess strontium ingestion has been shown to depress serum levels of 1,25-dihydroxyvitamin D in rats (Armbrecht et al. 1998). Since vitamin D insufficiency by itself can also cause rickets, measurement of both vitamin D levels and strontium levels in serum would be required to determine the role of strontium in a particular case. As mentioned above (Data Needs for Acute-Duration Studies), the proposed toxicity studies could be used to develop biomarkers for early effects following exposure to excess strontium. An array of biomarkers could possibly be developed to monitor the course of pathology before the signs of rickets fully appear.

Radioactive Strontium. A reduction in blood cell counts is a biomarker of effect for radioactive strontium. However, many other conditions can have the same result. Cytogenetic analysis of blood cells can reveal whether exposure to radioactive strontium has been sufficient to cause genotoxicity (see Table 3-5). A new method for evaluating DNA damage in cells exposed to gamma radiation has been developed using molecular biological techniques (Sutherland et al. 2000a, 2000b). It may be possible to

develop such an assay for evaluating exposure to radioactive strontium, which would also specifically identify the kind of DNA lesions produced.

Absorption, Distribution, Metabolism, and Excretion. More information is needed comparing the relative rates of absorption for different chemical forms of strontium that may vary in solubility. Solubility differences would affect the duration of residence of particles in the lung, which might have significant effects in the case of radiostrontium exposure. A comparison of gastrointestinal absorption rates for different chemical forms and for different vehicles of administration (food or water) has not been conducted. Results of such studies would help predict outcomes following different kinds of exposure. Nothing is known regarding dermal absorption of strontium taken up in soil, which is a type of exposure that children would be likely to encounter. However, studies of dermal absorption from soil would be of low priority given that significant dermal absorption of soluble strontium only occurred through abraded skin (See Section 3.5.1.3) and the amounts available from dry soil would be biologically insignificant under any realistic exposure scenario. Absorbed strontium is understood to distribute primarily to the bone and to be retained longer in the young than in adults. The combination of the ICRP PBPK model for strontium and animal-based studies on Observed Ratios of strontium and calcium (Comar and Wasserman 1964) is sufficient to estimate strontium turnover during pregnancy and lactation and in the elderly.

Comparative Toxicokinetics. The target organ for stable and radioactive strontium is the same in humans and animals, namely, bone. Young rats can serve as a model for children's exposures, but adult rats are less suitable, since the epiphyseal plate remains cartilaginous into adulthood (Leininger and Riley 1990). For this reason, adult rats could be expected to incorporate proportionally higher levels of strontium than adult humans. Furthermore, remodeling of bone in rats is not analogous to that in humans. The rat would probably not be a good model for evaluating placental transfer of strontium to the fetus because of differences in placental tissue organization.

Methods for Reducing Toxic Effects. Both stable and radioactive strontium are readily absorbed by the intestine, apparently through calcium transporter elements (Bianchi et al. 1999; Blumsohn et al. 1994; Milsom et al. 1987; Reid et al. 1986; Sips et al. 1994). Numerous methods have been tested for alleviating the effects of exposure to strontium (see Section 3.12). Oral administration of alginates with a high guluronic acid content or a single dose of aluminum phosphate antacid gel are currently recommended for reducing peak absorption of strontium shortly after exposure. The toxicities of excess stable and radioactive strontium are related to their rapid sequestration into bone. Most strategies for treatment involve high calcium in combination with other agents to enhance the replacement of strontium

in bone by calcium. There does not appear to be a need for new studies at this time. However, as mentioned in Section 3.6.2, polymorphisms in genetic factors that may affect rates of strontium absorption and bone mineralization are currently under investigation and potentially could regulate the effectiveness of treatment. If relevant polymorphisms are identified, then the existing methods for reducing toxic effects should be tested using stable strontium tracers to determine whether genetic factors affect the outcome of treatment.

Children's Susceptibility.

Stable Strontium. The effect of excess stable strontium ingestion on bone development is well documented: strontium-induced rickets has been reported in children and young animals. The particular vulnerability of children, because of the immaturity of the skeleton, is well understood. The intestinal rate of strontium absorption and the retention of strontium in the developing bone is known to be higher in infants and children than in adults. It is known that the fetus can be exposed to strontium following previous maternal exposure, but adequate information regarding changes in the rates of strontium mobilization from the maternal skeleton or changes in rates of intestinal absorption of strontium during the course of pregnancy is lacking. There is a need for studies to develop this information to fill in gaps in existing PBPK models for strontium; this effort would have the additional benefit of being applicable to other bone-seeking radioisotopes. Another issue to be considered is the relative bioavailability of strontium in the different chemical compounds (e.g., strontium chloride, strontium carbonate, strontium phosphate). Since children may be exposed to strontium by pica behavior, there is a need for animal studies that would investigate variations in absorption (bioavailability) when strontium is ingested in the form of soil.

Biomarkers of exposure and effect are established for children. Since the primary biomarker of effect, rickets, is a late-stage phenomenon, it would be useful to precisely establish a constellation of biomarkers that would identify a precursor condition. Such markers might include relative serum levels of vitamin D, calcium, phosphorus, and alkaline phosphatases, as well as strontium itself. The alginate method for reducing peak absorption of strontium has been validated in children (Sutton et al. 1971a).

Radioactive Strontium. Numerous oral exposures have demonstrated the enhanced risk of reproductive effects and cancer in animals exposed to radiostrontium *in utero* or during lactation. At the higher levels used in injection studies, teratogenic effects were observed on bone development. The possibility of neurological deficits from gestational exposure to radioactive strontium, resulting from radiostrontium incorporation into the cranium and subsequent irradiation of adjacent brain tissue, should be explored.

The toxicokinetic and bioavailability issues mentioned in the previous section on stable strontium apply to radioactive strontium. Low-level exposure studies should be conducted to evaluate possible impairment of immune function, which results from irradiation of bone marrow by radiostrontium incorporated into bone and which has been observed in animal studies at higher levels.

Radioactive strontium is its own biomarker of exposure in children and adults. The primary biomarkers of effect, also applicable to children and adults, are a reduction in lymphocyte and other blood cell counts, which closely match the intensity of exposure. The alginate method for reducing peak absorption, described above, has been validated for children (Sutton et al. 1971a). It is not clear whether another recommended treatment, a single dose of aluminum phosphate antacid gel, would be safe for children, since it can have toxic effects in children at high doses. Either method would only be effective if administered very soon after exposure (within an hour).

Data needs relating to both prenatal and childhood exposures and developmental effects expressed either prenatally or during childhood, are discussed in detail in the Developmental Toxicity subsection above.

Child health data needs relating to exposure are discussed in 6.8.1 Identification of Data Needs: Exposures of Children.

3.13.3 Ongoing Studies

Stable Strontium. Two currently funded research programs that specifically mention stable strontium are probably using it as a surrogate for calcium in physiological experiments. In a study sponsored by the National Institute of Mental Health, Dr. J.A. Dzubay (1997) of the Oregon Health Sciences University is conducting *in vitro* experiments on the activity of NMDA (N-methyl D-aspartate) channels in the hippocampus; these are membrane channels controlled by NMDA receptors that regulate the influx of calcium into neurons. In work funded by the National Institute of Neurological Disorders and Stroke, Dr. David Lovinger (1999) of Vanderbilt University Medical Center is studying glutamatergic and dopaminergic synaptic transmission in the neostriatum. In a third study, sponsored by the National Institute of General Medical Sciences, Dr. J. Bell (1998) of Fayetteville State University in North Carolina is examining the effect of metal salts on the fidelity of DNA synthesis. It appears that this research may provide additional genotoxicity information regarding stable strontium.

Radioactive Strontium. The single largest population available for studying the long-term health effects of radiostrontium is the Techa River cohort that was exposed from contaminated drinking water and food following releases from a plutonium processing plant between 1949 and 1956 (Akleyev et al. 1995; Bauchinger et al. 1998; Kossenko 1996; Kossenko et al. 1994, 1997, 2000; Shagina et al. 2000; Tolstykh et al. 1998). In addition to the studies reviewed in this toxicological profile, further analysis of this population is expected to continue under the auspices of the Urals Research Center for Radiation Medicine.

Additional information regarding the toxicity of radioactive strontium is likely to emerge from studies related to the therapeutic use of strontium isotopes. In programs funded by the National Heart Lung and Blood Institute, Dr. Sou-Tung Chiu-Tsao (1999) of the Beth-Israel Medical Center, New York, and Dr. Ravinder Nath (1999) of Yale University Medical Center, are investigating ^{90}Sr along with other isotopes for intravascular brachytherapy delivered at the time of angioplasty. Dr. Carl J. Pepine (1998) of the Department of Veterans Affairs Medical Center, Gainesville, Florida, is conducting a clinical trial to evaluate a commercial product for intravascular brachytherapy. Dr. Timothy Kuzel (1999) of the Department of Veterans Affairs Medical Center, Chicago, Illinois, is conducting a Phase I/II trial of ^{89}Sr in conjunction with mitoxantrone and hydrocortisone in the treatment of bone metastases in patients with hormone-refractory prostate cancer. In work funded by the National Center of Research Resources, Dr. Franco Muggia (1999) of the New York University Medical Center is conducting an open label Phase II study to evaluate the effect and toxicity of Doxil, a liposomal encapsulated doxirubicin, and ^{89}Sr in combination for treating hormone-refractory metastatic prostate cancer. In a study sponsored by the National Institute on Deafness and Other Communication Disorders, Dr. Gina M. Nelson (1999) of the University of Alabama at Birmingham is conducting laboratory tests in rodents in order to develop a radiation treatment for cancer of the mouth that will be less likely to destroy the sense of taste than current procedures. Radiostrontium will be held in a device to expose the tongue to beta radiation.

4. CHEMICAL, PHYSICAL, and RADIOLOGICAL INFORMATION

4.1 CHEMICAL IDENTITY

Strontium is an alkaline earth element in Group IIA of the periodic table. Because of its high reactivity, elemental (or metallic) strontium is not found in nature; it exists only as molecular compounds with other elements. The chemical information for elemental strontium and some of its compounds is listed in Table 4-1. Radioactive isotopes of strontium (e.g., ^{89}Sr and ^{90}Sr, see Section 4.2) are the primary cause of concern with regard to human health (see Chapter 3).

4.2 PHYSICAL, CHEMICAL, AND RADIOLOGICAL PROPERTIES

The physical properties of strontium metal and selected strontium compounds are listed in Table 4-2. The percent occurrence of strontium isotopes and the radiologic properties of strontium isotopes are listed in Table 4-3.

Strontium can exist in two oxidation states: 0 and +2. Under normal environmental conditions, only the +2 oxidation state is stable enough to be of practical importance since it readily reacts with both water and oxygen (Cotton and Wilkenson 1980; Hibbins 1997). There are 26 isotopes of strontium, 4 of which occur naturally. The four stable isotopes, ^{84}Sr, ^{86}Sr, ^{87}Sr, and ^{88}Sr, are sometimes referred to as stable strontium. The most important radioactive isotopes, ^{89}Sr and ^{90}Sr, are formed during nuclear reactor operations and during nuclear explosions by the nuclear fission of ^{235}U, ^{238}U, or ^{239}Pu. For example, ^{235}U is split into smaller atomic mass fragments such as ^{90}Sr by a nuclear chain reaction initiated by high energy neutrons of approximately 1 million electron volts (or 1 MeV). These smaller atomic mass fragments are referred to as fission by-products. This process is illustrated below:

$$^{235}\text{U} + {}^{1}\text{n} \rightarrow {}^{90}\text{Sr} + {}^{89}\text{Sr} + \text{other fission by-products}$$

^{90}Sr is the more dangerous of the two isotopes due to its long half-life (29 years). ^{90}Sr decays by emission of a beta-particle with a maximum energy of 0.546 MeV and the creation of an ^{90}Y isotope, or progeny product. Unlike other radioactive isotopes that decay by beta-emission, ^{90}Sr does not directly release high energy photons or gamma-ray radiation (γ). However, the progeny product of ^{90}Sr, ^{90}Y, is both a beta-particle (2.28 MeV maximum energy) emitter and to a minor degree for 0.02% of all disintegrations, a

Table 4-1. Chemical Identity of Strontium and Strontium Compounds

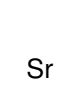
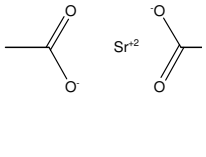
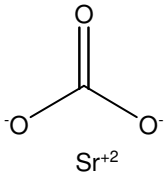
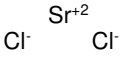
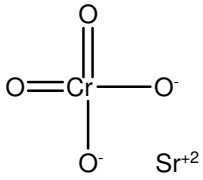
Property	Strontium (0)	Strontium acetate	Strontium carbonate	Strontium chloride	Strontium chromate
Chemical formula	Sr	$C_4H_6O_4Sr$	CO_3Sr	Cl_2Sr	CrH_2O_4Sr
Chemical structure	Sr	$Sr(O_2CCH3)_2$	$SrCO_3$	$SrCl_2$	$SrCrO_4$
					
Synonyms	None	Strontium diacetate	Carbonic acid, strontium salt (1:1); strontianite	Strontium dichloride	Chromic acid, strontium salt
Trade names	No data	No data	No data	No data	No data
Identification numbers					
CAS registry	7440-24-6	543-94-2	1633-05-2	10476-85-4	7789-06-2
NIOSH RTECS	WK7849000	AJ4725000	No data	WK8400000	GB3240000
EPA hazardous waste	No data	No data	No data	No data	D007
OHM/TADS	No data	No data	No data	No data	No data
DOT/UN/NA/IMO shipping	UN 1383/IMO 4.2	No data	No data	No data	9149/NA 9149
HSDB	2545	No data	5845	No data	2545
NCI	No data	75799	112224	No data	No data
STCC	No data	No data	No data	No data	49 633 77

Table 4-1. Chemical Identity of Strontium and Strontium Compounds

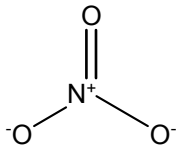
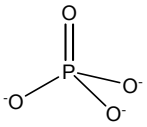
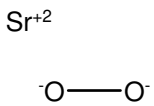
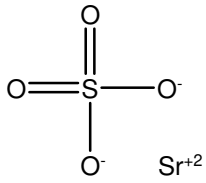
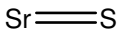
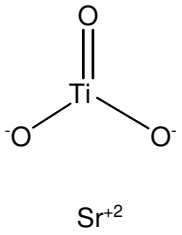
Property	Strontium fluoride	Strontium hydroxide	Strontium nitrate	Strontium phosphate	Strontium oxide
Chemical formula	F_2Sr	H_2O_2Sr	N_2O_6Sr	O_8P_2Sr3	OSr
Chemical structure	SrF_2	$Sr(OH)_2$	$Sr(NO_3)_2$	$Sr_3(PO_4)_2$	SrO
					
Synonyms	Strontium difluoride	Strontium hydrate	Nitrate de strontium (French); Nitric acid, strontium salt; strontium dinitrate; strontium(II) nitrate (1:2)	No data	Strontia, strontium monoxide
Trade names	No data	No data	No data	No data	No data
Identification numbers					
CAS registry	7783-48-4	18480-07-4	10042-76-9	7446-28-8	1314-11-0
NIOSH RTECS	WK8925000	WK9100000	WK9800000	No data	No data
EPA hazardous waste	No data	No data	No data	No data	No data
OHM/TADS	No data	No data	No data	No data	No data
DOT/UN/NA/IMO shipping	No data	No data	UN 1507 Oxidizer IMO 5.1	No data	No data
HSDB	No data	No data	No data	No data	No data
NCI	No data	No data	No data	No data	No data
STCC	No data	No data	49 187 54	No data	No data

Table 4-1. Chemical Identity of Strontium and Strontium Compounds

Property	Strontium peroxide	Strontium sulfate	Strontium sulfide	Strontium titanate
Chemical formula	O_2Sr	O_4SSr	SSr	O_3SrTi
Chemical structure	SrO_2 	$SrSO_4$ 	SrS 	$SrTiO_3$ 
Synonyms	Strontium dioxide	Celestine, celestite	Strontium monosulfide	No data
Trade names	No data	No data	No data	No data
Identification numbers				
CAS registry	1314-18-7	7759-02-6	1314-96-1	12060-59-2
NIOSH RTECS	WL0100000	No data	WL0400000	No data
EPA hazardous waste	No data	No data	P107/D003	No data
OHM/TADS	No data	No data	No data	No data
DOT/UN/NA/IMO shipping	UN 1509 Oxidizer IMO 5.1	No data	No data	No data
HSDB	788	No data	12	No data
NCI	No data	No data	No data	No data
STCC	49 187 55	No data	No data	No data

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; STCC = Standard Transportation Commercial Code

Source: ChemFinder 2002; HSDB 2002; Lide 2000

Table 4-2. Physical and Chemical Properties of Strontium and Strontium Compounds[a]

Property	Strontium (0)	Strontium acetate[b,c]	Strontium carbonate[b,c]	Strontium chloride[c]	Strontium chromate
Molecular weight, g/mole	87.62	205.71	147.63	158.53	203.62
Color	Pale yellow	White	White	White	Yellow
Physical state	Solid	Solid	Solid	Solid	Solid
Melting point	777 °C	Decomposes	1,497 °C[d]	875 °C	No data
Boiling point	1,382 °C	Not applicable	Decomposes at 1,100 °C	1,250 °C	No data
Density, g/cm^3	2.64	2.099	3.5	3.05	3.90
Odor	No data	No data	Odorless	No data	No data
Odor threshold:					
Water	No data	No data	No data	No data	No data
Air	No data	No data	No data	No data	No data
Solubility:					
Water	Decomposes	369 g/L (cold)	0.11 g/L at 18 °C	538 g/L at 20 °C	30 g/L at 100 °C
Organic solvents(s)	Alcohol	Alcohol, slightly	No data	Alcohol, acetone	Acetic acid
Partition coefficients:					
Log K_{ow}	No data	No data	No data	No data	No data
Log K_{oc}	No data	No data	No data	No data	No data
Vapor pressure	5 mmHg at 847 °C	No data	No data	No data	No data
Henry's Law constant	No data	No data	No data	No data	No data
Autoignition temperature	No data	No data	No data	No data	No data
Flashpoint	No data	No data	No data	No data	No data
Flammability limits	No data	No data	No data	No data	No data
Explosive limits	No data	No data	No data	No data	No data

Table 4-2. Physical and Chemical Properties of Strontium and Strontium Compounds[a]

Property	Strontium fluoride[e,c]	Strontium hydroxide[c]	Strontium nitrate[c]	Strontium phosphate[f]	Strontium oxide[c]
Molecular weight, g/mole	125.62	121.64	211.63	452.80	103.62
Color	White	Colorless	Colorless	White	Yellow
Physical state	Solid	Solid	Solid	Solid	Solid
Melting point	Decomposes >100 °C	375 °C	570 °C	No data	2,430 °C
Boiling point	2,489 °C	No data	645 °C	No data	3,000 °C
Density, g/cm^3	4.24	3.63	2.98	No data	4.56
Odor	No data	No data	Odorless	No data	No data
Odor threshold:					
Water	No data	No data	No data	No data	No data
Air	No data	No data	No data	No data	No data
Solubility:					
Water	0.12 g/L at 18 °C	470 g/L at 100 °C	790 g/L at 18 °C	Insoluble	229 g/L at 100 °C
Organic solvents(s)	Alcohol, acetone	Alcohol	Slightly in alcohol and acetone	No data	Slightly in alcohol
Partition coefficients:					
Log K_{ow}	No data	No data	No data	No data	No data
Log K_{oc}	No data	No data	No data	No data	No data
Vapor pressure	1 mmHg at 921 °C	No data	No data	No data	No data
Henry's Law constant	No data	No data	No data	No data	No data
Autoignition temperature	No data	No data	No data	No data	No data
Flashpoint	No data	No data	No data	No data	No data
Flammability limits	No data	No data	No data	No data	No data
Explosive limits	No data	No data	No data	No data	No data

Table 4-2. Physical and Chemical Properties of Strontium and Strontium Compounds[a]

Property	Strontium peroxide	Strontium sulfate	Strontium sulfide	Strontium titanate
Molecular weight, g/mole	119.63	183.68	119.70	183.52
Color	White	Colorless	Gray	White
Physical state	Solid	Solid	Solid	Solid
Melting point	Decomposes at 215 °C	1,605 °C	>2,000 °C	No data
Boiling point	No applicable	No data	No data	No data
Density, g/cm^3	4.56	3.96	3.70	4.810
Odor	Odorless	No data	Hydrogen sulfide in moist air	No data
Odor threshold:				
Water	Not applicable	No data	No data	No data
Air	Not applicable	No data	No data	No data
Solubility:				
Water	Decomposes	0.14g/L at 30 °C	Decomposes	Insoluble
Organic solvents(s)	Alcohol	Slightly in alcohol	No data	No data
Partition coefficients:				
Log K_{ow}	No data	No data	No data	No data
Log K_{oc}	No data	No data	No data	No data
Vapor pressure	No data	No data	No data	No data
Henry's Law constant	No data	No data	No data	No data
Autoignition temperature	No data	No data	No data	No data
Flashpoint	No data	No data	No data	No data
Flammability limits	No data	No data	No data	No data
Explosive limits	No data	No data	No data	No data

[a]Source: HSDB 2002, unless otherwise stated
[b]Merck 1989
[c]Lide 1995
[d]At 69 atmospheres pressure
[e]Sigma-Aldrich 2000
[f]Lide 2000

Table 4-3. Percent Natural Occurrence and Radioactive Properties of Isotopes of Strontium

Isotope	CAS registry number	Natural abundance (by weight %)	Beta energies, MeV	Half-life	Activity, Ci/gram
^{84}Sr	15758-49-3	0.56	No data	Stable	No data
^{85}Sr	13967-73-2	No data	1.065[a]	65 days	35,400
^{86}Sr	13982-14-4	9.86	No data	Stable	No data
^{87}Sr	13982-64-4	7.00	No data	Stable	No data
^{88}Sr	14119-10-9	82.58	No data	Stable	No data
^{89}Sr	14158-27-1	No data	1.495	51 days	27,800
^{90}Sr	10098-97-2	No data	0.546	29 years	143
^{91}Sr	14331-91-0	No data	2.707	10 hours	3.4×10^6
^{92}Sr	14928-29-1	No data	1.911	3 hours	1.1×10^7

[a]Decay mechanism by electron capture with gamma emission

Source: Lide 1995

beta-particle and gamma-ray (2.19 keV) emitter. The decay product of ^{90}Y is ^{90}Zr, a stable isotope. The reaction is:

$$^{90}Sr\ (t_{1/2}=29\ yrs) \rightarrow {}^{90}Y\ (t_{1/2}=64\ hrs) + \beta^-(0.546MeV) \rightarrow \begin{cases} {}^{90}Zr\ (stable) + \beta^-(2.28\ MeV) \quad (99.98\ \%) \\ \rightarrow\ {}^{90}Zr\ (stable) + \beta^-(0.523\ MeV) + \gamma(1.75\ MeV) \end{cases}$$

^{89}Sr, like ^{90}Sr, is a fission product of ^{235}U, ^{238}U, or ^{239}Pu. It decays to ^{89}Y by emission of a beta-particle of 1.495 MeV ^{89}Y. ^{89}Sr has half-life of 51 days (Lide 1995).

5. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL

5.1 PRODUCTION

Strontium is a naturally occurring element that makes up approximately 0.02–0.03% of the earth's crust. In nature, strontium is present in igneous rocks in amounts averaging 375 ppm. The principal strontium minerals of commercial interest are celestite ($SrSO_4$) and strontianite ($SrCO_3$). Strontium is also a minor component of other mineral deposits and may occur in or near sedimentary rocks associated with beds or lenses of gypsum, anhydrite, and rock salt; in veins associated with limestone and dolomite; or dispersed in shales, marls, and sandstones. In the United States, there are deposits of celestite in Texas, Washington, Arizona, Ohio, and California. The U.S. Geological Survey (USGS) estimated U.S. resources of celestite and strontianite at 2,500,000 tons, containing 1,130,000 tons of strontium (Adams 1975). However, domestic deposits of these minerals are not economically exploitable, and strontium has not been mined in the United States since 1959.

Celestite is converted to $SrCO_3$, the common commercial form of strontium. The black ash method (alternatively known as the calcining method) and the soda method (also known as direct conversion) are the two most common recovery techniques for strontium. The black ash method produces chemical grade strontium carbonates, which are 98% strontium carbonate and 2% byproducts and impurities. The soda ash method produces technical grade strontium carbonates, containing at least 97% strontium carbonate. The black ash method is the preferred means of strontium carbonate production because it yields a higher-grade product (USGS 1998).

During World War II, the U.S. government began stockpiling celestite for defense applications. In 1963, Congress determined that the stockpile was unnecessary, and by 1973, all of the stockpiled high-grade celestite was sold. The remaining low-grade celestite material, approximately 12,000 metric tons, has been listed by the Defense National Stockpile Center of the Defense Logistics Agency as valueless. In 1998, Congress authorized the remaining stockpile for disposal. The only U.S. strontium carbonate producer using celestite is the Chemical Products Corporation of Cartersville, Georgia. A number of U.S. companies manufacture strontium compounds from strontium carbonate. Mallinkrodt Inc. of St. Louis, Missouri, produces strontium chloride, and Rockwood Pigments Corporation of Beltsville, Maryland, produces strontium chromate. Production of other strontium compounds is on a limited scale (USGS 1998, 1999).

Radioactive strontium, or ^{89}Sr and ^{90}Sr, does not occur in nature. It is the direct result of anthropogenic activity. As discussed in Chapter 4, ^{89}Sr and ^{90}Sr are produced by nuclear fission. Nearly all of the ^{90}Sr generated in the United States is present in spent nuclear reactor fuel rods. These fuel rods are currently located at the commercial reactor facilities or at Department of Energy (DOE) facilities across the United States. After 1 year of decay of nuclear fuel rods, ^{90}Sr represents 3.7% by mass of the total fission product inventory. A limited amount of ^{89}Sr and ^{90}Sr is produced for industrial, scientific, and medicinal applications through the process of fission product recovery. During the period of 1974–1984, ^{90}Sr was recovered and converted into solid forms. Typically, ^{90}Sr is combined with fluorine to produce strontium fluoride ($^{90}SrF_2$) or with chlorine (Cl_2) to produce strontium chloride ($^{90}SrCl_2$). These solids were placed in double walled capsules to be used for commercial and medical applications. ^{90}Sr is available from Pacific Northwest National Laboratory located at the DOE facility in Hanford, Washington. The Hanford inventory of ^{90}Sr embodies one of the largest sources of this nuclide in the world (DOE 1996b, 1996c).

5.2 IMPORT/EXPORT

In 2001, 100% of celestite used in the United States was imported from Mexico. Of the 38,500 metric tons of strontium minerals and compounds imported in 2001, approximately 94% were imported from Mexico, 6% from Germany, and 2% from other countries. From the period of 1954–1974, demand for strontium imports (both mineral and compound) has steadily increased from approximately 3,200 to 16,000 metric tons. From 1994 to 2001, the importation of strontium minerals and compounds for consumption has remained relatively steady at approximately 31,000–38,500 metric tons. The apparent consumption of all strontium imports in the United States is 97%. The total export volume of strontium compounds during 1993–2001 was more than 20 times lower than the quantities of strontium minerals and compounds imported during the same period. Exports of strontium compounds has varied from 1,120 metric tons in 1994 to 1,040 metric tons in 2001 (USGS 1998, 1999, 2002).

5.3 USE

In 2001, more than 85% of all strontium consumed in the United States was used in the manufacture of ceramics and glass products, primarily in television faceplate glass and secondarily in ceramic ferrite magnets (strontium ferrite) and other ceramic and glass applications. All color televisions and other devices containing cathode-ray tubes (CRT) sold in the United States are required by law to contain

strontium in the faceplate glass of the picture tube to block x-ray emissions. Major manufacturers of television picture tube glass incorporate about 8% by weight of strontium oxide (SrO) into the glass faceplate material. Strontium is added to the glass melt in the form of strontium carbonate. Upon heating and solidification, it is transformed to SrO. Other uses for strontium compounds include pyrotechnics (strontium nitrate), paint pigments (strontium chromate), fluorescent lights (strontium phosphate), getters in zinc production (strontium carbonate), alloy (strontium metal), and medicines (strontium chloride, strontium peroxide). Strontium metal has limited commercial use. One minor use of strontium is as an alloy material for the production of aluminum castings. Most commercial uses of strontium compounds and products use strontium carbonate as the feed material (Hibbins 1997; USGS 1999, 2002).

The radioactive isotope ^{89}Sr (also known by the pharmaceutical brand name Metastron™) is used as a cancer therapeutic to alleviate bone pain. ^{85}Sr has been used in medical applications, such as radiologic imagining of bones, in minor commercial applications, such in radioisotope thermoelectric generators (RTG), as a beta-particle standard source, and in instruments that measure thickness and density of materials (Murray 1994). ^{90}Sr has been used in RTGs at remote locations (e.g., lighthouses) throughout the former Soviet Union (Alimov 2003). Many of these ^{90}Sr RTGs in the former Soviet Union are completely unguarded against potential thieves or intruders, lacking such minimal security measures as fences or even signs warning of radioactive dangers. The biggest danger coming from these unprotected RTGs is their availability to terrorists who can use the radioactive materials (e.g., ^{90}Sr) contained in them to make so-called “dirty bombs”, which are bombs that are triggered by standard explosives, but disperse radioactivity.

5.4 DISPOSAL

Most nonradioactive strontium minerals, strontium compounds, and strontium-containing materials do not require special disposal and handling requirements. However, some chemical forms may be classified as hazardous materials if the compound is chemically reactive, flammable, or toxic. Care should be taken to read and understand all of the hazards, precautions, and safety procedures for each specific chemical form. In addition, all federal, state, and local laws and regulations should be investigated and subsequently followed with regard to disposal and handling of the specific chemical form of the strontium compound or material.

Radioactive strontium does require special disposal and handling requirements and is regulated by the Nuclear Regulatory Commission (USNRC). Radioactive waste-containing radioactive strontium can be

grouped into three categories: low-level waste (LLW); high-level waste (HLW) and spent nuclear fuel; and mixed waste. As defined by the Nuclear Waste Policy Act, high-level radioactive waste is "the highly radioactive material resulting from the reprocessing of spent nuclear fuel, including liquid waste produced directly in reprocessing and any solid material derived from such liquid waste that contains fission products in sufficient concentration." However, most classifications of HLW also include spent nuclear fuel. Most HLW was generated from the production of plutonium. A small fraction is related to the recovery of enriched uranium from naval reactor fuel. This waste typically contains highly radioactive, short-lived high activity fission by-products as well as other long-lived isotopes, hazardous chemicals, and toxic heavy metals. ^{90}Sr contamination is only a small fraction of the activity of HLW. Liquid HLW is typically stored in large underground tanks of either stainless steel or carbon steel, depending on whether they are acid or alkaline solutions. There are about 100 million gallons of high-level liquid waste stored in underground tanks in Washington, South Carolina, Idaho, and New York. These tanks contain a variety of radioactive liquids, solids, and sludges. Some of the liquid wastes have been solidified into glass, ceramic slag, salt cakes, and sludges (DOE 1996a; Murray 1994).

Spent nuclear fuels, such as fuel elements and irradiated targets used in nuclear reactors, are currently disposed of at the commercial nuclear power plants and DOE facilities where they were produced. Spent fuel is highly radioactive due to the large concentration of fission products and must be stored in special water-cooled pools that shield and cool the material. Most of the ^{90}Sr remains trapped in the spent fuel rod matrix and is never released. Roughly all DOE spent fuel, about 3,000 metric tons, is stored at four sites: Hanford, Savannah River, Idaho National Engineering Laboratory, and West Valley, New York. Commercial reactors have generated more than 30,000 metric tons of spent fuel. The spent fuel from these facilities is stored at the more than 100 commercial nuclear reactor sites around the United States. The establishment of an HLW and spent fuel repository for both DOE and commercial waste is currently under evaluation at Yucca Flats, Nevada. It is not projected to be in operation until after the year 2010 (DOE 1996b; Eisenbud 1987; Murray 1994).

Mixed waste contains both radioactive and chemically hazardous materials such as toxic, corrosive, flammable, or explosive materials. The radioactive component may be either HLW or LLW. All liquid HLW is mixed waste, usually in the presence of organic solvents or heavy metals in addition to radioactive components. Disposal of mixed wastes is regulated by EPA under the Resource Conservation and Recovery Act (RCRA) and by the USNRC under the Atomic Energy Act. EPA and USNRC have developed special procedures on how to handle and dispose of this special category. DOE operates an incinerator in Oak Ridge, Tennessee that burns mixed hazardous radioactive wastes (DOE 1996a).

Low-level waste is all radioactive waste that cannot be classified as HLW, spent fuel, or mixed waste. Low-level does not necessarily mean low radioactivity or low environmental hazards. However, the bulk of LLW has relatively little radioactivity and practically no transuranic elements. Thus, LLW usually does not require shielding from radioactivity or heat removal equipment. Most LLW is acceptable for near-surface land disposal. LLW types that may be contaminated with ^{90}Sr include both wet and dry wastes. Examples of the physical form of LLW are spent ion exchange resins, filter sludges, filter cartridges, evaporator bottoms, compactable trash, non-compactable trash, irradiated components, ashes produced from the incineration of combustible material, contaminated detergents or solvents, organic liquids, and discarded contaminated equipment or tools. Of the LLW generated today, approximately 64% of the volume and 70% of the radioactivity are generated as a result of nuclear power plant activities or supporting fuel cycle operations. Other sources of LLW are industrial, academic, government, and medical. Radiostrontium contamination accounts for only a small fraction of the activity of LLW. LLW is typically packaged in drums or boxes and buried in shallow pits or trenches. Approximately 3 million cubic meters of LLW generated in the United States have been disposed of this way. LLW from DOE sources is currently disposed of at several DOE facilities across the United States. Only two sites accept non-DOE LLW, Barnwell, South Carolina and Richland, Washington. Over half of the LLW in the eastern United States is disposed of at the Barnwell site. As required by the Federal LLRW (Low Level Radioactive Waste) Policy Act in 1980 and in the 1985 amendments, states or interstate compacts are required to build facilities to contain LLW generated from sources within their boundaries. However, other than Barnwell, South Carolina and Richland, Washington sites, no other facility in the United States is currently accepting LLW from non-DOE sources. Currently, many generators store LLW on-site until additional facilities can be constructed in the future (DOE 1996a; Eisenbud 1987; Murray 1994).

6. POTENTIAL FOR HUMAN EXPOSURE

6.1 OVERVIEW

Strontium and ^{90}Sr have been identified in at least 102 and 12, respectively, of the 1,636 hazardous waste sites that have been proposed for inclusion on the EPA National Priorities List (NPL) (HazDat 2003). However, the number of sites evaluated for strontium and strontium-90 are not known. The frequency of these sites can be seen in Figures 6-1 and 6-2, respectively. Of these sites, all are located within the United States and none are located in the Commonwealth of Puerto Rico.

Strontium is widely distributed in the earth's crust and oceans. Strontium is released into the atmosphere primarily as a result of natural sources, such as entrainment of dust particles and resuspension of soil. Radioactive strontium is released into the environment as a direct result of anthropogenic activities. Stable strontium can neither be created nor destroyed. However, strontium compounds may transform into other chemical compounds. Radioactive strontium is formed by nuclear reactions. Radioactive decay is the only mechanism for decreasing the concentration of radiostrontium. The half-life of ^{90}Sr is 29 years. Eventually, all of the radioactive strontium will be converted to stable zirconium (see Section 4.2).

Strontium present in the atmosphere is in the form of wet or dry aerosols. The principal chemical species in the air is strontium oxide (SrO). Strontium oxide will react rapidly in the presence of moisture to form Sr^{+2} and $SrOH^{+}$ ions. Strontium is dispersed by atmospheric cycling and is subsequently deposited by wet deposition on the earth's surface. In surface water and groundwater, strontium exists primarily as a hydrated ion. Strontium can form ionic complexes with other inorganic or organic substances. Strontium is relatively mobile in water. However, the formation of insoluble complexes or sorption of strontium to soils can reduce its mobility in water. Strontium sorbs to soils by ion exchange, and tends to be more mobile in soils with a high concentration of exchangeable ions or in soils with low cation exchange capacities. Strontium is taken up and retained by aquatic and terrestrial plants and is concentrated in the boney tissues of animals that eat contaminated vegetation. The average concentration of strontium in urban air is 20 ng/m^3 (Dzubay and Stevens 1975). The concentration of ^{90}Sr in the atmosphere has steadily decreased since its maximum concentration in 1963. The mean concentration of strontium in U.S. surface water is <1 mg/L. Dissolved strontium has been detected in groundwater and surface water used for drinking water supplies with average concentrations of 0.81 and 1.1 mg/L, respectively (EPA

Figure 6-1. Frequency of NPL Sites with Strontium Contamination

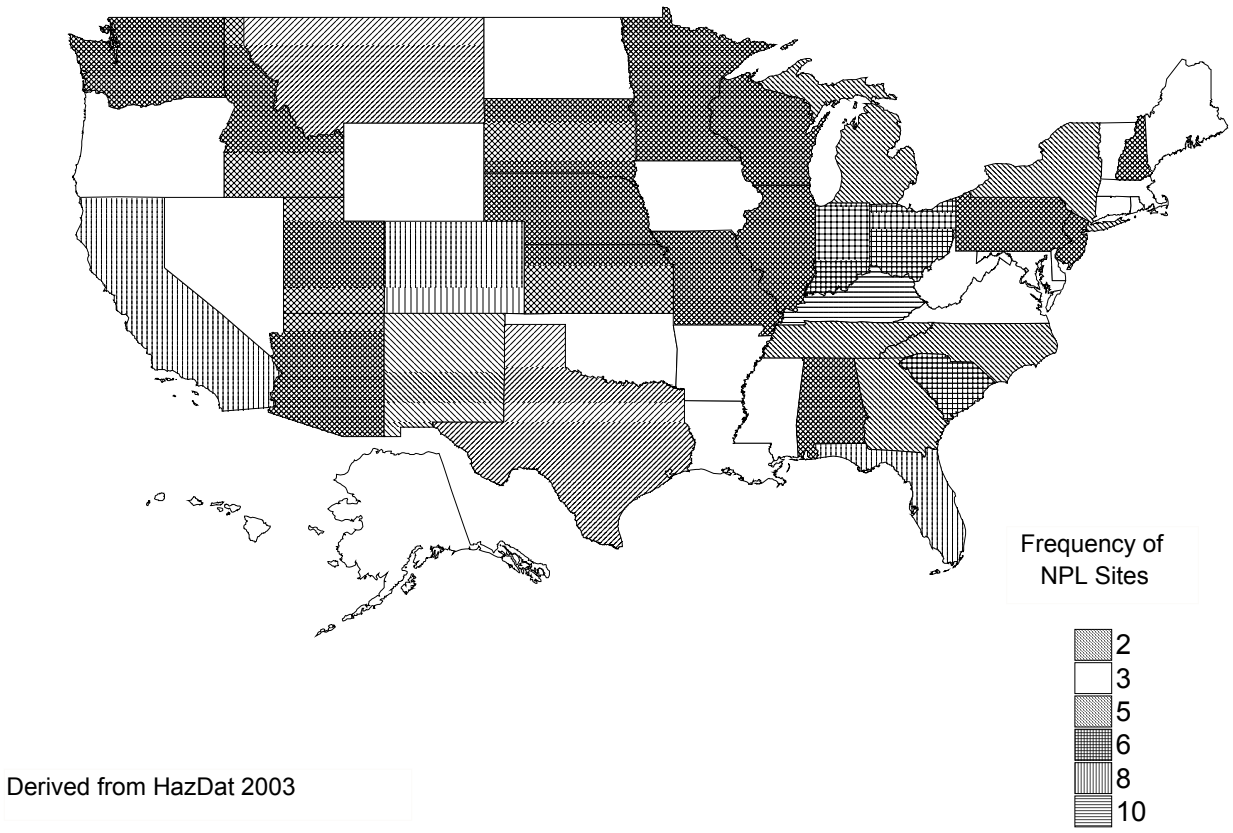


Figure 6-2. Frequency of NPL Sites with Strontium-90 Contamination

Derived from HazDat 2003

2002b). The median concentration of ^{90}Sr in drinking water for 1995 was 0.1 pCi/L (3.7 mBq/L). Human exposure to strontium and radiostrontium can result from consumption of food, drinking water, or incidental ingestion of soil or dust contaminated with strontium. Food and drinking water are the largest sources of exposure to strontium and radiostrontium. Grain, leafy vegetables, and dairy products contribute the greatest percentage of dietary strontium and radiostrontium to humans.

6.2 RELEASES TO THE ENVIRONMENT

The TRI data should be used with caution because only certain types of facilities are required to report. This is not an exhaustive list.

6.2.1 Air

Strontium naturally occurs in the earth's crust and is released into the atmosphere as a result of natural processes such as entrainment of dust particles, resuspension of soil by wind, and sea spray. Entrainment of soil and dust particles with significant concentrations of strontium would be most significant in areas with higher soil strontium concentrations. Coastal regions have higher concentrations of strontium due to sea spray (Capo et al. 1998). Human activities, including milling and processing of strontium compounds, burning of coal, land application of phosphate fertilizers, and using pyrotechnic devices, release strontium into the atmosphere (Lee and von Lehmden 1973; Ondov et al. 1989; Perry 1999; Que Hee et al. 1982; Raven and Loeppert 1997). The effect of these activities is illustrated by the deposition rates of strontium measured in peat cores of northern Indiana. Deposition has increased by a factor of 7 from 8.1 mg strontium/m^2/year in presettlement times (1339–1656) to 57.0 mg strontium/m^2/year between 1970 and 1973 (Cole et al. 1990).

Strontium discharged into the atmosphere from the operation of coal fired power plants depends on the strontium concentration in coal, the amount of coal burned, and the efficiency of fly ash recovery. Approximately 90% of coal mass is consumed during the combustion process, leaving 10% as a residual nonvolatile material (fly ash) containing 100–4,000 ppm (or mg/kg) of strontium (Furr et al. 1977). Atmospheric concentrations of strontium emitted from coal fired power plants have been found to range from 17 to 2,718 µg/m^3 in the western United States and are approximately 9,786 µg/m^3 in the eastern United States (Ondov et al. 1989; Que Hee et al. 1982). Phosphate fertilizers are known to contain between 20 and 4,000 µg strontium/g solid by weight (Lee and von Lehmden 1973; Raven and Loeppert

1997). Strontium can be released into the atmosphere in windblown soil to which phosphate fertilizers have been applied. Pyrotechnic displays release low levels of strontium on the order of 9 ng/m^3 in the immediate environment of the display (Perry 1999).

Strontium has been identified in air at 9 sites collected from the 102 NPL hazardous waste sites where it was detected in some environmental media (HazDat 2003).

Radioactive strontium (e.g., ^{90}Sr) was released into the atmosphere from aboveground testing of nuclear weapons during the period of 1945–1980. Nuclear weapon testing injects radioactive material into the stratosphere, which results in wide dispersal of radionuclides. However, atmospheric deposition of ^{90}Sr has steadily decreased from a high in 1963 of approximately 1.10x10^8 GBq (3.0 MCi) to <3,000 Ci in 1990, which suggests that global concentrations of ^{90}Sr in the atmosphere have declined (DOE 1996c). Other sources of regional contamination from radiostrontium include large-scale nuclear power plant accidents such as the Chernobyl disaster in the Ukraine (April 1986), which resulted in releases of about 2.2 MCi (8.1x10^7 GBq) of ^{89}Sr and 0.22 MCi (8.1x10^6 GBq) of ^{90}Sr into the atmosphere (Eisenbud 1987). However, although some ^{90}Sr reached the upper atmosphere and was subsequently transported around the world, most of the radiostrontium was deposited as regional fallout in eastern Europe (Eisenbud 1987). Routine releases of radiostrontium in 1993 from the operation of nuclear power plants around the United States are summarized in Table 6-1 (USNRC 1993a). In 1993, releases of radiostrontium (i.e., ^{89}Sr, ^{90}Sr, and ^{91}Sr) for boiling water reactors (BWR) and pressurized water reactors (PWR) (the two common designs of nuclear reactors in the United States) were 72.1 and 3.3 mCi (2.67 and 0.12 GBq), respectively. The total annual releases of radiostrontium from nuclear power plants in the United States (75.4 mCi or 2.79 GBq) are insignificant compared to releases of ^{90}Sr from the testing of nuclear weapons. In the former Soviet Union between the years 1949 and 1956, large-scale environmental contamination occurred in the region surrounding the Mayak plutonium production complex in the Ural region of Russia (Eisenbud and Gesell 1997). Releases of radioactive liquid wastes into the Techa River, both planned and accidental, of about 10^{17} Bq (2.7 MCi) resulted. ^{90}Sr contributed about 12% (or 0.23 MCi) to the total activity released (Tokareva et al. 2000). Other minor releases of ^{90}Sr have involved accidents with rockets or satellites that have disintegrated in the atmosphere. The Soviet satellite Cosmos 954 powered by a plutonium fueled nuclear reactor released 3.1x10^3 GBq (83 Ci) of ^{90}Sr to the regional atmosphere in northern Canada in 1978 (Eisenbud 1987). The Department of Energy (DOE) and its predecessor agencies have been involved in operations that have released radiostrontium into the atmosphere. Over the 43-year operating period at the DOE Savannah River Site in South Carolina, about 1.1x10^2 GBq (3 Ci) of ^{90}Sr were released into the atmosphere, primarily from the chemical separation and

Table 6-1. Radiostrontium Releases from Nuclear Power Plants for 1993

		Annual total site environmental releases for 1993						
		Water				Air		
Installation	Location[a]	^{89}Sr, mCi	^{90}Sr, mCi	^{91}Sr, mCi	^{92}Sr, mCi	^{89}Sr, mCi	^{90}Sr, mCi	^{91}Sr, mCi
Boiling Water Reactors								
Browns Ferry[b]	Decatur, AL	41.1	2.05	No data	0.40	0.19	No data	No data
Brunswick[b]	Wilmington, NC	No data	No data	No data	0.0062	0.099	0.0027	No data
Clinton	Clinton, IL	No data	No data	No data	No data	0.06	No data	No data
Cooper	Omaha, NE	4.69	15.8	No data	0.082	No data	No data	No data
Dresden[b]	Joliet, IL	0.056	0.085	No data	No data	0.67	0.004	No data
Duane Arnold	Cedar Rapids, IA	No data	No data	No data	No data	0.018	0.0009	No data
Edwin I. Hatch	Baxley, GA	6.29	0.43	5.20	0.65	12.0	0.24	No data
Fermi	Laguna Beach, MI	0.19	No data	No data	No data	0.14	0.0003	4.0
Grand Gulf	Vicksburg, MS	0.32	0.29	No data	No data	0.003	0.002	No data
Hope Creek	Wilmington, DE	No data	No data	No data	No data	No data	No data	No data
Humbolt Bay[b]	Eureka, CA	No data	36.5	No data	No data	No data	0.002	No data
James A. Fitzpatrick	Syracuse, NY	0.44	No data	No data	No data	0.045	7.3×10^{-7}	No data
LaCrosse[b]	LaCross, WI	No data	0.28	No data	No data	No data	0.0003	No data
LaSalle	Ottawa, IL	No data	No data	No data	No data	No data	No data	No data
Limerick	Phildelphia, PA	20.0	0.44	No data	No data	16.4	0.31	No data
Millstone	New London, CT	3.30	0.15	No data	0.55	0.22	0.0006	No data
Monticello	St.Cloud, MN	No data	No data	No data	No data	0.59	0.003	No data
Nine Mile Point	Oswego, NY	<0.0001	No data	No data	No data	5.90	0.004	No data
Oyster Creek	Toms River, NJ	No data	No data	No data	No data	1.17	0.014	No data
Peach Bottom	Lancaster. PA	0.19	0.056	No data	No data	4.9	0.021	3.76
Perry	Painesville, OH	0.22	0.008	No data	No data	1.8	0.009	4.87
Pilgram	Boston, MA	1.63	0.086	No data	No data	5.8	0.024	No data
Quad-Cites	Moline, IL	0.050	0.018	No data	0.12	0.61	0.0014	No data
River Bend	Baton Rouge, LA	5.3	0.31	No data	No data	0.30	0.0095	No data
Shoreham	Brookhaven, NY	0.025	No data	No data	No data	No data	No data	No data
Susquehanna	Berwick, PA	0.0088	No data	No data	0.0011	0.0003	No data	No data
Vermont Yankee	Brattleboro, VT	No data	No data	No data	No data	2.83	0.054	No data
WNP-2	Richland, WA	0.55	0.057	No data	No data	3.5	0.012	1.61

Table 6-1. Radiostrontium Releases from Nuclear Power Plants for 1993

		Annual total site environmental releases for 1993						
		Water				Air		
Installation	Location[a]	^{89}Sr, mCi	^{90}Sr, mCi	^{91}Sr, mCi	^{92}Sr, mCi	^{89}Sr, mCi	^{90}Sr, mCi	^{91}Sr, mCi
Total		84.4	56.6	5.20	1.81	57.2	0.72	14.2
Pressurized Water Reactors								
Arkansas One	Russellville, AR	2.81	1.17	No data	0.59	0.000955	No data	No data
Beaver Valley	Shippingport, PA	No data	No data	No data	0.08	No data	No data	No data
Big Rock Point	Charlevoix, MI	0.02	0.17	No data	No data	0.21	0.006	2.73
Braidwood	Joliet, IL	3.68	158.4	No data	0.017	No data	No data	No data
Byron	Byron, IL	152.4	0.56	No data	No data	No data	No data	No data
Callaway	Fulton, MO	17.6	1.12	No data	No data	0.004	No data	No data
Calvert Cliffs	Washington, DC	0.83	0.37	No data	No data	No data	No data	No data
Catawaba	Rock Hill, SC	No data	No data	No data	0.41	No data	No data	No data
Comache Peak	Glen Rose, TX	No data	No data	No data	0.029	No data	No data	No data
Crystal River	Tampa, FL	3.03	10.2	No data	3.57	0.001	0.001	No data
Davis-Besse	Toledo, OH	No data	No data	No data	No data	No data	No data	No data
Diablo Canyon	San Luis Obispo, CA	0.16	0.057	No data	0.003	No data	No data	No data
Donald C. Cook	St. Joseph, MI	No data	0.029	No data	No data	0.080	0.0005	No data
Fort Calhoun	Omaha, NE	0.61	0.77	No data	No data	No data	0.0007	No data
H.B. Robinson	Hartsville, SC	No data	No data	No data	No data	No data	No data	No data
Haddam Neck	Middletown, CT	0.076	1.52	No data	No data	0.0002	0.0002	No data
Harris[b]	Raleigh, NC	No data	No data	No data	No data	No data	No data	No data
Indian Point[b]	Peekskill, NY	0.077	0.007	No data	No data	No data	No data	No data
Joseph M. Farley	Dothan, AL	No data	0.028	No data	0.10	No data	No data	No data
Kewaunee	Green Bay, WI	0.92	0.051	No data	No data	No data	No data	No data
Maine Yankee	Wicassett, ME	0.15	No data	No data	No data	No data	No data	No data
McGuire	Charlotte, NC	0.20	No data	No data	No data	No data	No data	No data
North Anna[c]	NW Richmond, VA	No data	No data	No data	No data	No data	No data	No data
Oconee	Greenville, SC	No data	No data	No data	No data	No data	No data	No data
Palisades	South Haven, MI	0.003	0.012	No data	No data	0.011	0.0042	No data
Palo Verde	Phoenix, AZ	No data	No data	No data	No data	0.19	0.0009	No data
Point Beach	Manitowoc, WI	0.012	0.11	0.0052	No data	No data	0.0001	No data
Prairie Island	Minneapolis, MN	No data	No data	No data	0.029	0.0006	0.0003	No data
R.E. Ginna	Rochester, NY	0.30	0.090	No data	No data	No data	No data	No data

Table 6-1. Radiostrontium Releases from Nuclear Power Plants for 1993

		Annual total site environmental releases for 1993						
		Water				Air		
Installation	Location[a]	^{89}Sr, mCi	^{90}Sr, mCi	^{91}Sr, mCi	^{92}Sr, mCi	^{89}Sr, mCi	^{90}Sr, mCi	^{91}Sr, mCi
Rancho Seco[b]	Sacramento, CA	No data	0.0013	No data	No data	No data	No data	No data
San Onofre[b]	San Clemente, CA	4.26	0.36	No data	0.48	No data	No data	No data
Seabrook	Portsmouth, NH	No data	No data	No data	No data	No data	No data	No data
Sequoyah	Daisy, TN	0.35	0.29	0.023	0.54	No data	No data	No data
South Texas	Bay City, TX	No data	No data	No data	No data	No data	No data	No data
St. Lucie	Ft. Pierce, FL	1.21	1.83	No data	No data	No data	0.0012	No data
Summer	Columbia, SC	0.0007	0.021	No data	No data	No data	No data	No data
Surry	Newport News, VA	No data	No data	No data	No data	No data	No data	No data
Three Mile Island[b]	Harrisburg, PA	0.034	0.83	No data	No data	No data	0.0003	No data
Trojan[b]	Portland, OR	0.24	0.029	No data	No data	No data	No data	No data
Turkey Point[b]	Florida City, FL	12.7	3.55	No data	No data	No data	No data	No data
Vogtle	Augusta, GA	1.64	0.19	No data	No data	0.0025	0.0003	No data
Waterford	New Orleans, LA	No data	No data	No data	0.23	No data	No data	No data
Wolf Creek	Burlington, KS	No data	0.092	0.0087	No data	No data	No data	No data
Yankee Rowe[b]	Greenfield, MA	No data	No data	No data	No data	No data	No data	No data
Zion	Waukegan, IL	No data	No data	No data	5.93	No data	No data	No data
Total		207.1	182.8	0.04	11.5	0.50	0.02	2.73

[a]Post office state abbreviations used
[b]Facilities that are permanently or indefinitely shut down
[c]Air ^{85}Sr 8.17x10^{6}

Source: NRC 1993b

reprocessing of nuclear fuel (Carlton et al. 1998, 1999). Between 1944 and 1972, about 64 Ci ($2.4x10^3$ GBq) of ^{90}Sr and 700 Ci ($2.6x10^4$ GBq) of ^{89}Sr was released into the atmosphere at the DOE Hanford site in Washington state from the routine operation of chemical plants used to separate plutonium from spent reactor fuel (CDC 1994).

^{90}Sr has been identified in air at 3 sites collected from the 12 NPL hazardous waste sites where it was detected in some environmental media (HazDat 2003).

6.2.2 Water

Releases of strontium to surface water and groundwater results from the natural weathering of rocks and soils and from the discharge of waste water directly into streams and aquifers. Intentional and unintentional releases of radioactive strontium directly into streams have occurred at DOE sites across the country. Over the period of 1954–1989, about 104 Ci ($3.8x10^3$ GBq) of ^{90}Sr and 216 Ci ($8.0x10^3$ GBq) of ^{89}Sr were released to streams in the vicinity of the Savannah River Site (Carlton et al. 1998; Cummins et al. 1991). During the period from 1952 to 1991, >129 Ci of ^{90}Sr in waste water was discharged into pits, wells, and infiltration ponds at the Idaho Chemical Processing Plant in Idaho, some of which may have found its way into surface or groundwater (Bartholomay et al. 1995). Minor releases of radioactive strontium to water occur annually from nuclear power plants. Table 6-1 summarizes the releases of radioactive strontium from nuclear power plants into surface waters in 1993 (USNRC 1993a). Releases of radiostrontium (i.e., ^{89}Sr, ^{90}Sr, ^{91}Sr, and ^{92}Sr) into surface waters in 1993 from BWR and PWR were 146.2 mCi (5.41 GBq) and 401.4 mCi (14.9 GBq), respectively.

Strontium has been identified in surface water and groundwater at 25 and 55 sites, respectively, collected from the 102 NPL hazardous waste sites where it was detected in some environmental media. ^{90}Sr has been identified in surface water and groundwater at 3 and 7 sites, respectively, collected from the 12 NPL hazardous waste sites where it was detected in some environmental media (HazDat 2003).

6.2.3 Soil

Strontium is ubiquitous in the environment and is present in nearly all rocks and soils. It is released to land in solid waste and from the use of phosphate fertilizers. ^{90}Sr is found in nearly all soils in the United States. ^{90}Sr that is deposited at a specific site varies widely, depending primarily on rainfall. Intentional

and unintentional releases of radioactive strontium have occurred at DOE sites across the country. Between 1954 and 1989 at the Savannah River Site, 105 Ci ($3.9x10^3$ GBq) of ^{89}Sr and 299 Ci ($1.1x10^4$ GBq) of ^{90}Sr were released into onsite seepage basins (DOE 1991). About 100 million gallons of liquid HLW are stored in underground tanks in Hanford, Washington, Savannah River, South Carolina, Idaho National Engineering Laboratory, Idaho, and West Valley, New York; these tanks contain a variety of radioactive liquids, solids, and sludges with unknown characteristics. Sixty-seven tanks at the Hanford site have suspected leaks of HLW into the surrounding soil. The largest three confirmed leaks at the Hanford site have released 115,000, 70,000, and 55,000 gallons of HLW, respectively, which may contain ^{90}Sr as well as other radionuclides (DOE 1996a).

Strontium has been identified in soil and sediment at 32 and 16 sites, respectively, collected from the 102 NPL hazardous waste sites where it was detected in some environmental media. ^{90}Sr has been identified in soil and sediment at 3 and 1 sites, respectively, collected from the 12 NPL hazardous waste sites where it was detected in some environmental media (HazDat 2003).

6.3 ENVIRONMENTAL FATE

6.3.1 Transport and Partitioning

Strontium, present in crustal materials, is released by the weathering force of wind and water. Strontium leaves the oceans, the largest reservoir of dissolved strontium, by deposition in marine carbonate sediment. Some strontium is transported from oceans to the atmosphere in sea spray, returning to the terrestrial environment in the form of precipitation (Capo et al. 1998).

Strontium released into the atmosphere from natural and anthropogenetic activities is transported and redeposited on the earth by dry or wet deposition. Dry deposition results from gravitational settling, impact, and sorption on surfaces (NCRP 1984). Experimental data on dry deposition of strontium, present in the ambient atmosphere, is limited. Rain, sleet, snow, or other forms of moisture can wash airborne particles containing strontium from the atmosphere by the process of wet deposition. Wet deposition depends on conditions such as particle solubility, air concentration, rain drop size distribution, and rain fall rate (NCRP 1984). Hirose et al. (1993) examined the mechanism of aerial deposition of ^{90}Sr derived from the Chernobyl accident, and found that 96% of atmospheric ^{90}Sr returned to earth as wet deposition.

Like calcium, strontium has moderate mobility in soils and sediments, and sorbs moderately to metal oxides and clays (Hayes and Traina 1998). The Sr^{2+} ion is strongly hydrated and is firmly coordinated with six or more water molecules in aqueous solution. When Sr^{2+} ions sorb on negatively charged mineral surface sites, the hydration sphere is retained (O'Day et al. 2000). Strontium sorbs as hydrated ions on the surface of clay minerals (kaolinite), weathered minerals (amorphous silica), and iron oxides (Sahai et al. 2000). Sorbed carbonate on iron oxides enhances the sorption of Sr^{2+} and permits the nucleation of Sr^{2+} as strontium carbonate (Sahai et al. 2000). On calcite (calcium carbonate), Sr^{2+} sorption occurs by electrostatic attraction as hydrated ions. However, at higher concentrations, precipitation of strontianite (strontium carbonate) occurs, and strontium is likely to be less mobile (Parkman et al. 1998).

A wide variation of K_d values have been published in the literature for Sr^{2+} sorption (NCRP 1984) that reflect differences in soil and sediment conditions as well as the analytical techniques used (Bunde et al. 1997). The *in situ* K_d values of stable strontium and ^{90}Sr determined in soil cores taken from the fallout area of the 1945 blast in Nagasaki, Japan were 496 and 300 L/kg, respectively (Mahara 1993). Migration rates for ^{90}Sr in soils from this area were estimated to be 4.2 mm/year when the percolation rate of soil water was 2,500 mm/year. Most ^{90}Sr remained close to the soil surface in these soils. In 1996, at most sites in the contaminated zone near Chernobyl, the main content of ^{90}Sr (more than 95% of activity) was located in the upper 30-cm layer. Only at a few sites (<1% of all sites) had a significant part of the ^{90}Sr (>20%) migrate deeper than 30 cm (Kashparov et al. 2001). A high migration ability of ^{90}Sr is observed only in low-humus sands. In soils from Belarus near the Chernobyl accident site, K_d values were 43, 59, and 150 L/kg for soddy-podzolic, soddy-loamy sandy, and peaty-gley soils, respectively (Sokolik et al. 2001). Organic matter in soils has a substantial effect on the transport of strontium through soils into groundwater. K_d values decreased down the soil profile in Podzol forest soil with an organic rich top soil and lower clay layers, from 140 to 44 L/kg (Bunzl and Schimmack 1989). Sr^{2+} chemically complexes with organic matter by partially neutralizing exchangeable sites on organic matter resulting in the precipitation of organic matter-Sr^{2+} complexes (Helal et al. 1998a). High concentrations of ion exchangeable Ca^{2+} in soil enhances the complexation of Sr^{2+} with organic matter and increases the removal of Sr^{2+} from solution, which results in reduced Sr^{2+} mobility (Helal et al. 1998a). However, nitrate fertilizers inhibit the formation of Sr^{2+}-organic matter complexes and increase Sr^{2+} mobility (Helal et al. 1998b). K_d values of 15–40 L/kg were measured for $^{90}Sr^{2+}$ in aquifer sediments near Liquid Waste Disposal Facilities at the Hanford site in Washington, where rapid ion exchange dominates (DOE 1996d). K_d was measured for $^{90}Sr^{2+}$ in aquifer sediments beneath waste water ponds that contained high salt concentrations at the Idaho National Environmental and Engineering Laboratory (INEEL) (Bunde et al.

1998); and values ranged from 56 to 62 L/kg at initial concentrations of sodium and potassium of 300 and 150 mg/L, respectively. For initial aqueous concentrations of sodium between 1,000 and 5,000 mg/L, K_d values were 4.7 and 19 L/kg, respectively. At the Chalk River Nuclear Laboratory in Ontario, Canada, a ^{90}Sr waste plume in groundwater initially advanced rapidly as ^{90}Sr was out competed by high concentrations of Ca^{2+} and Mg^{2+} for sorption sites in sediments, and as concentrations of Ca^{2+} and Mg^{2+} declined, the migration of the ^{90}Sr plume slowed (Toran 1994). High salt concentrations (marine, brines, or high salinity water) can increase the mobility of $^{90}Sr^{2+}$ by decreasing strontium sorption to sediments (Bunde et al. 1997, 1998) and increase the transport of strontium with the environmental cycling of water.

Strontium is not necessary for growth or reproduction for most plants, but is typically absorbed to satisfy the plant's metabolic requirements for calcium (NCRP 1984). Soil to plant concentration ratios for strontium (the ratio of the concentration of strontium in wet vegetation to the concentration of strontium in dry soil) are 0.017–1.0 (NCRP 1984), and indicate that strontium can be easily absorbed into plants from soil. The uptake of strontium by plants is greatest in sandy soils having low clay and organic matter content (Baes et al. 1986). The concentration of nutritive mineral elements in soil such as calcium lower the intake of strontium to the aboveground phytomass. The average reduction of the soil-to-plant concentration ratios for ^{90}Sr caused by amendment with Ca or K is around 50–60% (Lembrechts 1993).

Strontium may be deposited on plant surfaces from the atmosphere, remain on the plant, be washed off, or be absorbed directly into the plant through leaves. Contamination by direct deposition on foliage surfaces is predominantly a short-term mechanism with a weathering half-life of approximately 14 days (Lassey 1979). Carini et al. (1999) examined the mechanism of translocation in three species of fruit-bearing plants exposed to aerial deposition of ^{85}Sr and found that translocation of ^{85}Sr is localized to the area of contamination on the plant. However, uptake of strontium through the leaves is minor compared to root uptake. Once absorbed in the plant, strontium translocates to other parts of the plant, such as the leaves or fruit. Translocation of strontium in plants is affected by the particular species and stage of organism growth, and the most metabolically active parts (growing) will accumulate higher concentrations of strontium (Kodaira et al. 1973).

Strontium, taken up by plants and translocated to the aboveground plant compartments, has been observed for deep-rooted plants such as chasima *(Chrysothamnus nauseosus)*, mulberry vegetation *(Morus alba)*, quaking aspen *(Populus tremuloides)*, and red maple *(Acer rubrum)* growing on top of low level waste burial sites or contaminated soils (Cooper and Rahman 1994; DOE 1995; Fresquez et al. 1996a). The top growth of the plant material releases strontium to the soil surface through leaf fall. Downward migration

of ^{90}Sr is slowed by recycling of the contaminated litter by vegetation (Cooper and Rahman 1994). Subsurface ^{90}Sr can be transported from soil to top soil by burrowing animals, and is spread to the surrounding environment via animal tissues and fecal deposits. At the Subsurface Disposal Area at the INEL, deer mice had the highest contamination of all animals from ingestion of ^{90}Sr-contaminated low level nuclear waste. In addition, the biotic intrusion of soils covering the waste site brings water infiltration into buried LLW (Arthur and Janke 1986).

The uptake or bioaccumulation of strontium by plants and organisms is the mechanism by which strontium in air, water, and soil enters into the food chain of humans. Bioconcentration factors (BCFs) have been measured by several investigators in both aquatic and terrestrial organisms for ^{90}Sr (NCRP 1984). BCF values for ^{90}Sr in aquatic, terrestrial, and wetland ecosystems at the Savannah River Site were reported by Friday (1996) and are summarized in Table 6-2. The study illustrates that the organisms with the highest uptake are aquatic organisms such as fish (large-mouthed bass), macroinvertebrates (insects), macrophytes (white-water lilies and bladderwort), and zooplankton. Because of the similarity of strontium to calcium, boney fish had a very high BCF, with a value >50,000 measured in the boney tissue (Friday 1996). In the muscle tissue of boney fish, BCF values for ^{90}Sr ranged from high (benthic invertebrate and fish feeders; 610) to very high (piscivores; 3,400). Because strontium and calcium are chemically similar, the concentration of calcium in water can influence the bioaccumulation of strontium in biota. Organisms such as fish bioaccumulate strontium with an inverse correlation to levels of calcium in water. However, this correlation is not universal and does not apply to other organisms such as algae and plants (NCRP 1984).

6.3.2 Transformation and Degradation

Because strontium is an element, its atoms do not degrade by environmental processes such as hydrolysis or biodegradation. However, radioactive strontium will be subject to radioactive decay and transformation to other elements. Eventually, all of the radioactive strontium will be transformed into stable zirconium by the process of radioactive decay (see Section 4.2):

$$^{90}\text{Sr}\ (t_{½} = 29\ \text{years}) - {}^{90}\text{Y}\ (t_{½} = 64\ \text{hours}) + \beta^{-} - {}^{90}\text{Zr}\ (\text{stable}) + \beta^{-}$$

Both radioactive and nonradioactive strontium compounds are subject to both biotic and abiotic transformation mechanisms.

Table 6-2. Selected Bioconcentration Factors for ^{90}Sr in Aquatic, Wetland, and Terrestrial Ecosystems at the Savannah River Site

Organism	Bioconcentration factors for ^{90}Sr		
	Minimum	Maximum	Mean
Algae		600	
Clam, shell		1,300	
Fish muscle			
Insect and bottom invertebrate feeders		<48	
Piscivores		3,400	
Benthic invertebrate and fish feeders		610	
Fish bone			
Insect and bottom invertebrate feeders		2,400	
Piscivores		63,000	
Benthic invertebrate and fish feeders		57,000	
Detritus and plankton feeders		51,000	
Macroinvertebrates, larvae	520	54,000	27,300
Macrohytes (rooted vascular)	2,100	8,500	5,500
Macrophytes (floating vascular)		9,400	
Zooplankton		3,900	
Corn			
Grain		0.15	
Leaves		13.1	
Pine tree, leaves	0.88	1.69	1.29
Soybeans		2.51	
Tree (maple, sweetgum, and poplar)			
Wood		0.81	
Bark		11	
Leaf		3.8	

Source: Friday 1996

6.3.2.1 Air

The presence of strontium and radioactive strontium compounds in the atmosphere results from both natural and anthropogenetic activities (see Section 6.2.1). Strontium is emitted into the atmosphere as strontium oxide (SrO) during thermal processes. SrO is unstable and reacts with moisture or carbon dioxide in the air to form strontium hydroxide ($Sr[OH]_2$) or strontium carbonate ($SrCO_3$), respectively. $Sr[OH]_2$ in contact with water in clouds or during washout by rain will ionize to form Sr^{2+} and $SrOH^+$ ions. There is no evidence in the literature for interaction of SrO with other compounds in the atmosphere.

6.3.2.2 Water

Strontium exists almost exclusively in the environment as a +2 cation, and will form different species, some of which are more soluble than others. Because the different species have different solubilities, they will have different mobilities in the environment and different exposure potentials. Strontium exists as a hydrated cation, an ionic solution complex, or an ionic salt. In the environment, typical solution species for strontium are Sr^{2+} and $SrOH^+$, and some strontium compounds ($SrCO_3$ and $SrSO_4$) are practically insoluble in neutral water (Cotton and Wilkenson 1980; see Table 4-2).

6.3.2.3 Sediment and Soil

The principal abiotic processes that transform strontium in soils and sediments are mediated by sorption and desorption reactions between the soil solution and matrix (precipitation, complexation, and ion exchange), and controlled by pH, ionic strength, solution speciation, mineral composition, organic matter, biological organisms, and temperature (see Section 6.3.1). For many soil systems, in the short term, strontium sorption is dominated by simple ion exchange, and strontium ions are readily exchangeable. At longer timescales, however, strontium ions may relocated into sterically hindered sites that are not readily exchangeable (Bunker et al. 2000).

In the vicinity of the Chernobyl accident site, ^{90}Sr has leached from “hot” fuel particles (which have dissolved) and now may interact with natural soil components (Sokolik et al. 2001). In situations where soil is incorporated into a nuclear fireball (e.g., Semipalatinsk Nuclear Test Site, Kazakhstan), the resulting fused silicates that form are usually comparatively insoluble. Typically, ^{90}Sr in these particles

are tightly bound with the majority of ^{90}Sr undergoing radioactive decay before being released by weathering (Gastberger et al. 2000).

6.3.2.4 Other Media

No data were located in the literature on the transport or degradation of stable or radioactive strontium in other media.

6.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

Strontium is widely distributed throughout the earth and has continuously cycled between the atmosphere, biosphere, hydrosphere, and lithosphere for many millions of years. Table 6-3 illustrates the average or range of concentrations of strontium in earth materials (Capo et al. 1998). Anthropogenic activities have increased local concentrations of strontium as a consequence of the development of an industrialized human society. Before the 1940s, radioactive strontium was not present in the environment at any measurable levels.

In the United States, commercial nuclear power plant operators are required to monitor and report any detectable quantities of radioactive materials released to the environment (USNRC 1996). Table 6-1 summarizes releases of radiostrontium isotopes with half-lives >8 hours to the atmosphere and water for 1993 from PWR and BWR nuclear power plants. Nearly all of the radioactive material reported as released in effluents are from planned releases from normal plant operation or anticipated operational occurrences. The latter includes unplanned releases of radioactive materials from miscellaneous actions such as equipment failure, operator error, or procedure error, and are not of such consequence as to be considered an accident (USNRC 1993a).

6.4.1 Air

According to two surveys, the strontium content in urban air ranges from 4 to 100 ng/m^3 and averages 20 ng/m^3 (Dzubay and Stevens 1975). The arithmetic mean concentration of strontium in urban air was measured as 29.1 ng/m^3 in the Los Angeles basin during 1985 (Witz et al. 1986). Urban air in Illinois between 1985 and 1988 averaged 0.9–4.8 ng/m^3 (Sweet et al. 1993). Areas where higher strontium

Table 6-3. Average or Ranges of Concentration of Strontium in Earth Materials

Material	Concentration of strontium
Geologic	(ppm)
Average crust	370
Exposed upper crust	337
Soil:	
Soil minerals	240
Soil (labile)	0.2–20
Individual rock types:	
Basalt	465
Carbonate	610
High-Ca granite	440
Low-Ca granite	100
Sandstone	20
Shale	300
Biologic	(ppm)
Wood	8–2,500
Roots (spruce)	19
Conifer needles	2–20
Hydrologic	(µg/L)
Seawater	7,620
Rivers	6–800
Rain	0.7–383
Snow	0.01–0.76

Source: Capo et al. 1998

concentrations are prevalent are near coal burning plants where strontium can be released with stack emissions (as discussed in Section 6.2.1).

Before the 1940s, radiostrontium was not present in the air at any significant concentrations. Concentrations of ^{90}Sr in the atmosphere peaked at about 10 MCi (0.37 GBq) in 1963 coincident with the period of extensive atmospheric nuclear weapons testing. Since the signing of the Nuclear Test Ban Treaty of 1963, the concentration of ^{90}Sr has steadily dropped through the latter 35 years by deposition and radioactive decay (DOE 1996c; Eisenbud 1987). Recent levels of ^{90}Sr in air were not located.

6.4.2 Water

Surveys of strontium in surface waters and municipal water supplies across the United States show that strontium is present in nearly all fresh waters in amounts <1 mg/L (USGS 1963). The National Drinking Water Contaminant Occurrence Database (NDOD), which contains data from public water supplies (PWS), where testing is performed at many points in the system, including the intake and at various points in the treatment and distribution systems, as well as at the point where the drinking water can be labeled "finished", lists the number of detections and concentrations of strontium. The average concentrations of strontium in PWS waters from the United States derived from surface water and groundwater were 1.10 (range, 0.2–3.68 mg/L) and 0.81 mg/L (range, 0.010–3.5 mg/L), respectively (EPA 2002b). The average concentrations of strontium in streams of the United States are between 0.5 and 1.5 mg/L. Strontium concentrations >1 mg/L are found in streams of the southwest, where the total dissolved solids content is the highest of any area of the continental United States. Streams of most of the Atlantic slope basins, southern United States, upper Great Lakes region, and Pacific northwest contain concentrations of strontium that are generally <0.5 mg/L strontium (USGS 1963). Some exceptions are areas where there are celestite-rich limestone deposits, such as regions of northwestern Ohio and eastern Florida (USGS 1963). The average concentration of strontium in sea water is approximately 8 mg/L (Demayo 1986). In groundwater, the average concentration of strontium is <0.5 mg/L. High concentrations of strontium, >1 mg/L, have been in observed in the southwestern United States. Unusually high concentrations of strontium, >20 mg/L, have been observed for some wells in central Wisconsin (USGS 1963). The NDOD lists the number of detections and concentrations of strontium in groundwater and surface water at several locations around the United States from ambient water samples (EPA 2002b). Dissolved strontium was detected in groundwater at 4,353 of 4,383 sites (99.3% of sites), with an average concentration of 1.6 mg/L (range, 0.0009–200 mg/L). The average dissolved strontium concentration in lake/reservoirs and springs were 1.09 mg/L (97.6% of sites; range, 0.002–170 mg/L) and

0.64 mg/L (100% of sites; range, 0.028–3.2 mg/L), respectively. In other surface waters, dissolved strontium was detected at 1,572 of 1,595 sites (98.6% of sites), with an average concentration of 362 µg/L (range, 0.0005–30 mg/L). The concentration of dissolved strontium in publicly owned treatment works (POTW) influents was between 0.025 and 0.45 mg/L (EPA 1981). The average concentrations of strontium in rain and snow were 0.7–383 and 0.01–0.76 µg/L, respectively (Capo et al. 1998).

^{90}Sr concentration in surface waters of the north Pacific Ocean has decreased steadily since the early 1960s to present day levels of approximately 23–81 pCi/m^3 (1–3 Bq $^{90}Sr/m^3$) sea water. This value is estimated by dividing the concentration levels for ^{137}Cs by the global fallout activity ratio measured for $^{137}Cs/^{90}Sr$ of 1.5 (Hamilton et al. 1996). The EPA ERAMS program monitors ambient concentrations of ^{90}Sr in drinking water at 78 sites. ERAMS data serve to assess trends and anomalies in concentrations, and to compare with standards set forth in the EPA National Interim Primary Drinking Water Regulations. Table 6-4 summarizes drinking water composite samples for the period of January–December in 1995 taken at the 78 sites in major population centers or near selected nuclear facilities (EPA 2000a). The median concentration of ^{90}Sr in drinking water for this period was 0.1 pCi/L (4 mBq). Sites with above average levels of ^{90}Sr, Detroit and Niagara Falls, recorded levels of 0.4 and 0.5 pCi/L (~15 mBq/L), respectively. In a 1974 study, a concentration of 0.09 pCi/L ^{90}Sr (3 mBq/L) in drinking water was measured in Los Angeles, California (Kraybill 1983). In a survey that examined 169 wells used for public drinking water in California (Storm 1994), 16 wells measured recordable concentrations of ^{90}Sr, with an average concentration of 105 pCi/L (4 Bq/L). The NDOD lists the number of detections of ^{90}Sr in ambient groundwater at several locations around the United States. Dissolved ^{90}Sr was detected in groundwater at 18 out of 104 sites (17%), with an average concentration of 1.46 nCi/L (53.9 Bq) (EPA 2002b). The concentrations of ^{90}Sr in groundwater at the 91 waste sites located at 18 DOE facilities were between 0.05 and 231,000 pCi/L (2 mBq and 9 kBq) (DOE 1992). River water taken from the Ebro River basin (Northeast Spain) during 1994 had a mean ^{90}Sr level of 6.6 mBq (0.18 pCi) and ranged from 5.9 to 7.6 mBq/L (0.16 to 0.21 pCi/L) (Pujol and Sanchez-Cabeza 2000). ^{90}Sr in the Ebro River waters could be attributed solely to global fallout. The DOE Environmental Measurements Laboratory program measures the ^{90}Sr content of wet deposition in selected sites across the world to determine global trends in ^{90}Sr deposition. The data for the year 1990 are presented in Table 6-5 for cities in the United States. The average total annual wet deposition of ^{90}Sr in the United States was 5 pCi/m^2 (0.2 Bq/m^2) during this period. The precipitation samples with the highest total ^{90}Sr concentrations were obtained from New York City and Nome, Alaska with annual totals of 10 and 8 pCi/m^2 (0.4 and 0.3 Bq/m^2), respectively. In all cases, the ^{90}Sr concentrations in rain were low, which suggests that the atmospheric content of ^{90}Sr in 1990 was small and decreasing (DOE 1996c).

Table 6-4. ^{90}Sr in Drinking Water (Composites) for January–December 1995

State[a]	City	Total solids (mg/L)	^{90}Sr	
			pCi/L	±2σ
AK	Fairbanks	162.0	0.0	0.2
AL	Dothan	160.0	0.1	0.1
AL	Montgomery	55.2	0.1	0.2
AL	Muscle Shoals	82.0	0.2	0.2
AL	Scottsboro	87.0	0.2	0.2
AR	Little Rock	28.8	0.0	0.2
CA	Berkeley	8.0	0.1	0.2
CA	Los Angeles	318.0	0.0	0.1
CO	Denver	140.0	0.0	0.2
CO	Platteville	138.0	0.0	0.2
CT	Hartford	36.6	0.3	0.2
DE	Dover	191.0	ND	—
FL	Miami	150.0	0.2	0.2
FL	Tampa	252.0	0.3	0.2
GA	Baxley	165.0	0.0	0.2
GA	Savannah	147.0	ND	—
HI	Honolulu	208.0	0.1	0.1
IA	Cedar Rapids	121.0	0.1	0.2
ID	Boise	95.5	ND	—
ID	Idaho Falls	219.0	ND	—
IL	Morris	474.0	ND	—
IL	West Chicago	337.0	0.1	0.1
KS	Topeka	364.0	0.2	0.2
LA	New Orleans	226.0	0.2	0.2
MA	Lawrence	93.8	0.2	0.2
MD	Baltimore	89.8	0.1	0.2
MD	Conowingo	155.0	0.1	0.2
ME	Augusta	85.2	0.3	0.2

Table 6-4. ^{90}Sr in Drinking Water (Composites) for January–December 1995

State[a]	City	Total solids (mg/L)	^{90}Sr	
			pCi/L	±2σ
MI	Detroit	79.8	0.4	0.2
MI	Grand Rapids	125.0	0.3	0.2
MN	Minneapolis	93.8	0.3	0.2
MN	Red Wing	238.0	0.0	0.2
MO	Jefferson City	283.0	0.0	0.2
MS	Jackson	86.8	0.2	0.2
MS	Port Gibson	313.0	0.0	0.1
MT	Helena	61.8	0.1	0.2
NC	Charlotte	46.8	0.1	0.2
NC	Wilmington	110.0	0.2	0.2
ND	Bismarck	329.0	0.0	0.2
NE	Lincoln	305.0	0.1	0.2
NH	Concord	81.2	0.1	0.2
NJ	Trenton	92.7	0.1	0.2
NJ	Waretown	52.0	0.0	0.2
NM	Santa Fe	279.0	ND	—
NV	Las Vegas	248.0	0.1	0.2
NY	Albany	68.8	0.3	0.2
NY	New York City	44.5	0.0	0.2
NY	Niagara Falls	99.2	0.5	0.2
NY	Syracuse	94.8	0.3	0.2
OH	Cincinnati	198.0	0.2	0.2
OH	Columbus	362.0	0.0	0.3
OH	East Liverpool	215.0	0.3	0.2
OH	Painesville	126.0	0.2	0.3
OH	Toledo	148.0	0.3	0.3
OK	Oklahoma City	62.6	0.3	0.2
OR	Portland	19.2	0.1	0.2

Table 6-4. ^{90}Sr in Drinking Water (Composites) for January–December 1995

State[a]	City	Total solids (mg/L)	^{90}Sr pCi/L	^{90}Sr ±2σ
PA	Columbia	121.0	0.1	0.2
PA	Harrisburg	51.2	0.1	0.2
PA	Philadelphia	165.0	0.0	0.2
PA	Philadelphia-Queen	207.0	0.1	0.2
PA	Philadelphia-Baxter	101.0	0.2	0.2
PA	Pittsburgh	178.0	0.2	0.2
PC	Corozal	71.6	0.1	0.2
RI	Providence	52.8	0.3	0.2
SC	Barnwell	73.6	0.0	0.2
SC	Columbia	28.2	0.0	0.2
SC	Jenkinsville	165.0	ND	—
SC	Seneca	35.2	0.1	0.2
TN	Chattanooga	82.2	0.2	0.2
TN	Knoxville	93.8	0.0	0.2
TX	Austin	180.0	0.0	0.2
VA	Doswell	193.0	0.0	0.2
VA	Lynchburg	45.2	0.1	0.2
VA	Virginia Beach	91.2	0.3	0.2
WA	Richland	77.2	0.1	0.2
WA	Seattle	29.8	0.0	0.2
WI	Genoa City	194.0	ND	—
WI	Madison	234.0	ND	—

[a]Post office state abbreviations used

ND = not detected;
2σ = counting error term reported at the 2σ (95%) confidence level

Source: EPA 1995

Table 6-5. Quarterly and Annual Deposition of ^{90}Sr in Selected U.S. Cites for the Year 1990

	Quarter								Annual total	
	First		Second		Third		Fourth			
Location	^{90}Sr Deposition[a]	Precipitation[b]	^{90}Sr Deposition[a]	Precipitation[b]	^{90}Sr Deposition[a]	Precipitation[b]	^{90}Sr Deposition[a]	Precipitation[b]	^{90}Sr Deposition[a]	Precipitation[b]
Anchorage, Alaska	0.0	8.5	0.0	6.5	—	15.9	—	29.7	0.0	60.5
Argonne, Illinois	0.1	18.6	0.1	33.4	0.1	26.9	0.0	29.5	0.2	108.4
Birmingham, Alabama	0.1	50.6	0.0	22.2	0.0	14.7	0.0	31.7	0.1	119.3
Chester, New Jersey	0.0	23.2	0.1	44.7	0.1	39.2	0.1	39.3	0.2	146.4
Cold Bay, Alaska	0.0	20.3	0.0	14.7	0.1	29.5	0.0	31.1	0.1	95.5
Fairbanks, Alaska	0.0	3.4	0.0	5.6	0.1	25.9	0.1	12.1	0.2	47.1
Houston, Texas	0.0	31.4	0.0	26.0	0.0	22.0	0.0	21.8	0.0	101.2
Lihue, Hawaii	0.0	36.7	0.0	14.5	0.0	12.2	0.1	36.6	0.1	100.0
Mauna Loa, Hawaii	0.0	54.5	0.0	0.3	0.1	7.5	0.0	44.9	0.1	107.2
Miami, Florida	0.0	9.4	0.0	54.8	0.0	48.0	0.1	19.1	0.2	131.1
New York, New York	—	28.7	0.1	42.5	0.1	46.0	0.1	37.5	0.4	154.7
Nome, Alaska	0.1	5.4	0.0	10.8	0.2	27.0	0.1	13.2	0.3	56.3
Vermillion, South Dakota	0.0	5.5	0.0	28.7	0.0	20.6	0.0	6.0	0.1	60.7
West Los Angeles, California	0.1	16.7	0.1	5.3	0.1	0.1	0.0	4.1	0.2	26.2
Wooster, Ohio	0.0	16.5	0.1	28.0	0.0	43.5	0.0	36.9	0.1	124.8
Average	0.03	22.0	0.03	22.5	0.06	25.3	0.04	26.2	0.2	96.0

[a]In Bq/m^3
[b]In cm

Source: DOE 1996d

6.4.3 Sediment and Soil

Table 6-3 summarizes the average or range of concentrations of strontium in soils and bedrock minerals. The average concentrations of strontium in the earth's crust and the exposed upper crust are 370 and 337 mg/kg, respectively. Soils, on average, have approximately 240 mg/kg Sr (Capo et al. 1998; EPA 1995a). Some materials, such as soil amendments, are routinely applied to agricultural lands. Typical concentrations of strontium in soil amendments are: POTW sewage sludges, 250±192 ppm (mg/kg dry weight); phosphate fertilizers, 610 mg/kg; limestone, 610 mg/kg; and manure, 80 mg/kg dry weight (EPA 1995a; Mumma et al. 1984).

The background level of ^{90}Sr in soils of the United States from global fallout will depend upon the historical transport and deposition inventory at that particular location. The mean regional background concentration of ^{90}Sr in soils in proximity to the Los Alamos National Laboratory from 1974 to 1994 was 320±250 pCi/kg dry weight soil (Fresquez et al. 1996b). This value has decreased with time due to radioactive decay of ^{90}Sr. The range of concentrations for ^{90}Sr in soils and sediments at 91 waste sites located at the 18 DOE facilities around the United States was 0.02–540,000 pCi/kg (DOE 1992). The total content of ^{90}Sr on surface soil in the 30 km contaminated zone around Chernobyl accident site in the Ukraine (not including the reactor site and waste storage) was about $8.1x10^{14}$ Bq ($2.2x10^{7}$ Ci) in 1997, which corresponds to about 0.4–0.5% of the Chernobyl reactor inventory at the time of the accident (Kashparov et al. 2001). Ten years after the accident, about 95% of the ^{90}Sr activity is associated with the upper 10–20 cm layer of soil for most of the soils in this area. Mean ^{90}Sr activity in soil at a Chernobyl-contaminated field site in the Ukraine was 36 Bq dry weight (0.97 nCi dry weight) (Malek et al. 2002). Levels of ^{90}Sr in soils from Belarus situated at a distance of ~40 km from the Chernobyl accident site ranged from 50 to 640 kBq/m^2 (1.4–17 μCi/m^2), while levels at a distance of 200–250 km ranged from 10–80 kBq/m^2 (270–2,200 nCi/m^2) (Sokolik et al. 2001).

The mean activity of ^{90}Sr in lacustrine and marine sediments from Antarctica in 1989–1996 ranged from 0.17 to 0.76 Bq/kg dry weight (4.59–20.5 pCi/kg dry weight) and from <0.10 to 0.21 Bq/kg dry weight (<2.7–5.78 pCi/kg dry weight), respectively (Jia et al. 1999). The ^{90}Sr activities in marine sediments ranged from 117 to 1,277 mBq/kg (3.16 and 34.5 pCi/kg) and from 304 to 1,799 mBq/kg (8.21–48.6 pCi/kg) at two sites off atomic power stations in South Korea (Yang et al. 2002). $^{90}Sr^{2+}$ ions in sediments are characterized by reversible ion exchange processes that lead to low ^{90}Sr activity in sediments (Jia et al. 1999).

6.4.4 Other Environmental Media

The range of concentrations of strontium in fruits and vegetables is summarized in Table 6-6 (Barnes 1997). The highest concentrations are observed in leafy vegetables, such as cabbage (64.2 mg Sr/kg dry weight) (USGS 1980).

The range of concentrations of ^{90}Sr in food stuffs is summarized in Table 6-7. The highest concentrations were observed in fresh vegetables (8.8 pCi/kg dry weight=0.33 Bq/kg dry weight) and dry beans (15.9 pCi/kg dry weight=0.59 Bq/kg dry weight) (Eisenbud 1987). The U.S. Food and Drug Administration Radionuclides in Foods program monitors radionuclides (e.g., ^{90}Sr) in the food supply as part of the Total Diet Study (TDS). For the years 1994 and 1995, about 60 foods with historically high ^{90}Sr levels were analyzed (Capar and Cunningham 2000). ^{90}Sr was detected in about 65% of these foods. The greatest concentration was in mixed nuts at 2 Bq/kg (50 pCi). Approximately 200 reactor-survey food test portions, including raw vegetables, food crops (primarily fruits), fish, and milk, were collected in the vicinities of 33 nuclear reactors (Cunningham et al. 1994). Ninety-four percent of the reactor-survey food test portions had ^{90}Sr activities between 0 and 0.74 Bq/kg (0 and 20 pCi), and 6% had activity concentration between 0.74 and 7.4 Bq/kg (20 and 200 pCi/kg). The EPA ERAMS program monitors ambient concentrations of ^{90}Sr in pasteurized milk at 42 sites in major population centers, and is used to assess trends and anomalies in concentrations. Table 6-8 summaries pasteurized milk samples for the period of July 1997 (EPA 2002b). The average concentration of ^{90}Sr in pasteurized milk during this period for the 42 sites was 0.9 pCi/L (33 mBq/L). Sites with above average levels of ^{90}Sr in pasteurized milk were observed at (listed in order of decreasing activity of ^{90}Sr): Minot, North Dakota; Grand Rapids, Michigan; Spokane, Washington; Cleveland, Ohio; Cincinnati, Ohio; Memphis, Tennessee; St. Paul, Minnesota; Chicago, Illinois; Detroit, Michigan; San Francisco, California; Baltimore, Maryland; and Wilmington, Delaware. Dietary intake of ^{90}Sr peaked in 1965 at 1.1 Bq/day (30 pCi/day), during a period of atmospheric testing of nuclear weapons, and has continued to decline to <0.05 Bq/day (<1.2 pCi/day) after 1987 (Cunningham et al. 1989). Dietary intake of ^{90}Sr in the United States from 1961 to 1991 is illustrated in Figure 6-3.

Sato et al. (1977) determined the concentration of strontium in tobacco leaves as 141 µg/g. The average concentration of strontium in the ash of 12 brands of cigarettes was measured as 373 µg/g (Iskander 1986). No significant difference was observed in the concentration of strontium in the cigarette filter before and after smoking (Sato et al. 1977). The ranges of concentrations of strontium in waste materials are: municipal solid waste (MSW) 11–35 µg/g; incineration fly ash 110–220 µg/g (Lisk 1988); coal fly

Table 6-6. Concentration of Strontium in Fruit Juices and Produce

Fruit juice and produce	Average liquid concentration (µg/L)[a]	Average solid concentration (ppm)[b]
Apple		13.58
Apple juice	0.1271	
Banana	0.1297	
Bean:		
Dry		6.63
Snap		21.7
Blackberry	0.2619	
Boysenberry	0.9523	
Cabbage		64.17
Corn:		
Sweet		0.416
Cucumber		24
Currant:		
Red	1.251	
Grape:		
American		25.6
Concord	0.3661	
European		38.4
Red	0.1086	
White	0.6318	
Kiwi	1.744	
Lemon products:		
Lemon	0.0986	
Bottled	0.5334	
Lemonade	0.1653	
Lettuce		22.26
Lime	0.3464	
Mango	0.5121	
Orange		25.56
Orange juice		
Brazilian	0.0417	
California	0.5368	
Florida	0.0933	
Navel	0.5209	
Pineapple	0.1612	
Papaya	1.690	
Peach		3.082
Pear	0.5912	
Pineapple	0.0604	

Table 6-6. Concentration of Strontium in Fruit Juices and Produce

Fruit juice and produce	Average liquid concentration (µg/L)[a]	Average solid concentration (ppm)[b]
Potato		2.562
Raspberry	2.232	
Strawberry	0.3001	
Tangerine	0.0828	
Tomato		9.96
Tomato sauce	0.8894	

[a]Barnes 1997
[b]USGS 1980; values are parts per million, dry weight

Table 6-7. ^{90}Sr in the Human Diets During 1982

				New York City			San Francisco		
Diet category	Intake kg/year	g Ca/year	Percent yearly intake Ca	pCi ^{90}Sr/kg	pCi ^{90}Sr/year	Percent yearly intake ^{90}Sr	pCi ^{90}Sr/kg	pCi ^{90}Sr/year	Percent yearly intake ^{90}Sr
Dairy products	200	216.0	58	3.2	641	32	1.0	200	21
Fresh vegetables	48	18.7		8.8	422		2.4	116	
Canned vegetables	22	4.4		5.4	119		2.9	64	
Root vegetables	10	3.8		3.4	34		3.8	38	
Potatoes	38	3.8		2.3	88		2.1	79	
Dry beans	3	2.1		15.9	48		7.9	54	
Total (vegetables)			9			36			36
Fresh fruit	59	9.4		2.6	152		1.3	77	
Canned fruit	11	0.6		1.1	12		0.8	9	
Fruit juice	28	2.5		1.7	48		1.4	40	
Total (fruits)			3			11			13
Bakery products	44	53.7		3.0	131		1.9	84	
Flour	34	6.5		4.5	153		3.5	119	
Whole grain products	11	10.3		6.2	69		2.9	32	
Macaroni	3	0.6		2.4	7		2.3	7	
Rice	3	1.1		0.6	2		0.8	2	
Total (grains)			20			18			25
Meat	79	12.6		0.4	35		0.4	31	
Poultry	20	6.0		0.3	6		0.3	5	
Eggs	15	8.7		0.6	10		0.6	8	
Fresh fish	8	7.6		0.2	1		0.1	1	
Shell fish	1	1.6		0.2	<1		0.7	1	
Total (meat, eggs, and fish)	-	-	10	-	-	3	-	-	5
Yearly intake									
Ca (total)		370 g							
^{90}Sr (total)					1978 pCi			967 pCi	
Ratio of ^{90}Sr/Ca					5.3 pCi ^{90}Sr/g Ca			2.6 pCi ^{90}Sr/g Ca	
Daily intake					54 pCi/day			2.6 pCi/day	

1 pCi=37 mBq (conversion factor)
Source: DOE 1984

Table 6-8. ^{90}Sr in Pasteurized Milk in July 1997

State[a]	City	^{90}Sr (pCi/L)
AL	Montgomery	0.98
CA	Los Angeles	0.66
CA	Sacramento	0.26
CA	San Francisco	1.24
CO	Denver	0.41
CT	Hartford	1.31
DE	Wilmington	1.00
FL	Tampa	0.59
GA	Atlanta	0.56
HI	Honolulu	0.38
IA	Des Moines	0.40
IL	Chicago	1.38
IN	Indianapolis	0.96
KY	Louisville	0.20
MA	Boston	0.77
MD	Baltimore	1.06
MI	Detroit	1.34
MN	Grand Rapids	1.78
MN	St. Paul	1.44
MO	Kansas City	1.14
MS	Jackson	—
NC	Charlotte	1.25
ND	Minot	2.12
NJ	Trenton	0.75
NM	Albuquerque	0.53
NV	Las Vegas	0.20
NY	Buffalo	0.75
NY	Syracuse	0.94
OH	Cincinnati	1.60

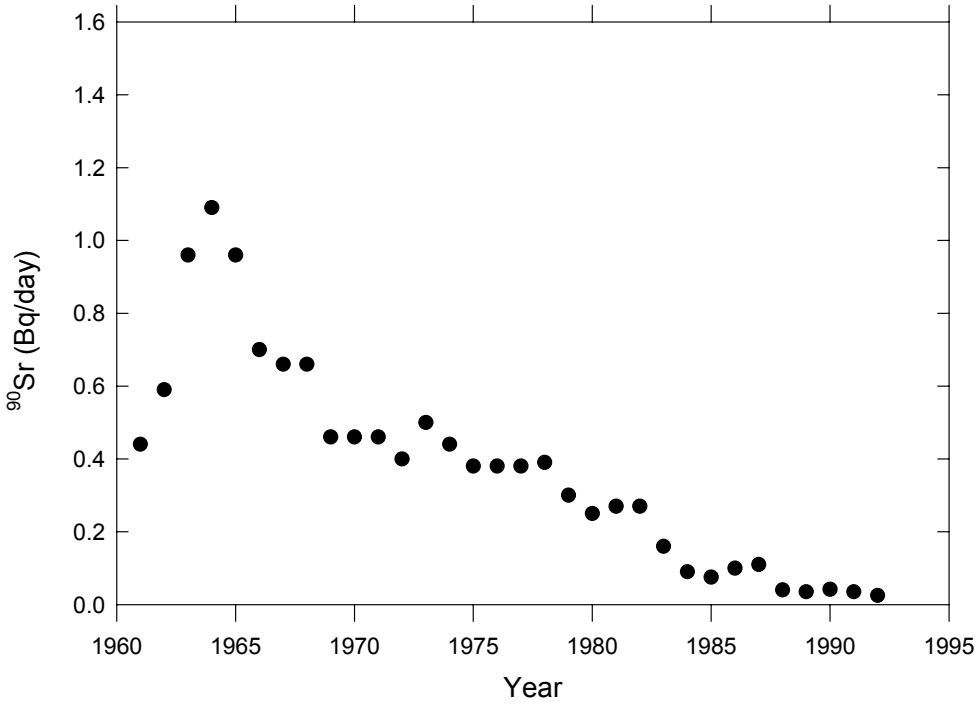
Table 6-8. ^{90}Sr in Pasteurized Milk in July 1997

State[a]	City	^{90}Sr (pCi/L)
OH	Cleveland	1.60
OR	Portland	0.79
PA	Philadelphia	0.84
PA	Pittsburgh	0.23
PC	Cristobal	0.27
PR	San Juan	0.51
SC	Charleston	0.73
TN	Memphis	1.54
TX	Austin	0.29
TX	Ft. Worth	0.50
VA	Norfolk	0.89
VT	Burlington	1.10
WA	Seattle	0.49
WA	Spokane	1.71

[a]Post office state abbreviations used

Source: EPA 2000b

Figure 6-3. U.S. Daily Dietary Intake of ^{90}Sr, 1961–1992



Source: Cunningham et al. 1994

ash 30–7,600 µg/g; coal bottom ash 170–6,400 µg/g; flue-gas desulfurization by-products 70–3,000 µg/g; oil ash 50–920 µg/g; (Eary et al. 1990); and compost 260–420 µg/g (Evans and Tan 1998).

Levels of ^{90}Sr were measured in tissue samples of animals killed by motorists near the low-level radioactive disposal site at Los Alamos National Laboratory and from background locations. The mean concentration of ^{90}Sr in tissues from deer and elk killed near the low-level radioactive disposal site were 460 and 230 mBq/kg (12 and 7.0 pCi), respectively, while concentrations at background locations were 130 and 6.3 mBq/kg (3.5 and 1.7 pCi), respectively (Ferenbaugh et al. 2002). Between 1994 and 1996, levels of skeletal ^{90}Sr in small mammals in the Exclusion Zone at Chernobyl, Ukraine averaged 297 Bq/g (8.0 nCi/g) (Chesser et al. 2000).

6.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

The primary routes of human exposure to strontium are from inhalation of aerosols and ingestion of food and drinking water containing strontium. The intake of strontium, therefore, depends upon the concentration of strontium in air, drinking water, and in the food items that comprise a person's diet, which may be highly variable. The average concentration of strontium in urban air is about 20 ng strontium/m^3 (see Section 6.4.1). Assuming that an adult breathes approximately 20 m^3 of air per day, the inhalation exposure would be 400 ng strontium/day. This value may be somewhat higher for persons living near sources of strontium emission. Workers employed at industrial facilities that produce, process, and use strontium and strontium compounds will have higher exposures. Similarly, strontium is taken into the body by ingestion of drinking water. Using the concentration of strontium in U.S. drinking water to be 1 mg/L (see Section 6.4.2), and the consumption rate as 2 L/day, the strontium intake from drinking water would be 2 mg/day. In a 1994 total diet study in the United Kingdom, the total dietary exposure to stable strontium was estimated at 1.3 mg/day (Ysart et al. 1999). As part of an Australian Market Basket Survey in 1994, the estimated daily intakes of strontium for female adults ranged from 0.89 to 1.2 mg/day (Gulson et al. 2001). Combining air, water, and diet exposures estimates, the total daily exposure to strontium is ~3.3 mg/day.

External exposure to ^{90}Sr is not a concern because of minor emission of penetrating radiation from ^{90}Sr. No estimate of the concentration of ^{90}Sr in air is available (see Section 6.4.1). However, it is assumed that ambient concentrations of ^{90}Sr in the atmosphere are small relative to exposures from water and diet. If the concentration of ^{90}Sr in average U.S. drinking water is estimated as 0.1 pCi/L (4 mBq/L) or one radiochemical event per 5–10 minutes (see Section 6.4.2), and the consumption rate of drinking water by

a normal adult is assumed to be 2 L/day, then the exposure from drinking water would be 0.2 pCi (7 mBq) per day. Since the inception of the TDS Radionuclides in Foods program in 1961, intake levels of ^{90}Sr in food have steadily declined from a peak level in 1965 of 1.1 Bq/day (30 pCi/day), to below 0.2 Bq/day (5 pCi/day) (Cunningham et al. 1989). A DOE Environmental Measurements Laboratory study estimated the average dietary intake of ^{90}Sr from 19 diet categories for individuals living in the urban areas of New York City and San Francisco. Table 6-6 summarizes the data from this study (DOE 1984). For both locations, vegetables accounted for more than a third of the yearly dietary intake of ^{90}Sr at 36%. In the vegetable group, fresh vegetables were the largest contributors of ^{90}Sr dietary intakes. The next largest contributor of ^{90}Sr was grains and dairy products. Using a conservative estimate of total dietary exposure for ^{90}Sr of 5 pCi/day (0.19 Bq/day) and drinking water exposure of 0.2 pCi/day (7 mBq/day), the total estimated daily exposure to strontium is approximately 5.2 pCi/day (0.19 Bq/day). Current population exposure levels to ^{90}Sr will be lower than this value as a result of decreasing concentrations of ^{90}Sr in the environment. However, this value may be somewhat higher for persons living near sources of ^{90}Sr, such as DOE facilities, and for workers employed at government facilities that produce, process, and use ^{90}Sr and ^{90}Sr waste compounds.

Table 6-9 summarizes measurements of concentrations of strontium in human tissues and body fluids resulting from consumption of food and water and from natural background sources (Tsalev 1984); these are nonoccupationally exposed populations. The highest concentrations of strontium are in the bones and teeth (Iyengar et al. 1978; Tsalev 1984).

The distributions of ^{90}Sr in the body are significantly different for males and females. As expected, the highest concentrations of ^{90}Sr are measured in the boney tissue. Males and females averaged 10.4 and 65 pCi/kg (0.38 and 2.4 Bq/kg) wet weight, respectively. Males had a much higher concentration of ^{90}Sr in the muscular tissue compared to females. The heart and psoas muscles had respective concentrations of ^{90}Sr for men averaging 13.9 and 18.7 pCi/kg (0.51 and 0.69 Bq) wet weight versus respective concentrations of 7.4 and 1.9 pCi/kg (0.27 Bq/kg and 70 mBq/kg) wet weight for females (Baratta and Ferri 1966). Approximately 1,000 human teeth, collected in southern Ukraine in 1990–1991, had ^{90}Sr activities ranging from 1.0 to 16.3 mBq/g ash (0.027–0.44 pCi/q ash) (Kulev et al. 1994).

Strontium can be released into the atmosphere as a result of glass manufacturing. In one study, the median ambient air concentration of strontium that both art glass makers and formers were chronically exposed was 0.1 μg strontium/m^3 (Apostoli et al. 1998). A National Occupational Exposure Survey conducted by NIOSH during 1981–1983 estimated the number of workers potentially exposed to

Table 6-9. Strontium Concentrations in Human Body Fluids and Tissues

Sample	Units[a]	Mean	Range
Blood	µg/L	27	No data
Bone	µg/g	138	63–281
Brain	µg/g	0.08	No data
Dental plaque	µg/g	48	<0.5–1,880
Erythrocytes	µg/L	7.2	No data
Feces	µg/day	1.5	No data
Hair	µg/g	4.2	0.75–10.8
Kidney	µg/g	0.1	No data
Liver	µg/g	0.15	No data
Lung	µg/g	0.38	No data
Milk	µg/L	20	17–295
Muscle	µg/g	0.05	No data
Nails (finger)	µg/g(dry weight)	No data	0.43–0.86
Plasma or serum	µg/L	40	10–70
Saliva	µg/L	11	8–63
Sweat	mg/7 hour	0.96	No data
Tooth (dentin)	µg/g	115	14–286
Tooth (enamel)	µg/g	128	14–286
Urine	µg/L	No data	<0.01–0.03

[a]Values are per wet weight unless otherwise noted.

Source: Tsalev 1984

strontium compounds in the workplace: strontium chloride (8,289), strontium fluoride (5,607), strontium hydroxide (385), and strontium nitrate (1,895) (NOES 1983).

Workers engaged in nuclear fuel cycle operations, such as the handling of radioactive strontium wastes, decontamination and decommissioning workers, contaminated soils, and waters may be potentially exposed to radioactive strontium. A case of accidental inhalation and dermal exposure to strontium titanate contaminated with ^{90}Sr used for lightning rods was recorded, which resulted in an exposure of approximately 10^5 Bq (2.7 mCi) to the workers (Navarro and Lopez 1998).

6.6 EXPOSURES OF CHILDREN

This section focuses on exposures from conception to maturity at 18 years in humans. Differences from adults in susceptibility to hazardous substances are discussed in 3.7 Children's Susceptibility.

Children are not small adults. A child's exposure may differ from an adult's exposure in many ways. Children drink more fluids, eat more food, breathe more air per kilogram of body weight, and have a larger skin surface in proportion to their body volume. A child's diet often differs from that of adults. The developing human's source of nutrition changes with age: from placental nourishment to breast milk or formula to the diet of older children who eat more of certain types of foods than adults. A child's behavior and lifestyle also influence exposure. Children crawl on the floor, put things in their mouths, sometimes eat inappropriate things (such as dirt or paint chips), and spend more time outdoors. Children also are closer to the ground, and they do not use the judgment of adults to avoid hazards (USNRC 1993a).

As part of an Australian Market Basket Survey in 1994, the estimated daily intakes of strontium for 6-month-old infants fed exclusively breast milk or infant formula were 47 and 254 µg/day, respectively (Gulson et al. 2001). The mean concentration of strontium in amniotic fluid and placenta ranged from 0.03 to 0.05 mg/L and from 1.6 to 3.2 µg/L, respectively, for mothers from Portugal (Carvalho et al. 2001). Harrison (1965) notes that strontium in human breast milk is transferred to newborns during breast feeding.

Specific information on the exposure of children to radiostrontium is limited. As for adults in the general population, small exposures to children occur from normal ingestion of food and drinking water and inhaling air. These exposures may be higher in areas near nuclear fuel processing sites and hazardous

waste sites containing radiostrontium. Future accidental exposures could potentially occur from nuclear weapons detonation and consequent contamination of air, water, and food.

Children typically ingest a higher percentage of diary products compared to adults. Levels of ^{90}Sr in body tissues tend to increase with age (Glowiak and Pacyna 1978). In a study in the Soviet Union between 1959 and 1971, children were reported to have elevated levels of ^{90}Sr in bone tissue between the ages of 1 and 4 years (Marei et al. 1976). The elevated levels of ^{90}Sr for children of this age were determined to be a direct result of diet, primarily from ^{90}Sr contaminated cow's milk. In a 1978 study in Poland, females between 0 and 20 years of age had the highest level of ^{90}Sr accumulation in the gonad tissues for all age levels (Glowiak and Pacyna 1978). No explanation as to a cause for this accumulation was provided. For 1979–1994 births, the average concentration of ^{90}Sr in deciduous teeth from children of Western Suffolk County (New York), Eastern Suffolk County (New York), Dade County (Miami, Florida), and Ocean County (New Jersey) were 1.56, 1.02, 2.80, and 1.54 pCi/g calcium, respectively (Gould et al. 2000). No additional information is available on whether children differ from adults in their weight-adjusted intake of strontium. There is no information on ^{90}Sr levels in amniotic fluid, meconium, cord blood, neonatal blood, or breast milk.

At hazardous waste sites, radiostrontium that is found in excess of natural background levels is most likely to be in soil and presents a special hazard for young children. Hand-to-mouth activity resulting in inadvertent soil consumption or intentional consumption of soil (pica behavior) will result in oral exposure to radiostrontium. Young children often play close to the ground and frequently play in dirt, which increases their dermal exposure to radiostrontium in dust and soil. The degree of hazard in each case depends on the form of strontium present at the waste site.

Compared to adults, the potential for radiostrontium exposure is greater for children who consume foods (e.g., milk, grains) produced in areas with elevated concentrations of radiostrontium in the soil and for children with elevated concentrations of radiostrontium in their drinking water. Children are more likely to be exposed to ^{90}Sr in cow's milk produced in contaminated areas. Table 6-8 summaries pasteurized milk samples in the United States for July 1997 (EPA 2002b). The average concentration of ^{90}Sr in pasteurized milk during this period was 0.9 pCi/L (33 mBq/L).

Other home exposures are unlikely since no household products or products used in crafts, hobbies, or cottage industries contain significant amounts of radiostrontium. Radiostrontium exposure to children from parents' work clothes, skin, hair, tools, or other objects from the workplace is possible if the parent

is exposed to radiostrontium at work. However, no specific cases of home contamination with radiostrontium were located in the literature.

6.7 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

Cigarettes and tobacco leaves are known to contain strontium, and individuals who smoke may be exposed to higher levels of strontium. Strontium has been found in the tobacco leaves and ash of cigarettes at average levels of 141 and 373 mg/kg, respectively (Iskander 1986).

The potential for ^{90}Sr exposure is greater for individuals who consume foods grown in areas with elevated concentrations of ^{90}Sr in soil, and for individuals with elevated concentrations of ^{90}Sr in drinking water. Industries where higher exposures to ^{90}Sr are known to occur include nuclear weapons test sites, nuclear weapons production, and nuclear reactors facilities. Populations with potentially high exposure include DOE employees involved in heavy construction, decontamination activities, chemical processing, and fabrication.

Populations with a relatively short food chains (e.g., Arctic peoples) and a higher per capita consumption of country foods that have elevated levels of contamination from radionuclides, will have a higher exposure to ^{90}Sr (Barrie et al. 1992). Caribou or reindeer feeding on arctic vegetation are more likely to accumulate higher body burdens of ^{90}Sr in edible tissues than other herbivorous animals with less restrictive diets (Witkamp 1966). Concentrations of ^{90}Sr in caribou meat per gram of calcium were high (150 pCi/g Ca) compared with those of Alaskan-grown cabbage (6 pCi/g Ca) and potatoes (8 pCi/g Ca), marine fish (5 pCi/g Ca), and whale meat (1 pCi/g Ca). Arctic peoples, who depend on caribou and reindeer for sustenance, may have an elevated body burden of ^{90}Sr compared to other people who consume a more varied diet (Witkamp 1966). However, the 1966 peak levels reported in this study are expected to have fallen to minuscule levels since the Test Ban Treaty of 1962.

6.8 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 strontium 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 strontium.

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 the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

6.8.1 Identification of Data Needs

Physical and Chemical Properties. Relevant data on the physical and chemical properties of strontium and strontium compounds are available in the literature and are sufficient to permit estimation of its environmental fate (ChemFinder 2002; Cotton and Wilkenson 1980; Hibbins 1997; HSDB 2002; Lide 1995, 2000; Merck 1989; Sigma-Aldrich 2000). The physical and chemical properties of radiostrontium and radiostronium compounds are expected to be equivalent to those for stable strontium. Data on the radioactive properties of isotopes of strontium are available (Lide 1995).

Production, Import/Export, Use, Release, and Disposal. Data regarding the past and present production and import/export volumes for strontium are available (Adams 1975; USGS 1998, 1999, 2002). The uses of strontium and strontium compounds are well known with more than 85% of all strontium consumed in the United States used in the manufacture of ceramics and glass products (Hibbins 1997; USGS 1999, 2002). Strontium is found in food products such as fruits and vegetables (Barnes 1997; USGS 1980). Since strontium is not covered under Superfund Amendments and Reauthorization Act (SARA), Title III, manufacturers and users are not required to report releases to the EPA's Toxics Release Inventory (TRI). Most nonradioactive strontium minerals, strontium compounds, and strontium-containing materials do not require special disposal and handling requirements.

Data regarding the past and present production and import/export volumes for radiostrontium are limited (DOE 1996b, 1996c). The uses of radiostrontium and radiostrontium compounds are restricted primarily to medicinal, analytical, and power generation applications (Alimov 2003; Murray 1994). Radioactive strontium (e.g., ^{90}Sr) was released into the atmosphere from aboveground testing of nuclear weapons during the period of 1945–1980. Nuclear weapon testing injects radioactive material into the stratosphere, which results in wide dispersal of radionuclides. However, atmospheric deposition of ^{90}Sr

has steadily decreased from a high in 1963 of approximately $1.10x10^8$ GBq (3.0 MCi) to <3,000 Ci in 1990, which suggests that global concentrations of ^{90}Sr in the atmosphere have declined (DOE 1996c). The disposal of radiostrontium and radiostrontium contaminated wastes is governed by the U.S. Nuclear Regulatory Commission (USNRC) regulations, and releases of radiostrontium and radiostrontium contaminated wastes are governed by USNRC and EPA regulations.

Environmental Fate. Information about the partitioning and mobility of strontium and strontium compounds in the environment is available (Bunde et al. 1997; Bunzl and Schimmack 1989; Hayes and Traina 1998; Helal et al. 1998a, 1998b; O'Day et al. 2000; Parkman et al. 1998; Sahai et al. 2000). Strontium released into the atmosphere from natural and anthropogenetic activities is transported and redeposited on the earth by dry or wet deposition (NCRP 1984). Because strontium is an element, its atoms do not degrade by environmental processes such as hydrolysis or biodegradation.

Information about the partitioning and mobility of ^{90}Sr in environment is available (Bunde et al. 1997, 1998; DOE 1996d; Kashparov et al. 2001; Mahara 1993; Sokolik et al. 2001; Toran 1994). Radiostrontium released into the atmosphere from anthropogenetic activities is transported and redeposited on the earth by dry or wet deposition (NCRP 1984). Radiostrontium does not degrade by environmental processes such as hydrolysis or biodegradation. However, radioactive strontium will be subject to radioactive decay and transformation to other elements. Eventually, all of the radioactive strontium will be transformed into stable zirconium by the process of radioactive decay. Additional information on the environmental fate of ^{90}Sr in different forms of mixed waste may be beneficial. Studies investigating mixed waste matrixes may be useful information for accessing the current and potential risk of the storage of liquid HLW in buried underground tanks. Mixed waste forms that pose the highest potential risk include mixtures such as metals-radiostrontium, metals-radiostrontium-organic acids, metals-radiostrontium-complexing agents, and metals-radiostrontium-ketones (DOE 1992).

Bioavailability from Environmental Media. The absorption and distribution of strontium and radiostrontium as a result of inhalation, dermal, or oral exposures have been discussed in Sections 3.5.1 and 3.5.2. Limited information on the bioavailability of strontium and radiostrontium from environmental media (e.g., plants and animals) is available. Additional studies on the bioavailability of strontium and radiostrontium from environmental media would be useful.

Food Chain Bioaccumulation. The uptake or bioaccumulation of strontium and radiostrontium by plants and organisms is the mechanism by which strontium and radiostrontium in air, water, and soil enter

into the food chain of humans. Information on tissue levels of strontium and radiostrontium indicating storage in the organism as a result of exposure to contaminated media would be useful. Information on whether strontium and radiostrontium are biomagnified (increased levels in predators resulting from the consumption of contaminated prey organisms) would also be helpful.

Exposure Levels in Environmental Media. Strontium has been detected in air (Dzubay and Stevens 1975; Sweet et al. 1993; Witz et al. 1986), water (Capo et al. 1998; EPA 1981, 2002b; USGS 1963), soil (Capo et al. 1998; EPA 1995a), plants (Sato et al. 1977), and foodstuff (Barnes 1997; USGS 1980). Reliable monitoring data for the levels of strontium in contaminated media at hazardous waste sites are needed so that the information obtained on levels of strontium in the environment can be used in combination with the known body burden of strontium to assess the potential risk of adverse health effects in populations living in the vicinity of hazardous waste sites. In a 1994 total diet study in the United Kingdom, the total dietary exposure to stable strontium was estimated at 1.3 mg/day (Ysart et al. 1999). As part of an Australian Market Basket Survey in 1994, the estimated daily intakes of strontium for female adults ranged from 0.89 to 1.2 mg/day (Gulson et al. 2001). Combining air, water, and diet exposures estimates, the total daily exposure to strontium is ~3.3 mg/day.

Radiostrontium has been detected in air (DOE 1996c; Eisenbud 1987), water (DOE 1992, 1996c; EPA 2000a, 2002b; Hamilton et al. 1996; Kraybill 1983; Pujol and Sanchez-Cabeza 2000), soil (DOE 1992; Fresquez et al. 1996b; Kashparov et al. 2001; Malek et al. 2002; Sokolik et al. 2001), and foodstuffs (Capar and Cunningham 2000; Cunningham et al. 1989, 1994; Eisenbud 1987; EPA 2002b). Information on levels of radiostrontium is needed. Exposure levels of ^{90}Sr in environmental media have decreased as a result of radioactive decay from a high in the 1960s. However, updated information on the concentration levels in air, water, soil, and food (e.g., milk products) may be useful. Specific monitoring of radiostrontium in airborne particulates may also be beneficial. Reliable monitoring data for the levels of radiostrontium in contaminated media at hazardous waste sites may be useful so that the information obtained on levels of radiostrontium in the environment can be used in combination with the known body burden of radiostrontium to assess the potential risk of adverse health effects in populations living in the vicinity of hazardous waste sites. Using a conservative estimate of total dietary exposure for ^{90}Sr of 5 pCi/day (0.19 Bq/day) (Cunningham et al. 1989) and drinking water exposure of 0.2 pCi/day (7 mBq/day) (EPA 2000a), the total estimated daily exposure to strontium is approximately 5.2 pCi/day (0.19 Bq/day).

Exposure Levels in Humans. Strontium has been detected in human tissues, as illustrated in Table 6-9 (Tsalev 1984). The highest concentrations of strontium are in the bones and teeth (Iyengar et al. 1978; Tsalev 1984). However, these data are not current (within 3 years). Additional human tissue monitoring data for strontium is needed for populations surrounding hazardous waste sites. This information is necessary for assessing the need to conduct health studies on these populations.

^{90}Sr has been detected in human tissues with the highest concentrations measured in boney tissues (Baratta and Ferri 1966; Kulev et al. 1994). However, these data are not current (within 3 years). Exposure levels of humans to ^{90}Sr have decreased as a result of radioactive decay from a high in the 1960s. Additional human tissue monitoring data for radiostrontium is needed for populations surrounding hazardous waste sites. This information is necessary for assessing the need to conduct health studies on these populations.

Exposures of Children. Children are exposed to strontium in the same manner as adults, primarily by food and water intake. No information was available on unique exposure pathways for children (e.g., pica children, dermal). However, children typically ingest a higher percentage of diary products compared to adults. Data exist on the levels of strontium in human breast milk (Gulson et al. 2001). Additional body burden studies on children are needed for strontium. Additional studies are needed to determine whether children are different in their weight-adjusted intake of strontium. Better and more recent information on exposure levels of strontium to children may be beneficial.

Children are exposed to radiostrontium in the same manner as adults, primarily by food and water intake. No information was available on unique exposure pathways for children (e.g., pica children, dermal). However, children typically ingest a higher percentage of diary products compared to adults. Exposure levels of children to ^{90}Sr have decreased as a result of radioactive decay from a high in the 1960s. Data exist on the levels of ^{90}Sr in deciduous teeth (Gould et al. 2000). Additional body burden studies on children are needed for radiostrontium. Additional studies are needed to determine whether children are different in their weight-adjusted intake of radiostrontium. Better and more recent information on exposure levels of radiostrontium to children may be beneficial.

Child health data needs relating to susceptibility are discussed in Section 3.13.2 Identification of Data Needs: Children's Susceptibility.

Exposure Registries. No exposure registries for strontium or radiostrontium were located. These substances are not currently compounds for which a subregistry has been established in the National Exposure Registry. These substances 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 exposure to this substance.

6.8.2 Ongoing Studies

The Federal Research in Progress (FEDRIP 2002) database provides additional information obtainable from a few ongoing studies that may fill in some of the data needs identified in Section 6.8.1. These studies are summarized in Table 6-10.

Table 6-10. Ongoing Studies on the Environmental Effects of Strontium[a]

Investigator	Affiliation	Study	Sponsor
Ron, Elaine	NIH	Studies of populations exposed to occupational sources of radiation	NIH
Helt, JE	ANL	Waste volume reduction using surface characterization and decontamination by laser ablation	DOE-OEM
Todd, Terry A	INEEL	Laboratory radioactive waste solvent extraction and ion exchange	DOE-OEM
Smith, Robert W	INEEL	Calcite precipitation and trace metal partitioning in groundwater and the vadose zone: Remediation of ^{90}Sr and other divalent metals and radionuclides in arid western environments	DOE-OEM
Louie, Gary D	PNNL	Chemical separations for nuclear waste disposal	DOE-OEM
Louie, Gary D	PNNL	Chemical speciation of strontium, americium, and curium in waste	DOE-OEM

ANL = Argonne National Laboratory; DOE-OEM = Department of Energy-Office of Environmental Management; INEEL = Idaho National Engineering and Environmental Laboratory; NIH = National Institute of Health; PNNL = Pacific Northwest National Laboratory

[a]Source: FEDRIP 2002

7. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting, measuring, and/or monitoring strontium, its metabolites, and other biomarkers of exposure and effect to strontium. The intent is not to provide an exhaustive list of analytical methods. Rather, the intention is to identify well-established methods that are used as the standard methods of analysis. Many of the analytical methods used for environmental samples are the methods approved by federal agencies and organizations 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 modify previously used methods to obtain lower detection limits and/or to improve accuracy and precision.

Its companion manual, the Draft Multi-Agency Radiological Laboratory Analytical Protocols (MARLAP) manual, robustly describes relevant analytical equipment and methods, and became available for public comment in July 2001 (MARLAP 2001).

7.1 BIOLOGICAL MATERIALS

Strontium can enter the human body through inhalation, ingestion, or penetration through the skin. Measurement of the quantities of radiostrontium in the body can be performed by two primary methods, *in vivo* measurements and *in vitro* measurements. These types of measurements are called bioassays. *In vivo* techniques measure the quantities of internally deposited radiostrontium directly using a whole body counter, while *in vitro* techniques permit estimation of internally deposited strontium by analysis of body fluids, excreta, or (in rare instances) tissues obtained through biopsy or postmortem tissue sectioning. Some of these analytical methods are summarized in Table 7-1.

7.1.1 Internal Strontium Measurements

In vivo (or direct) measurements of radioactive strontium in the body are made with radiation detector systems and associated electronics called whole body counters that measure radiation as it leaves the body from internally deposited radioactive strontium. This system measures the emission of gamma rays or x-rays from internally deposited radionuclides. These counters are insensitive to beta particles emitted

Table 7-1. Analytical Methods for Determining Strontium in Biological Samples

Sample matrix	Sample preparation	Analytical method	Detection limit	Percent recovery	Reference
Blood	Acidification with nitric acid; dilution; addition of La matrix modifier	GFAAS	0.13 mg/L	94.5–102.5	Burguera et al. 1999
Blood	Acid digestion; iron extraction; clean-up by ion exchange; thin film deposition	TRXF	0.04 µg/mL	No data	Prange et al. 1989
Blood	Acid digestion; dilution	ICP-AES	0.3 µg/L	113	NIOSH 1994; Piette et al. 1994
Blood serum	Dry ashing; neutron activation; chemical separation	TNA	0.02 µg/mL	75–90	Teree and Cohn 1966
Blood serum	Acidification and dilution	ICP-MS	No data	99	Muñiz et al. 1999
Bone	Acidification with nitric acid; dilution; addition of La matrix modifier.	GFAAS	0.13 mg/L	96.5–102.9	Burguera et al. 1999
Bone	Acid digestion	ICP-MS	6 µg/g dry weight	No data	Outridge et al. 1996
Bone ash	Acid dissolution; clean-up by coprecipitation and scavenging	β-GPC	No data	No data	Mutschke and Pribilla 1967
Hair	Ashed	PIXE	1 µg/g	No data	Clayton and Wooller 1985
Tissues	Acid digestion; dilution	ICP-AES	No data	113	NIOSH 1994
Tissues	Complexometric digestion in TMAH/EDTA matrix with heat	GFAAS	2.2 ng/g	99±4.2	D'Haese et al. 1996
Urine	Acidification with nitric acid; dilution; addition of La matrix modifier	GFAAS	0.13 mg/L	98.8–101.5	Burguera et al. 1999
Urine	Coprecipitation with calcium phosphate; sample wet ashed with nitric acid; extraction and separation on Crown ether loaded chromatographic column	LSC	7 dpm/L (0.82 Bq/L or 22 pCi/L)	95±5	Dietz et al. 1991
Urine	Wet ashed; precipitation with oxalate; acid dissolution; chemical extraction	LSC	0.6 pCi (22 mBq)	100	Kramer and Davies 1982

β-GPC (total radioactive strontium) = beta gas proportional counter; Bq = Becquerel; dpm = disintegrations per minute; EDTA = ethylenediamine tetraacetic acid; GFAAS (total strontium) = graphite furnace atomic absorption spectroscopy; ICP-AES (total strontium) = inductively coupled plasma atomic emission spectroscopy; ICP-MS (isotopic strontium composition) = inductively coupled plasma-mass spectrometry; La = Lanthanum; LSC (isotopic quanitification of ^{89}Sr and ^{90}Sr) = liquid scintillation counting; pCi = pico curies (10^{-12} curies); PIXE (total strontium) = proton induced x-ray emission; TMAH = tetramethylammonium hydroxide; TNA (total strontium) = thermal neutron activation and radiometric measurement; TRXF (total strontium) = total-reflection x-ray fluorescence

from radiostrontium; thus, the utility for radiostrontium is limited to high exposure measurements. *In vivo* assays are the most direct method of quantifying internally deposited radioactive materials. The determinations of ^{90}Sr levels are achieved by measuring, with a phoswich detector, the bremsstrahlung of the ^{90}Y beta rays (photons with energies ranging from 30 to 160 keV). The most commonly used detectors for measurement of ^{90}Y bremsstrahlung (i.e., electromagnetic radiation) by *in vivo* counting are sodium iodide or phoswich (NaI and CsI sandwich) (Tokareva et al. 2000). For whole-body counting, a scanning-bed geometry in a special shielding room is typically used. Although whole body counters may be used in many configurations, a chest counter is usually used for inhaled radioactive materials. *In vivo* analysis is widely used throughout the nuclear industry, both commercial and government, for quantifying levels of insoluble radioactive materials in the body (Kozheurov 1994).

In vivo counting systems are calibrated using tissue-equivalent phantoms. These phantoms have shapes similar to the human torso and are made of polystyrene or other tissue equivalent material. Standard radioactive strontium sources of known activity are inserted at locations where strontium would be expected to accumulate in a human body. Relationships are determined between the radioactive strontium activity measured by the detection system and the known activity in the phantom (Kozheurov 1994).

7.1.2 *In Vivo* and *In Vitro* Radiostrontium Measurements

In vitro radioactive strontium analyses are routinely performed in support of a personnel monitoring program or in cases where the size of an operation does not justify the cost of whole body counter facilities. These analyses are usually done on urine samples, but other types of body materials (e.g., feces or blood) may also be used. Urinalysis is effective for analysis of transportable or soluble strontium. Strontium may also be measured in fecal material using the same methods identified above for urinalyses, except that this matrix requires extensive preparation.

7.2 ENVIRONMENTAL SAMPLES

Two types of methods are commonly used for measurement of strontium and radiostrontium in environmental samples. The first is field surveys using portable survey instruments, and the second is analysis of samples procured in the field that are returned to the laboratory for quantification.

7.2.1 Field Measurements of Radiostrontium

Radiostrontium measurements in the field are typically qualitative in nature in that the instruments simply respond to beta emissions, regardless of their origin. However, the levels can be measured quantitatively if key parameters are known, such as the relative abundances of all beta-emitting isotopes present, the thickness of the layer being assessed, and the detection efficiency of the instrument for the type of surface being assessed. Measurements in the past have typically been made using portable, hand-held Geiger-Mueller or beta scintillation detectors equipped with a count rate meter, which detect beta radiation while discriminating against other forms of ionizing radiation in the same area. Survey instruments can provide a quick estimate or a measure of the level of activity that might be present. However, more accurate measurements of radioactive strontium may require that samples be taken for laboratory analyses.

7.2.2 Laboratory Analysis of Environmental Samples

Analytical methods for measuring strontium in environmental samples are summarized in Table 7-2. The available methods can be divided into two groups: chemical methods to determine the total mass of strontium in a sample and radiological methods to determine amounts of radioactive isotopes. Environmental media that have been tested for strontium include air filters, swipes, biota, water, soil, and others. A full range of laboratory analysis methods has been used to quantify the total strontium or its radioactive isotopes.

The chemical methods for detecting total strontium include spectrophotometry, fluorometry, kinetic phosphorescence, atomic absorption spectroscopy (e.g., flame and graphite furnaces), energy dispersive x-ray analysis (i.e., EDAX), x-ray fluorescence spectrometry, and inductively coupled plasma spectroscopy-atomic emission and mass spectrometry applications (i.e., ICP-AES and ICP-MS).

The quantity of radioactive strontium is typically determined by gas-flow proportional, liquid scintillation, and Cherenkov counting techniques (Scarpitta et al. 1999). The standard EPA analytical procedure to determine radiostrontium in water is Method 905.0, and several methods are permutations of this procedure. A stable strontium carrier is added to the water sample so that ^{89}Sr and ^{90}Sr are precipitated as insoluble carbonates. The sample then undergoes a preliminary counting that represents the total strontium activity ($^{89, 90}Sr$) plus a small fraction of ^{90}Y that has grown in by radioactive decay.

Table 7-2. Analytical Methods for Determining Strontium in Environmental Samples

Sample matrix	Sample preparation	Analytical method	Sample detection limit	Percent recovery	References
Air	Particulate collection on cellulose filter; acid digestion	FAAS (Method D4185)	No data	No data	ATSM 1999
Water	Acid digestion	Spectrophotometric measurement (total strontium) (Method 911.03)	No data	No data	AOAC 1990
Water	Filtration; acid digestion; add matrix modifier	FAAS (Method D3920; 7780)	No data	No data	ASTM 1999; OSW 1992
Water	Wet acid digestion	ICP-AES (Method 200.15)	No data	No data	EMMI 2000a
Drinking, raw, and waste water	Wet acid digestion; addition of Sr carrier and precipitation as $SrCO_3$; extraction of Yttrium; precipitation of Yttrium oxalate.	β-GPC (Method 973.66; 7500-Sr)	No data	93–99	AOAC 1990; APHA 1992
Water	Complex EDTA; ion chromatography; precipitate Sr effluent fraction as $SrCO_3$	β-GPC (Method 008)	No data	No data	EMMI 2000b
Water (high Sr concentration)	Ion chromatography; dilution	β-GPC	No data	No data	EMMI 2000c, 2000d
Saline water	Dilution	FAAS (Method D3352)	No data	100–106	ASTM 1999
Soils and sediments	Digest organic matter; pyrosulfate fusion; dissolve condensed phosphates	β-GPC	No data	No data	EMMI 2000c, 2000d
Soils and sediments	Fuse with NaOH-Na_2CO_3; dissolve in acid; ion exchange	β-GPC (Method 008-S)	No data	No data	EMMI 2000b
Vegetation and food	Dry ash; complexation with EDTA; ion exchange chromatography; precipitate Sr effluent fraction as $SrCO_3$	β-GPC (Method 008-V)	No data	No data	EMMI 2000b
Milk	Complexation of Y in growth; extraction; precipitation as oxalate	β-GPC (Method 974.37)	No data	No data	AOAC 1990

^{89}Sr and ^{90}Sr measured separately by measuring ^{90}Y in-growth

ß-GPC (total radioactive strontium) = beta gas proportional counter; EDTA = ethylenediamine tetraacetic acid; FAAS (total strontium) = flame atomic absorption spectroscopy; ICP-AES (total strontium) = inductively coupled plasma atomic emission spectroscopy

The ^{90}Y is allowed to reach equilibrium (e.g., approximately a 2-week period) and then is separated with stable yttrium-carrier as yttrium hydroxide (i.e., $Y(OH)_3$). The $Y(OH)_3$ precipitates are converted to the oxalate and the solid oxalate is beta counted in a low background gas-flow proportional counter. The ^{90}Sr concentration is determined from the ^{90}Y activity and the ^{89}Sr concentration by difference. Variations of the above method involve different techniques of selectively separating strontium from environmental samples. Using the various separation methods already described, Cherenkov counting, in conjunction with liquid scintillation, has also been use to detect ^{90}Sr by measuring the concentration of its progeny, ^{90}Y, in solution (Scarpitta et al. 1999).

Horwitz et al. (1991) developed an extraction chromatography technique in which strontium can be selectively separated from other interfering radionuclides such as alkaline and alkaline earth element ions. The technique uses an extraction column (e.g., Sr-resin) with a crown ether (4,4'(5')-bis(tert-butylcyclohexano)-18-crown-6) sorbed on an inert polymeric porous support. A sample with ^{90}Sr digested in concentrated nitric acid is diluted and loaded on the Sr-resin column in ~3 M nitric acid. Interfering elements are removed from the column with ~1 M nitric acid and strontium ions are subsequently eluted with a dilute acid solution. ^{90}Sr ions are then beta counted using a low background gas flow proportional counter or Cherenkov counting of ^{90}Y as previously discussed (Grahek et al. 1999; Torres et al. 2000, 2002). One disadvantage with this technique is some ions interfere with the strontium separation. For example, potassium diminishes the capacity of the Sr-resin column to retain strontium; lead also shows a very strong retention on the Sr-resin and irreversibly blocks Sr adsorption sites (Miró et al. 2002). Recently, improvements have been made to the extraction process using a wetting film technique, which has been shown to reduce ionic interferences (Miró et al. 2002).

7.3 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 strontium 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 strontium.

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 the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

7.3.1 Identification of Data Needs

Methods for Determining Biomarkers of Exposure and Effect. Analytical methods with satisfactory sensitivity and precision are available to determine the levels of strontium in human tissues and body fluids. Strontium and radiostrontium are found in essentially all food, water, and air, so everyone is exposed to some levels. Recently, Sutherland et al. (2000a, 2000b) developed a molecular biological strategy to identify clustered lesions in DNA resulting from *in vitro* cellular exposure to gamma radiation. It is possible that this technique might be adapted to evaluate genetic damage in blood cells following exposure to radioactive strontium. This method, however, will not be specific for ^{90}Sr effects.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Analytical methods with the required sensitivity and accuracy are available for quantification of strontium, both total and isotopic, in environmental matrices (Table 7-2). Knowledge of the levels of strontium in various environmental media, along with the appropriate modeling (see Chapters 3 and 5), can be used to evaluate potential human exposures through inhalation and ingestion pathways.

7.3.2 Ongoing Studies

No ongoing studies investigating new methods for detection and speciation of strontium or radiostrontium were identified in the Federal Research in Progress database (FEDRIP 2002).

8. REGULATIONS AND ADVISORIES

The international, national, and state regulations and guidelines regarding stable strontium in air, water, and other media are summarized in Table 8-1. The regulations and guidelines regarding radioactive strontium are summarized in Tables 8-2 and 8-3.

Stable Strontium. An MRL of 2.0 mg strontium/kg/day for intermediate-duration oral exposure to strontium was calculated by dividing a NOAEL of 140 mg strontium/kg/day for skeletal toxicity in young rats (Storey 1961) by an uncertainty factor of 30 and a modifying factor of 3 (see Appendix A).

The EPA derived a chronic reference dose (RfD) of 0.6 mg/kg/day for strontium (IRIS 2002). The RfD is based on a NOAEL of 190 mg strontium/kg/day for skeletal toxicity in young rats (Storey 1961).

The EPA has not classified stable strontium for human carcinogenicity (IRIS 2002). A number of agencies have classified strontium chromate as a human carcinogen by the inhalation route, on the basis of occupational and animal studies. The carcinogenicity of strontium chromate is attributed to the hexavalent chromium ion and not to strontium. The American Conference of Governmental Industrial Hygienists (ACGIH) has given strontium chromate the classification A2, suspected human carcinogen, and has established an 8-hour time-weighted-average (TWA) of 0.0005 mg/m^3 for occupational exposure (ACGIH 2002). The International Agency for Research on Cancer (IARC) has assigned strontium chromate, along with other chromates, to Group 1, as a human carcinogen (IARC 1990, 2002a). No other stable strontium compound is listed by IARC.

Radioactive Strontium. No MRLs were derived for inhalation or oral exposures to radioactive strontium. The EPA has not derived reference concentrations (RfCs) or RfDs for radioactive strontium (IRIS 2002), nor does the Integrated Risk Information System (IRIS) database provide cancer assessments for radioisotopes of strontium. This function is the responsibility of the EPA Office of Radiation and Indoor Air (ORIA). All radionuclides, including radioisotopes of strontium, are classified as known human (Group A) carcinogens. This classification is based on results of epidemiological studies of Japanese atomic bomb survivors, underground uranium miners, radium dial painters, and patients subjected to a variety of radiation treatments, as well as results of laboratory animal research and mammalian tissue culture studies. ORIA has published cancer slope factors (mortality and morbidity cancer risk estimates) for all known radionuclides, by various exposure routes (inhalation, drinking water ingestion, food ingestion, soil ingestion, immersion in a cloud, and external exposure from contaminated soil) for five age

Table 8-1. Regulations and Guidelines Applicable to Stable Strontium

Agency	Description	Information	Reference
INTERNATIONAL			
Guidelines:			
IARC	Carcinogenicity classification		IARC 1990, 2001a
	Strontium chromate	Group 1[a]	
NATIONAL			
Regulations and Guidelines:			
a. Air			
ACGIH	TLV (8-hour TWA)		ACGIH 2002
	Strontium chromate	$10x5^{-4}$ mg/m^3	
EPA	HAP		HSDB 2001
	Strontium chromate		
NIOSH	REL	No data	
OSHA	PEL	No data	
b. Water			
EPA	Drinking water guideline	4 mg/L	HSDB 2001
	Health Advisories		EPA 2000d
	10-kg child		
	1 Day	25 mg/L	
	10 Day	25 mg/L	
	Lifetime	4 mg/L	
	DWEL	20 mg/L	
USNRC	Maximum ambient environmental level in potable water	10 mg/L	HSDB 2001
c. Food		No data	
d. Other			
ACGIH	Carcinogenicity classification		ACGIH 2002
	Strontium chromate	A2[b]	
EPA	Carcinogenicity classification	Group D[c]	EPA 2000d
	RfD	$6x10^{-1}$ mg/kg/day	IRIS 2001
	Reportable quantity		EPA 2001a
	Strontium chromate	1,000 pounds	40CFR302.4
	Toxic pollutants and hazardous substances required to be identified		EPA 2001b 40CFR122, Appendix D
STATE			
a. Air		No data	
b. Water			
Florida	Drinking water guideline	4.2 mg/L	HSDB 2001
Maine	Drinking water guideline	2.4 mg/L	HSDB 2001
c. Food		No data	
d. Other			
Arizona	Soil remediation levels		BNA 2001
	Residential	$4.6x10^4$ mg/kg	
	Non residential	$1x10^6$ mg/kg	

Table 8-1. Regulations and Guidelines Applicable to Stable Strontium

Agency	Description	Information	Reference
STATE (*cont.*)			
Florida	Toxic substances in the workplace; Florida substance list	Strontium chromate	BNA 2001

[a]Group 1: carcinogenic to humans (refers to hexavalent chromium)
[b]A2: suspected human carcinogen (refers to hexavalent chromium)
[c]Group D: not classifiable as to human carcinogenicity

ACGIH = American Conference of Governmental Industrial Hygienists; BNA = Bureau of National Affairs; CFR = Code of Federal Regulations; DWEL = drinking water equivalent level; EPA = Environmental Protection Agency; HAP = hazardous air pollutant; HSDB = Hazardous Substances Data Bank; IARC = International Agency for Research on Cancer; IRIS = Integrated Risk Information System; NIOSH = National Institute for Occupational Safety and Health; OSHA = Occupational Safety and Health Administration; PEL = permissible exposure limit; REL = recommended exposure limit; RfD = reference dose; TLV = threshold limit values; TWA = time-weighted averages; USNRC = National Research Council

Table 8-2. Regulations and Guidelines Applicable to Radioactive Strontium

Agency	Description	Information	Reference
INTERNATIONAL			
Guidelines:			
a. Occupational			
ICRP	Recommended dose limits[a]; effective dose	20 mSv per year, averaged over defined period of 5 years[b]	ICRP 1994b
	Annual equivalent dose		
	Lens of the eye	150 mSv	
	Skin[c]	500 mSv	
	Hands and feet	500 mSv	
b. General Population			
IARC	Carcinogenicity classification	Group 1[d]	IARC 2001b, 2001c
ICRP	Recommended dose limits[a]		ICRP 1994b
	Effective dose	1 mSv per year[e]	
	Annual equivalent dose in		
	Lens of the eye	15 mSv	
	Skin[c]	50 mSv	
	Hands and feet	No data	
NATIONAL			
Regulations:			
a. Air			
EPA	Concentration levels for environmental compliance for ^{90}Sr	1.9×10^{-14} Ci/m^3	EPA 2001d 40CFR61, Appendix E
	Methods for estimating radionuclide emissions		EPA 2001m 40CFR61, Appendix D
	Test method for measuring radionuclide emissions from stationary sources	Method 114	EPA 2001e 40CFR61, Appendix B
OSHA	Safety and health regulations for construction for ionizing radiation	10CFR20 regulations apply	OSHA 2001 29CFR1926.53
	Toxic and hazardous substances for ionizing radiation		OSHA 2000 29CFR1910.1096
USNRC	Effluent concentrations in air		USNRC 2001g 10CFR20, Appendix B
	^{90}Sr		
	Class D[f]	3×10^{-11} µCi/mL	
	Class Y[g]	6×10^{-12} µCi/mL	
	Occupational values via inhalation	ALI (µCi) / DAC(µCi/mL)	USNRC 2001g 10CFR20, Appendix B
	^{90}Sr		
	Class D[f]	2×10^{1} / 8×10^{-9}	
	Class Y[g]	4×10^{0} / 2×10^{-9}	

Table 8-2. Regulations and Guidelines Applicable to Radioactive Strontium

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
b. Water			
EPA	Analytical methods for radioactivity of ^{90}Sr	Radio chemical	EPA 2001g 40CFR141.25 (a)
	Detection limits for man-made beta particle and photon emitters for ^{90}Sr	2 pCi/L	EPA 2001g 40CFR141.25 (c)(2), Table B
	Maximum contaminant levels in community water systems; average annual concentrations assumed to produce a total body or organ dose of 4 millirem/year		EPA 2001f 40CFR141.16
	^{90}Sr	8 pCi/L	
	Critical organ	Bone marrow	
	Monitoring frequency for radioactivity in community water systems; annual monitoring	Analysis of four quarterly samples	EPA 2001h 40CFR141.26 (b)(4)
USNRC	Effluent concentrations in water		USNRC 2001g 10CFR20, Appendix B
	^{90}Sr		
	Class D[f]	$5x10^{-7}$ µCi/mL	
	Releases to sewers; monthly average concentration		USNRC 2001g 10CFR20, Appendix B
	^{90}Sr		
	Class D[f]	$5x10^{-6}$ µCi/mL	
c. Food			
FDA	Sources of radiation used for inspection of food; sealed units producing radiation	≤2.2 million electron volts	FDA 2000 21CFR179.21
d. Other: Occupational			
DOE	Individual monitoring		DOE 2001a 10CFR835.402
	Limits for members of the public entering a controlled area (total effective dose equivalent in a year)	0.01 rem (0.001 Sv)	DOE 2001b 10CFR835.208
	Limits for the embryo/fetus from conception to birth	0.5 rem (0.005 Sv)	DOE 2001c 10CFR835.206
	Occupational dose limits for general employees; total effective dose equivalent	5 rems (0.05 Sv)	DOE 2001d 10CFR835.202

Table 8-2. Regulations and Guidelines Applicable to Radioactive Strontium

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
DOE	Occupational dose limits for general employees; sum of the deep dose equivalent for external exposures and the committed dose equivalent to any organ or tissue other than the lens of the eye	50 rems (0.5 Sv)	DOE 2001d 10CFR835.202
	Occupational dose limits for general employees		DOE 2001d 10CFR835.202
	Lens of the eye dose equivalent	15 rems (0.15 Sv)	
	Shallow dose equivalent to the skin or to any extremity	50 rems (0.5 Sv)	
	Planned special exposures		
	Occupational dose limits for minors (total effective dose equivalent in a year)	0.1 rem (0.001 Sv)	DOE 2001e 10CFR835.207
	Radiation standards; inhaled air DAC for lung retention		DOE 2000b 10CFR835, Appendix A
	^{90}Sr		
	Class D[h]	$8x10^{-9}$ µCi/mL	
	Class W[i]	No data	
	Class Y[j]	$2x10^{-9}$ µCi/mL	
DOT	Activity values for radio-nuclides		DOT 2001b 49CFR173.435
	^{90}Sr		
	A_1	5.41 Ci	
	A_2	2.70 Ci	
	Carriage by public highway; requirements for Class 7 (radioactive material); total transport index number	50	DOT 2001c 49CFR177.842
	General requirements for shipments and packages; Class 7 (radioactive) materials		DOT 2001d 49CFR173 Subpart I
	Scope and definitions		49CFR173.401 thru 403
	General design requirements		49CFR173.410
	Table of activity limits-excepted quantities and articles		49CFR173.425
	General requirements for shipments and packages; Class 7 (radioactive) materials		DOT 2001d 49CFR173 Subpart I

Table 8-2. Regulations and Guidelines Applicable to Radioactive Strontium

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
DOT	Requirements for determining A1 and A2 values for radionuclides and for the listing of radionuclides on shipping papers and labels		DOT 2001d 49CFR173.433
	Radiation level limitations; any normally occupied space except carriers operating under the provisions of a state or federally regulated radiation protection program and wearing radiation dosimetry devices	0.02 mSv/hour (2 mrem/hour)	DOT 2001e 49CFR173.441
	Radiation level limitations; any point 2 meters (6.6 feet) from the outer lateral surfaces, excluding top and underside	0.1 mSv/hour (10 mrem/hour)	DOT 2001e 49CFR173.441
	Radiation level limitations; external surface radiation level not to be exceeded under conditions normally incident to transportation packages exceeding the radiation limit	2 mSv/hour (200 mrem/hour) and the transport index (TI) is less than 10	DOT 2001e 49CFR173.441
	Transport by exclusive use shipment		
	Conditional maximum radiation level	10 mSv/hour (1,000 mrem/hour)	
	Outer surface of vehicles including top and underside	2 mSv/hour (200 mrem/hour)	
	Superfund; reportable quantity for ^{90}Sr	0.1 pounds	DOT 2001a 49CFR172.101, Appendix A, Table 2
e. Other: General Population			
EPA	Annual possession quantities for environmental compliance of ^{90}Sr		EPA 2001d 40CFR61, Appendix E
	Gaseous form	5.2×10^{-4} Ci/year	
	Liquid/powder forms	5.2×10^{-1} Ci/year	
	Solid form	5.2×10^{2} Ci/year	

Table 8-2. Regulations and Guidelines Applicable to Radioactive Strontium

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
EPA	Environmental standards for management and storage of spent nuclear fuel, high-level and transuranic radioactive wastes; applicability and definitions		EPA 2001i 40CFR191, Subpart A
	Whole body	25 mrem	
	Thyroid	75 mrem	
	Other critical organs	25 mrem	
	Environmental standards for disposal of spent nuclear fuel, high-level and transuranic radioactive wastes; applicability, definitions, containment and individual protection requirements		EPA 2001i 40CFR191, Subpart B
	Environmental standards for groundwater protection of spent nuclear fuel, high-level and transuranic radioactive wastes; applicability and definitions; release limits for containment requirements of ^{90}Sr	1,000/1,000 MTHM	EPA 2001i 40CFR191, Subpart C
	Hazardous waste injection restrictions; waste specific prohibitions; newly listed and identified wastes	D004–D011 wastes	EPA 2001j 40CFR148.18
	Land disposal restrictions; effective dates of injected prohibited hazardous wastes		EPA 2001l 40CFR268, Appendix VIII
	Radioactive waste; release limits for containment requirements[k] for ^{90}Sr	1,000 Ci	EPA 2001c 40CFR191, Appendix A
	Reportable quantity of ^{90}Sr	$1x10^{-1}$ Ci	EPA 2001e 40CFR302.4, Appendix B
	Standards for the control of residual radioactive materials from inactive uranium processing sites; definitions; control of residual radioactive materials and their listed constituents		EPA 2001k 40CFR192, Subpart A

Table 8-2. Regulations and Guidelines Applicable to Radioactive Strontium

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
EPA	Standards for cleanup of land and buildings contaminated with residual radioactive materials from inactive uranium processing sites		EPA 2001k 40CFR192, Subpart B
	Guidance for implementation		EPA 2001k 40CFR192, Subpart C
	Standards for management of uranium byproduct materials pursuant to Section 84 of the Atomic Energy Act of 1954, as amended		EPA 2001k 40CFR192, Subpart D
	Standards for management of thorium byproduct materials pursuant to Section 84 of the Atomic Energy Act of 1954, as amended		EPA 2001k 40CFR192, Subpart E
	Underground injection control regulations for Class V injection wells		EPA 2001n 63FR40586
USNRC	Activity values for radionuclides (^{90}Sr) A_1 A_2 Specific gravity	 5.41 Ci 2.70 Ci 1.4×10^{2} Ci	USNRC 2001i 10CFR71, Table A-1
	Byproduct material listing (^{90}Sr) Column 1 Column 2	 1×10^{-2} Ci 1×19^{-4} Ci	USNRC 2001b 10CFR33.100, Schedule A
	Byproduct material listing	0.1 µCi	USNRC 2001a 10CFR30.71, Schedule B
	Dose to an embryo/fetus (dose equivalent during the entire pregnancy)	0.5 rem (5 mSv)	USNRC 2001m 10CFR20.1208
	Licensing ice detection devices (^{90}Sr)	≤50 µCi	USNRC 2001c 10CFR31.10
	Occupational dose limits for adults (total effective dose equivalent) in a year	5 rems (0.05 Sv)	USNRC 2001n 10CFR20.1201
	Sum of the deep-dose equivalent and the committed dose equivalent to any individual organ or tissue other than the lens of the eye	50 rems (0.5 Sv)	USNRC 2001n 10CFR20.1201

Table 8-2. Regulations and Guidelines Applicable to Radioactive Strontium

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
USNRC	Annual limits to the lens of the eye, to the skin, and to the extremities		USNRC 2001n 10CFR20.1201
	Lens dose equivalent	15 rems (0.15 Sv)	
	Shallow-dose equivalent to the skin or to any extremity	50 rems (0.50 Sv)	
	Occupational dose limits for minors	10% of the annual dose limits specified for adult workers in 10 CFR 20.1201	USNRC 2001o 10CFR20.1207
	Occupational values for oral ingestion (ALI) of ^{90}Sr		USNRC 2001g 10CFR20, Appendix B
	Class D[f]	$3x10^{1}$ µCi (bone surf) $4x10^{1}$	
	Medical use—^{90}Sr as a use of unsealed byproduct material for uptake, dilution, and excretion studies		USNRC 2001k 10CFR35.100
	Medical use—^{90}Sr as a sealed source in an applicator for treatment of superficial eye conditions		USNRC 2001j 10CFR35.4000
	Physical protection for spent nuclear fuel and high-level radioactive waste		USNRC 2001p 63FR26955
	Radioactive waste; classification of ^{90}Sr		USNRC 2001l 10CFR61.55
	Column 1[l]	0.04 Ci/m^3	
	Column 2	150 Ci/m^3	
	Column 3	7,000 Ci/m^3	
	Standards for protection against radiation—dose limits for individual members of the public; total effective dose equivalent to individual	0.1 rem/year	USNRC 2001q 10CFR20.1301
	Standards for protection against radiation; dose limits for individual members of the public; dose from external source	0.002 rem/hour	USNRC 2001q 10CFR20.1301
	Quality assurance—^{90}Sr		USNRC 2001h 10CFR32.62
	Quantity of licensed material requiring labeling containing ^{90}Sr	$1.2x10^{-1}$ µCi	USNRC 2001d 10CFR30, Appendix B

Table 8-2. Regulations and Guidelines Applicable to Radioactive Strontium

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
USNRC	Quantity of radioactive material requiring need for an emergency plan for responding to a release (^{90}Sr)		USNRC 2001f 10CFR30.72, Schedule C
	Release fraction	0.01%	
	Quantity	90 Ci	
	Standards for protection against radiation; quantity of licensed material requiring labeling (^{90}Sr)	$1x10^{-1}$ µCi	USNRC 2001e 10CFR20, Appendix C
NATIONAL Guidelines:			
a. Air			
ACGIH	TLV-TWA (^{90}Sr)	Rdiation exposures must be kept as low as reasonable achievable	ACGIH 2002
	Effective dose		ACGIH 2002
	Any single year	50 mSv	
	Averaged over 5 years	20 mSv	
	Annual equivalent dose to		ACGIH 2002
	Lens of the eye	150 mSv	
	Skin	500 mSv	
	Hands and feet	500 mSv	
	Embryo-fetus exposures once the pregnancy is known		ACGIH 2002
	Monthly equivalent dose	0.5 mSv	
	Dose to the surface of women's abdomen (lower trunk)	2 mSv for the remainder of the pregnancy	
	Intake of radionuclide	1/20 ALI	
NIOSH	REL (TWA)	No data	
b. Water			
EPA	MCLG for beta particles	No final MCLG, but zero proposed in 1991	EPA 2000d
	MCL for beta particles	4 mrem	EPA 2000d
	Health advisory for beta particle activity in drinking water	4 mrem/year at 10^{-4} cancer risk	EPA 2000d
	Cancer group	Group A[m]	EPA 2000d
c. Food			
FDA	Derived intervention level[n] (DIL; Bq/kg food) for in accidentally-contaminated human food		FDA 1998
	^{89}Sr	400[o]	
	^{90}Sr	160[p]	

Table 8-2. Regulations and Guidelines Applicable to Radioactive Strontium

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
d. Other			
EPA	Effective dose equivalent		EPA 1987
	Adult	5 rem/year	Federal Register
	Lens of the eye	15 rem/year	Part II
	All other organs	50 rem/year	
	Juvenile workers (<18 years old)	0.5 rem/year	
	Pregnant workers	0.5 rem/gestation period	
	Carcinogenicity slope factors[q] Ingestion—lifetime excess total cancer risk/pCi		EPA 2002
	Water		
	^{82}Sr	3.13×10^{-11}	
	^{85}Sr	2.26×10^{-12}	
	^{85m}Sr	1.67×10^{-14}	
	^{89}Sr	1.28×10^{-11}	
	^{90}Sr	5.59×10^{-11}	
	$^{90+disentegration}Sr$	7.40×10^{-11}	
	^{91}Sr	3.22×10^{-12}	
	^{92}Sr	2.25×10^{-12}	
	Carcinogenicity slope factors[q] Ingestion—lifetime excess total cancer risk/pCi		EPA 2002
	Food		
	^{82}Sr	4.48×10^{-11}	
	^{85}Sr	3.11×10^{-12}	
	^{85m}Sr	2.31×10^{-14}	
	^{89}Sr	1.84×10^{-11}	
	^{90}Sr	6.88×10^{-11}	
	$^{90+disentegration}Sr$	9.53×10^{-11}	
	^{91}Sr	4.66×10^{-12}	
	^{92}Sr	3.26×10^{-12}	
	Carcinogenicity slope factors[q] Ingestion—lifetime excess total cancer risk/pCi		EPA 2002
	Soil		
	^{82}Sr	8.47×10^{-11}	
	^{85}Sr	5.03×10^{-12}	
	^{85m}Sr	3.74×10^{-14}	
	^{89}Sr	3.47×10^{-11}	
	^{90}Sr	9.18×10^{-11}	
	$^{90+disentegration}Sr$	1.44×10^{-10}	
	^{91}Sr	8.81×10^{-12}	
	^{92}Sr	6.18×10^{-12}	

Table 8-2. Regulations and Guidelines Applicable to Radioactive Strontium

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
EPA	Carcinogenicity slope factors[r] Inhalation—lifetime excess total cancer risk/pCi		EPA 2002
	^{82}Sr	$3.69x10^{-11}$	
	^{85}Sr	$2.56x10^{-12}$	
	^{85m}Sr	$8.32x10^{-15}$	
	^{89}Sr	$2.34x10^{-11}$	
	^{90}Sr	$1.05x10^{-10}$	
	$^{90+disentegration}Sr$	$1.13x10^{-10}$	
	^{91}Sr	$1.70x10^{-12}$	
	^{92}Sr	$1.03x10^{-12}$	
	Carcinogenicity slope factors[s] External exposure—risk/year per pCi/g in soil		EPA 2002
	^{82}Sr	$5.00x10^{-11}$	
	^{85}Sr	$2.20x10^{-6}$	
	^{85m}Sr	$8.21x10^{-7}$	
	^{89}Sr	$7.19x10^{-9}$	
	^{90}Sr	$4.82x10^{-10}$	
	$^{90+disentegration}Sr$	$1.96x10^{-8}$	
	^{91}Sr	$3.30x10^{-6}$	
	^{92}Sr	$6.69x10^{-6}$	
NCRP	Occupational exposures[t] Effective dose limits		NCRP 1993
	Annual	50 mSv	
	Cumulative	10 mSv x age	
	Occupational exposures[t] Equivalent dose annual limits for tissues and organs		NCRP 1993
	Lens of eye	150 mSv	
	Skin, hands, and feet	500 mSv	
	Public exposures (annual) Effective dose limit, continuous or frequent exposure[s]	1 mSv	NCRP 1993
	Public exposures (annual) Effective dose limit, infrequent exposure[t]	5 mSv	NCRP 1993
	Public exposures (annual) Equivalent dose limits for tissues and organs[t]		NCRP 1993
	Lens of eye	15 mSv	
	Skin, hands, and feet	50 mSv	

Table 8-2. Regulations and Guidelines Applicable to Radioactive Strontium

Agency	Description	Information	Reference
STATE			
a. Air			
Arkansas	Concentrations in air above natural background (^{90}Sr)		BNA 2001
	Occupational	S1x10^{-9} µCi/mL I 5x10^{-9} µCi/mL	
	Non occupational	S3x10^{-11} µCi/mL I 2x10^{-10} µCi/mL	
Illinois	Concentrations in air above natural background	S3x10^{-11} µCi/mL I 2x10^{-10} µCi/mL	BNA 2001
New Jersey	Maximum permissible average concentrations of radioactive materials in air (^{85m}Sr)		BNA 2001
	Occupational	S4x10^{-5} µCi/mL I 3x10^{-5} µCi/mL	
	Non occupational	S1x10^{-6} µCi/mL I 1x10^{-6} µCi/mL	
b. Water			
Alabama	Drinking water guidelines	8 pCi/L	HSDB 2001
Alaska	MCL for drinking water (^{90}Sr)	8 pCi/L	ADEC 2000
Arkansas	Concentrations in water above natural background (^{90}Sr)		BNA 2001
	Occupational	S1x10^{-5} µCi/mL I 1x10^{-3} µCi/mL	
	Non occupational	S3x10^{-7} µCi/mL I 4x10^{-5} µCi/mL	
California	Drinking water guidelines	8 pCi/L	HSDB 2001
	Primary MCL (^{90}Sr)	8 pCi/L	CA Department of Health Services 2000
Colorado	Standards applicable to surface waters	8 pCi/L	BNA 2001
	Groundwater quality standards	8 pCi/L	BNA 2001
Connecticut	Drinking water guidelines	8 pCi/L	HSDB 2001
Florida	Drinking water guidelines	4,200 µg/L	HSDB 2001
	MCL for groundwater (^{90}Sr)	8 pCi/L	FL DEP 2000
Idaho	Primary constituent standards for groundwater (^{90}Sr)	8 pCi/L	ID Department of Health & Welfare 1999
Illinois	Drinking water guidelines	8 pCi/L	HSDB 2001
	Water quality standard (^{90}Sr)	1 and 2 pCi/L	IL Environmental Protection Agency 1999

Table 8-2. Regulations and Guidelines Applicable to Radioactive Strontium

Agency	Description	Information	Reference
STATE (*cont.*)			
New Jersey	Maximum permissible average concentrations of radioactive materials in water (^{85m}Sr)		BNA 2001
	Occupational	S0.2 µCi/mL I 0.2 µCi/mL	
	Non occupational	S0.007 µCi/mL I 0.007 µCi/mL	
Indiana	Maximum contaminant levels in community water systems; average annual concentrations assumed to produce a total body or organ dose of 4 millirem/year		IN General Assembly 2000
	^{90}Sr	8 pCi/L	
	Critical organ	Bone marrow	
Maine	Drinking water guidelines	2,400 µg/L	HSDB 2001
Michigan	Maximum contaminant levels in community water systems; average annual concentrations assumed to produce a total body or organ dose of 4 millirem/year		MDEQ 2000
	^{90}Sr	8 pCi/L	
	Critical organ	Bone marrow	
New Hampshire	Drinking water guidelines	8 pCi/L	HSDB 2001
Wisconsin	Drinking water guidelines	8 pCi/L	HSDB 2001
c. Food		No data	
d. Other			
Arkansas	Determination of A_1 and A_2 quantities (^{90}Sr)		BNA 2001
	A_1	10 Ci	
	A_2	0.4 Ci	
	Specific gravity	$1.5x10^2$ Ci/g	
	Standard for protection against radiation	0.1 µCi	BNA 2001
Colorado	Determination of A_1 and A_2 (^{90}Sr)		BNA 2001
	A_1	5.41 Ci	
	A_2	2.70 Ci	
Delaware	Average annual concentration assumed to produce a total body or organ dose of 4 rem/year (^{90}Sr)		BNA 2001
	Critical organ (bone marrow)	8 pCi/L	
Nevada	Quantities of radioactive material for signs, labels, and signals	0.1 µCi	BNA 2001

Table 8-2. Regulations and Guidelines Applicable to Radioactive Strontium

Agency	Description	Information	Reference

[a]The limits apply to the sum of the relevant doses from external exposure in the specified period and the 50-year committed dose (to age 70 years for children) from intakes in the same period.
[b]With the further provision that the effective dose should not exceed 50 mSv in any single year. Additional restrictions apply to the occupational exposure of pregnant women.
[c]The limitation on the effective dose provides sufficient protection for the skin against stochastic effects. An additional limit is needed for localized exposures in order to prevent deterministic effects.
[d]Group 1: human carcinogen
[e]In special circumstances, a higher value of effective dose could be allowed in a single year, provided that the average over 5 years does not exceed 1 mSv per year.
[f]Class D: all soluble compounds except SrTiO
[g]Class Y: all insoluble compounds and SrTiO
[h]Class D: refers to materials with retention times in the pulmonary region of <10 days
[i]Class W: refers to materials with retention times in the pulmonary region of 10–100 days
[j]Class Y: refers to materials with retention times in the pulmonary region of >100 days
[k]Release limit per 1,000 metric tons of heavy metal (MTHM) or other unit of waste
[l]Column 1: The sum of the fractions rule for mixtures of radionuclides. For determining classification for waste that contains a mixture of radionuclides, it is necessary to determine the sum of fractions by dividing each nuclide's concentration by the appropriate limit and adding the resulting values. The appropriate limits must all be taken from the same column of the same table. The sum of the fractions for the column must be less than 1.0 if the waste class is to be determined by the column. Example: A waste contains ^{90}Sr in a concentration of 50 Ci/m^3 and ^{137}Cs of 22 Ci/m^3. Since the concentrations both exceed the values in Column 1, Table 2, they must be compared to Column 2 values. For ^{90}Sr fraction 50/150=0.33; for ^{137}Cs fraction, 22/44=0.5; the sum of the fractions=0.83. Since the sum is less than 1.0, the waste is Class B.
[m]Group A: human carcinogen
[n]Derived intervention levels (DIL) are concentrations of radioactivity in food whose consumption would deliver a committed effective dose equivalent equal to the most limiting of the protection action guides (PAGs) developed by FDA (1998).
[o]The FDA-recommended Derived Intervention Level (DIL) for radionuclides of ^{89}Sr, is defined as the DIL for the most sensitive age group (3 months) that was calculated from the most limiting Protective Action Goal (PAG; 50 mSv committed dose equivalent to the bone).
[p]The FDA-recommended Derived Intervention Level (DIL) for radionuclides of ^{90}Sr, is defined as the DIL for the most sensitive age group (15 years) that was calculated from the most limiting Protective Action Goal (PAG; 50 mSv committed dose equivalent to the bone).
[q]Radioactive slope factors calculated by EPA's Office of Radiation and Indoor Air (ORIA). Slope factors are central estimates in a linear model of the age-averaged, lifetime attributable radiation cancer incidence (fatal and nonfatal cancer) risk per unit of activity ingested, expressed as risk per picocurie (pCi).
[r]Inhalation slope factors are central estimates in a linear model of the age-average, lifetime attributable radiation cancer incidence (fatal and nonfatal cancer) risk per unit of activity inhaled, expressed as risk per picocurie (pCi).
[s]External slope factors are central estimates of the lifetime attributable radiation cancer incidence risk for each year of exposure to external radiation from photon-emitting radionuclides distributed uniformly in a thick layer of soil, expressed as risk/year per pCu per gram of soil.
[t]Sum of external and internal exposures but excluding doses from natural sources.

ACGIH = American Conference of Governmental Industrial Hygienists; ADEC = Alaska Department of Environmental Conservation; ALI = annual limits on intake; BNA = Bureau of National Affairs; CFR = Code of Federal Regulations; DAC = derived air concentration; DEP = Department of Environmental Protection; DOE = Department of Energy; DOT = Department of Transportation; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; HSDB = Hazardous Substances Data Bank; I = insoluble; IARC = International Agency for Research on Cancer; ICRP = International Commission on Radiological Protection; MCL = maximum contaminant level; MCLG = maximum contaminant level goal; MDEQ = Michigan Department of Environmental Quality; mSv = millisievert; MTHM = metric tons of heavy metal; NCRP = National Council on Radiation Protection; NIOSH = National Institute for Occupational Safety and Health; USNRC = Nuclear Regulatory Commission; OSHA = Occupational Safety and Health Administration; PAG = protective action guide; REL = recommended exposure limit; S = soluble; TWA = time-weighted average

Table 8-3. Effective Dose Coefficients[a] (e(50)) and Annual Limits on Intake[b] (ALI) for Occupational Exposures to Radioactive Strontium Isotopes

Radio-nuclide			Inhalation, 1μm AMAD[c]			Inhalation, 5μm AMAD			Ingestion		
Half-life	Absorp-tion type	f1[d]	e_{inh} (50)	ALI (Bq)	ALI (mCi)	e_{inh} (50)	ALI (Bq)	ALI (mCi)	e_{ing} (50)	ALI (Bq)	ALI (mCi)
^{80}Sr											
1.67 hr	fast	0.3	7.6×10^{-11}	2.6×10^{8}	7.11	1.3×10^{-10}	1.5×10^{8}	4.158	3.4×10^{-10}	5.9×10^{7}	1.590
	slow	0.01	1.4×10^{-10}	1.4×10^{8}	3.86	2.1×10^{-10}	9.5×10^{7}	2.574	3.5×10^{-10}	5.7×10^{7}	1.544
^{81}Sr											
0.425 hr	fast	0.3	2.2×10^{-11}	9.1×10^{8}	24.57	3.9×10^{-11}	5.1×10^{8}	13.860	7.7×10^{-11}	2.6×10^{8}	7.020
	slow	0.01	3.8×10^{-11}	5.3×10^{8}	14.22	6.1×10^{-11}	3.3×10^{8}	8.861	7.8×10^{-11}	2.6×10^{8}	6.93
^{82}Sr											
25.0 d	fast	0.3	2.2×10^{-9}	9.1×10^{6}	0.245	3.3×10^{-9}	6.1×10^{6}	0.164	6.1×10^{-9}	3.3×10^{6}	0.089
	slow	0.01	1.0×10^{-8}	2.0×10^{6}	0.054	7.7×10^{-9}	2.6×10^{6}	0.070	6.0×10^{-9}	3.3×10^{6}	0.090
^{83}Sr											
1.35 d	fast	0.3	1.7×10^{-10}	1.2×10^{8}	3.179	3.0×10^{-10}	6.7×10^{7}	1.801	4.9×10^{-10}	4.1×10^{7}	1.103
	slow	0.01	3.4×10^{-10}	5.9×10^{7}	1.589	4.9×10^{-10}	4.1×10^{7}	1.103	5.8×10^{-10}	3.5×10^{7}	0.932
^{85}Sr											
64.8 d	fast	0.3	3.9×10^{-10}	5.1×10^{7}	1.386	5.6×10^{-10}	3.6×10^{7}	0.965	5.6×10^{-10}	3.6×10^{7}	0.965
	slow	0.01	7.7×10^{-10}	2.6×10^{7}	0.702	6.4×10^{-10}	3.1×10^{7}	0.845	3.3×10^{-10}	6.1×10^{7}	1.638
^{85m}Sr											
1.16 hr	fast	0.3	3.1×10^{-12}	6.5×10^{9}	174.00	5.6×10^{-12}	3.6×10^{9}	96.53	6.1×10^{-12}	3.3×10^{9}	88.61
	slow	0.01	4.5×10^{-12}	4.4×10^{9}	120.00	7.4×10^{-12}	2.7×10^{9}	73.05	6.1×10^{-12}	3.3×10^{9}	88.61
^{87m}Sr											
2.8 hr	fast	0.3	1.2×10^{-11}	1.7×10^{9}	45.05	2.2×10^{-11}	9.1×10^{8}	24.57	3.0×10^{-11}	6.7×10^{8}	18.02
	slow	0.01	2.2×10^{-11}	9.1×10^{8}	24.57	3.5×10^{-11}	5.7×10^{8}	15.44	3.3×10^{-11}	6.1×10^{8}	16.38
^{89}Sr											
50.5 d	fast	0.3	1.0×10^{-9}	2.0×10^{7}	0.540	1.4×10^{-9}	1.4×10^{7}	0.386	2.6×10^{-9}	7.7×10^{6}	0.208
	slow	0.01	7.5×10^{-9}	2.7×10^{6}	0.072	5.6×10^{-9}	3.6×10^{6}	0.097	2.3×10^{-9}	8.7×10^{6}	0.235
^{90}Sr											
29.1 yr	fast	0.3	2.4×10^{-8}	8.3×10^{5}	0.023	3.0×10^{-8}	6.7×10^{5}	0.018	2.8×10^{-8}	7.1×10^{5}	0.019
	slow	0.01	1.5×10^{-7}	1.3×10^{5}	0.004	7.7×10^{-8}	2.6×10^{5}	0.007	2.7×10^{-9}	7.4×10^{6}	0.200
^{91}Sr											
9.5 hr	fast	0.3	1.7×10^{-10}	1.2×10^{8}	3.180	2.9×10^{-10}	6.9×10^{7}	1.864	6.5×10^{-10}	3.1×10^{7}	0.832
	slow	0.01	4.1×10^{-10}	4.9×10^{7}	1.318	5.7×10^{-10}	3.5×10^{7}	0.948	7.6×10^{-10}	2.6×10^{7}	0.711
^{92}Sr											
2.7 hr	fast	0.3	1.1×10^{-10}	1.8×10^{8}	4.914	1.8×10^{-10}	1.1×10^{8}	3.003	4.3×10^{-10}	4.7×10^{7}	1.257
	slow	0.01	2.3×10^{-10}	8.7×10^{7}	2.350	3.4×10^{-10}	5.9×10^{7}	1.590	4.9×10^{-10}	4.1×10^{7}	1.103

[a]ICRP (1994)
[b]For internal exposures, ICRP (1994) recommends an effective dose limit of 100 mSv over 5 years (averaging 20 mSv per year). The Annual Limits on Intake (ALI in Bequerels) were calculated by dividing the annual effective dose limit (0.02 Sv) by the dose coefficient (e(50)) in Sieverts/Bequerel.
[c]ICRP (1994) calculated inhalation dose coefficients for particles with AMAD of 1 or 5 μm.
[d]Fractional absorption factor used by ICRP (1994: Annexes E and F) to calculate effective dose coefficients. A value of 0.3 was used for unspecified strontium compounds and 0.01 was used for strontium titanate.

ALI = Annual Limits on Intake; AMAD = Activity Median Average Diameters; Bq = Bequerels; Ci = Curies; d = day; hr = hour; yr = year

groups and 14 radiogenic cancer cites (EPA 2000e). These factors are used to calculate the lifetime excess total cancer risk per unit intake or exposure to radiation (under the different exposure scenarios). Slope factors for radioactive strontium isotopes are listed in Table 8-2. IARC has determined that all internally deposited beta emitters, including radioactive strontium, are carcinogenic to humans and has assigned them to Group 1 (IARC 2001, 2002b).

Because of the potential for ionizing radiation to cause deterministic (acute radiation syndrome) and nondeterministic (cancer) health effects in exposed individuals, safe dose guidelines and regulations have been established for radionuclides in air and water by a number of international and national agencies (Tables 8-2 and 8-3). Regulations and guidelines that protect against deterministic effects are based on identified acute thresholds doses for those effects, with a reduction to protect sensitive populations and provide safety margins to account for uncertainties. Those that protect against nondeterministic effects use the observed frequencies with which those effects occur at high doses, account for uncertainties that may exist, and assume a linear dose-effect relationship to calculate the doses at which the effects would be presumed to occur at some acceptable frequency, such as the range of 10^{-4}–$10^{-}6$, which EPA often considers. This proportionality assumes a linear no threshold (LNT) dose effect curve. During the last decade, there have been reductions in LNT-based public radiation dose limits and site cleanup levels that have increased the scope and cost of medical, occupational, and environmental radiation protection efforts. Some recent studies found a reduction in health effects when the dose was delivered at lower dose rates, indicating a potential application to future protection guidelines and regulations.

The International Commission on Radiological Protection (ICRP) provides guidance on the fundamental principles regarding the biological effects of exposure to ionizing radiation and recommends exposure limits based on these analyses. In the United States, the National Council on Radiation Protection and Measurements (NCRP) was chartered in 1964 by the U.S. Congress to: (1) disseminate information of public interest and recommend radiation levels to protect the public, (2) support cooperation among organizations concerned with radiation protection, (3) develop basic concepts about radiation protection, and (4) cooperate with the ICRP and the International Commission on Radiation Units and Measurements. Even though the NCRP is a nongovernmental organization, it provides recommendations that guide the establishment of federal radiation policies, agency requirements, and statutory laws. Through the governmental agencies that rely on NCRP recommendations, the work of this organization has a significant impact on the many activities in the United States involving the use of radiation and radioactive materials.

The EPA sets radiation safety policy and basic safety standards. The execution of this policy is assigned to the various regulatory agencies, including the EPA itself, for application to the specific activities that they regulate. The U.S. Nuclear Regulatory Commission (USNRC), an independent government agency, regulates commercial nuclear power reactors; research/test/training reactors; fuel cycle facilities; and the transport, storage, and disposal of nuclear materials and waste (USNRC 1997). The EPA is responsible for protecting the public and the environment and for cleanup of radioactively contaminated sites (EPA 1997a).

The Food and Drug Administration (FDA) develops standards for radioactive material concentrations in food (FDA 1998) and in medical devices used in radiation therapy (FDA 1997). The FDA recently updated its guidance document that presents recommended action levels for accidental radioactive contamination of foods, both domestic and imported (FDA 1998). These derived intervention levels (DILs) are estimated levels in food that could lead to individuals receiving a radiation equivalent dose equal to the FDA protection action guide (PAG) that is set as the more limiting of either 0.5 rem (5 mSv) for committed effective dose or 5 rem (50 mSv) committed dose equivalent to any individual tissue or organ. Derived intervention levels, which are based on food intake rates, are calculated for different age groups and the DIL for the most vulnerable group is then adopted to provide a conservative margin of safety for the entire population. For ^{90}Sr, with a half-life of 29 years, the DIL is based on the dose to the bone surface in 15-year-old individuals, who have the highest rate of bone growth. For ^{89}Sr, with a half-life of 50.5 days, 3-month-old infants represent the most sensitive group because of the higher doses to the lower intestine from milk consumption. Table 8-2 presents the DILs adopted for the two strontium isotopes.

Transport of radioactive materials is regulated by the Department of Transportation (DOT) in conjunction with the USNRC. Coordinating government emergency response to accidents involving radioactive materials is the responsibility of the Federal Emergency Management Administration (FEMA).

National regulations governing the occupational exposure to ionizing radiation include USNRC regulations (10 CFR 20), the Occupational Safety and Health Administration (OSHA) standards for ionizing radiation (29 CFR 1910.1096), and the Department of Energy (DOE) standards for occupational radiation protection (10 CFR 835). National regulations concerning general population exposure to radiation have been developed as proposed by the EPA and as finalized by the USNRC based on the dose limit recommendations of the ICRP (ICRP 1996) and the NCRP (NCRP 1993). The EPA and USNRC

also use the BEIR reports of the National Academy of Sciences and the UNSCEAR reports on biological effects to help develop the U.S. standards in line with the NCRP and the ICRP consensus standards.

Currently, there are 29 "NRC Agreement States." An agreement state is any state that has entered into an agreement with the USNRC under Section 274 of the Atomic Energy Act of 1954, as amended. The USNRC relinquishes to these states the majority of its regulatory authority over source, by-product, and special nuclear material in quantities not sufficient to form a critical mass. However, the regulation of nuclear reactors is under USNRC jurisdiction. In the remaining states, USNRC still handles all of the inspection, enforcement, and licensing responsibilities.

The basic philosophy of radiation safety is to minimize unnecessary radiation exposure. The specific objectives of radiation safety guidance as stated by NCRP are (1) to prevent the occurrence of severe radiation-induced deterministic (nonstochastic) disease, and (2) to limit the risk of the nondeterministic (stochastic) effects (fatal cancer and genetic effects) to a reasonable level compared with nonradiation risks and in relation to societal needs, benefits gained, and economic factors. In addition to regulations that set upper limits on radiation dose, the concept of ALARA (As Low As Reasonably Achievable) was introduced to ensure that workplace endeavors resulting in exposures to radiation provide sufficient benefits that offset any potential detriment they cause (ACGIH 2002). The goal is not to eliminate all radiation exposure, which would not be possible, but instead to strive for an appropriate balance between protection of public health and reasonable costs (economic, social, etc.) while maintaining desirable dose limits. The ACGIH has adopted the occupational exposure guidance of the ICRP (ACGIH 2002).

9. REFERENCES

Aarkrog A. 1971. Prediction models for strontium-90 and caesium-137 levels in the human food chain. Health Phys 20:297-311.

Aarkrog A. 1972. Are the rate factors in the ^{90}Sr prediction models constant? Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 447-456.

Aarkrog A, Dahlgaard H, Nielsen SP. 1999. Marine radioactivity in the Arctic: A retrospect of environmental studies in Greenland waters with emphasis on transport of ^{90}Sr and ^{137}Cs with the east Greenland current. Sci Total Environ 237/238:143-151.

Aberg B, Crabo B, Ekman L, et al. 1968. Rapid uptake of radiostrontium in sperm. Acta Physiol Scand 74:381-383.

*ACGIH. 1999a. Strontium. 1999 TLVs and BEIs: Threshold limit values for chemical substances and physical agents biological exposure indices. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.

*ACGIH. 1999b. Strontium chromate. 1999 TLVs and BEIs: Threshold limit values for chemical substances and physical agents biological exposure indices. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.

*ACGIH. 2002. Strontium chromate. 2000 TLVs and BEIs: Threshold limit values for chemical substances and physical agents biological exposure indices. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.

*Adams WT. 1975. Strontium. In: Bureau of Mines. Mineral facts and problems. 1975 edition. U.S. Department of the Interior. Bulletin 667, 1049-1056.

*ADEC. 2000. Maximum contaminant levels (MCLs). Title 18 environmental conservation: Chapter 80. Drinking water 18 AAC 80. Alaska Department of Environmental Conservation. http://www.state.ak.us/local/akpages/ENV.CONSERV/title18/aac80ndx.htm. June 13, 2000.

*Adinolfi M. 1985. The development of the human blood-CSF-brain barrier. Dev Med Child Neurol 27:532-537.

Adler SS, Trobaugh FE. 1978. Hemopoiesis in diffusion chambers in strontium-89 marrow-ablated mice (40328). Proc Soc Exp Biol Med 159:260-265.

*Adlercreutz H. 1995. Phytoestrogens: Epidemiology and a possible role in cancer protection. Environ Health Perspect Suppl 103(7):103-112.

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* Cited in text

9. REFERENCES

*Agency for Toxic Substances and Disease Registry. 1989. Agency for Toxic Substances and Disease Registry. Decision guide for identifying substance-specific data needs related to toxicological profiles; Notice. Federal Register 54(174):37618-37634.

*Agency for Toxic Substances and Disease Registry. 1990. Biomarkers of organ damage or dysfunction for the renal, hepatobiliary, and immune systems. Subcommittee on Biomarkers of Organ Damage and Dysfunction, Agency for Toxic Substances and Disease Registry, Atlanta, GA.

*Agency for Toxic Substances and Disease Registry. 1999. Toxicological profile for ionizing radiation. Agency for Toxic Substances and Disease Registry, Atlanta, GA.

*Agency for Toxic Substances and Disease Registry. 2000. Toxicological profile for chromium. Atlanta, GA: Agency for Toxic Substances and Disease Registry.

*Aghajanian GK, Marek GJ. 1999. Serotonin, via 5-HT_{2A} receptors, increases EPSCs in layer V pyramidal cells of prefrontal cortex by an asynchronous mode of glutamate release. Brain Res 825:161-171.

Akerley W. 2000. Secondary leukemia. Twice a coincidence? Cancer 88(3):497-499.

*Akleyev AV, Kossenko MM, Silkina LA, et al. 1995. Health effects of radiation incidents in the southern Urals. Stem Cells 13(Suppl. 1):58-68.

*Alda JO, Escanero JF. 1985. Transport of calcium, magnesium and strontium by human serum proteins. Rev Esp Fisiol 41:145-150.

Alexakhin RM, Ginsburg LR, Mednik IG, et al. 1994. Model of ^{90}Sr cycling in a forest biogeocenosis. Sci Total Environ 157:83-91.

*Alexander FW, Clayton BE, Delves HT. 1973. The uptake and excretion by children of lead and other contaminants. International Symposium of Environmental and Health Aspects of Lead, Amsterdam, Oct. 2-6, 1972.

*Alexander FW, Clayton BE, Delves HT. 1974. Mineral and trace-metal balances in children receiving normal and synthetic diets. Quart J Med XLIII:89-111.

Alexander FW, Delves HT, Clayton BE. 1973. The uptake and excretion by children of lead and other contaminants. In: International Symposium of Environmental and Health Aspects of Lead, Amsterdam, Oct. 2-6, 1972, 319-331.

*Alfrey AC, Rudolph H, Smythe WR. 1975. Mineral metabolism in uremia. Kidney Int (Suppl.):85-89.

Allain P, Mauras Y, Premel-Cabic A, et al. 1991. Effects of an EDTA infusion on the urinary elimination of several elements in health subjects. Br J Clin Pharmacol 31:347-349.

*Alimov R. 2003. Radioisotope thermoelectric generators: Bellona's working paper. http://www.bellona.no/en/international/russia/navy/northern fleet/incidents/31772.html. December 08, 2003.

*Alm PE, Bloom GD. 1981a. Effects of norepinephrine on transmembrane calcium transport in rat mast cells. Int Arch Allergy Appl Immunol 66:427-438.

*Alm PE, Bloom GD. 1981b. What - if any - is the role of adrenergic mechanisms in histamine release from mast cells? Agents Actions 11(1/2):60-66.

*Altman PL, Dittmer DS. 1974. In: Biological handbooks: Biology data book. Vol. III. 2nd ed. Bethesda, MD: Federation of American Societies for Experimental Biology, 1987-2008, 2041.

Amano H, Yanase N. 1990. Measurement of ^{90}Sr in environmental samples by cation-exchange and liquid scintillation counting. Talanta 37(6):585-590.

*Andersen ME, Krishnan K. 1994. Relating in vitro to in vivo exposures with physiologically based tissue dosimetry and tissue response models. In: Salem H, ed. Animal test alternatives: Refinement, reduction, replacement. New York, NY: Marcel Dekker, Inc., 9-25.

*Andersen ME, Clewell HJ III, Gargas ML, et al. 1987. Physiologically based pharmacokinetics and the risk assessment process for methylene chloride. Toxicol Appl Pharmacol 87:185-205.

Anderson HL, Brady PV, Gruenhagen SE, et al. 1999a. Cs, Sr, and Ba sorption on clays and Fe-oxides. DE 2001 7898.

Anderson J, Kahn B, LaBone T, et al. 1999b. Solubility of various forms of strontium titanate in lungs: In vitro* and in vivo studies. Health Phys 76(6):628-634.

Anderson JJB. 1968. Effect of time on distribution of injected radiostrontium in the skeleton of young pigs. Health Phys 15:237-241.

Anderson JJB. 1972. Whole-body retention of single injections of ^{85}Sr in swine and dogs as a function of age: A review. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 31-38.

Anderson JJB, Comar CL. 1968. Strontium retention as a function of age in the dog. Radiat Res 34:153-169.

Anderson JJB, Balk MW, Crackel WC, et al. 1971a. Effects of calcitonin on ^{85}Sr whole body retention in the dog. Nature (London) New Biol 232:93-94.

Anderson JJB, Crackel WC, Norton HW. 1972. Effect of time on distribution of injected radiostrontium in the skeleton of six-month-old swine. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 123-136.

Anderson JJB, Greenfield JW, Posada JR, et al. 1970. Effect of estrogen on bone mineral turnover in mature female rats as measured by strontium-85. Proc Soc Exp Biol Med 135(3):883-886.

Anderson JJB, Milin L, Crackel WC. 1971b. Effect of exercise on mineral and organic bone turnover in swine. J Appl Physiol 30(6):810-813.

Ando A, Ando I. 1994. Biodistributions of radioactive bipositive metal ions in tumor-bearing animals. BioMetals 7(2):185-192.

9. REFERENCES

Andreyeva LP, Shvedov VL. 1977. [Changes in the rat hemopoietic system when exposed to Strontium 89 and Iodine 131 simultaneously]. Radiobiologiia 17(5):752-757. (Russian)

Anger KS, Aigner S, Bühler M, et al. 1980. [Quantitative whole-body bone scintigraphy. II. Pharmacokinetics of osteotropic radiopharmaceuticals]. Nuklearmedizin 19(3):97-107. (German)

Angeyo KH, Patel JP, Mangala JM, et al. 1998. Measurement of trace element levels in Kenyan cigarettes with the energy dispersive x-ray fluorescence spectroscopy technique. J Trace Microprobe Tech 16(2):233-246.

Anonymous. 1966a. Mopping up strontium. Br Med J 2(521):1024.

Anonymous. 1966b. Strontium metabolism. Br Med J 2(524):1215-1216.

Anonymous. 1969a. Calcium, phosphorus, and strontium metabolism in infants. Nutr Rev 27(9):254-256.

Anonymous. 1969b. Strontium-90 contamination down. Nature 222:210.

*AOAC. 1990. Official methods of analysis of the association of official analytical chemists. 15th ed. Methods 911.03, 973.66, 974.37.

*APHA. 1992. Strontium. Standard methods for the examination of water and wastewater, 18th ed. American Public Health Association.

Apostoaei AI. 2002. Absorption of strontium from the gastrointestinal tract into plasma in healthy human adults. Health Phys 83(1):56-65.

*Apostoli P, Giusti S, Bartoli D, et al. 1998. Multiple exposure to arsenic, antimony, and other elements in art glass manufacturing. Am J Ind Med 34:65-72.

Apostoli P, Porru S, Morandi C, et al. 1997. Multiple determination of elements in human seminal plasma and spermatozoa. J Trace Elem Med Biol 11:182-184.

*Apostolidis N, Paradellis T, Karydas A, et al. 1998. Calcium and strontium metabolic studies in patients on CAPD. Perit Dial Int 18(4):410-414.

Appelgren LE, Nilsson A, Ullberg S. 1963. Autoradiographic localization of strontium 85 in osteosarcomas. Acta Radiol Ther Phys Biol 1(6):459-464.

Appleton J. 1993. The structure of dentine after the injection of strontium chloride by backscattered electron imaging in the scanning electron microscope. Arch Oral Biol 38(1):1-4.

*Appleton J. 1995. Changes in the plasma electrolytes and metabolites of the rat following acute exposure to sodium fluoride and strontium chloride. Arch Oral Biol 40(4):265-268.

Arden NK, Major P, Poole JR, et al. 2002. Size at birth, adult intestinal calcium adsorption and 1,25(OH)2 vitamin D. Q J Med 95:15-21.

9. REFERENCES

Ardissino G, Schmitt CP, Bianchi ML, et al. 2000. No difference in intestinal strontium absorption after oral or IV calcitrol in children with secondary hyperparathyroidism. Kidney Int 58:981-988.

Argiro G, Atzei G, Boemi S, et al. 1998. A process for the recovery of strontium from the urine of patients injected with ^{89}Sr. Appl Radiat Isot 49(7):777-778.

Argyris BF, Reif AE. 1981. Lack of suppressor cell activity in the spleens of mice with radiation-induced osteogenic sarcomas. Cancer Res 41:839-844.

*Armbrecht HJ, Boltz MA, Christakos S, et al. 1998. Capacity of 1,25-dihydroxyvitamin D to stimulate expression of calbindin D changes with age in the rat. Arch Biochem Biophys 352(2):159-164.

*Armbrecht HJ, Wasserman RH, Bruns MEH. 1979. Effect of 1,25-dihydroxyvitamin D_3 on intestinal calcium absorption in strontium-fed rats. Arch Biochem Biophys 192(2):466-473.

Arner A, Lövgren B, Uvelius B. 1983. The effects of Ca^{2+} and Sr^{2+} at different modes of activation in the smooth muscle of the rat portal vein. Acta Physiol Scand 117:541-545.

Arskan Z, Tyson JF. 1999. Determination of calcium, magnesium and strontium in soils by flow injection flame atomic absorption spectrometry. Talanta 50:929-937.

Artalejo CR, Garcia AG, Aunis D. 1987. Chromaffin cell calcium channel kinetics measured isotopically through fast calcium, strontium, and barium fluxes. J Biol Chem 262(2):915-926.

*Arthur WJ, Janke DH. 1986. Radionuclide concentrations in wildlife occurring at a solid radioactive waste disposal area. Northwest Sci 60(3):154-165.

Arthur WJ, Markham OD. 1982. Radionuclide export and elimination by coyotes at two radioactive waste disposal areas in southeastern Idaho. Health Phys 43(3):493-500.

*Ash P, Loutit JF. 1977. The ultrastructure of skeletal haemangio-sarcomas induced in mice by strontium-90. J Pathol 122:209-218.

Ashrafi MH, Spector PC, Curzon MEJ. 1980. Pre- and posteruptive effects of low doses of strontium on dental caries in the rat. Caries Res 14:341-346.

Assimakopoulos PA, Divanes K, Pakou AA, et al. 1995. Radiostrontium transfer to sheep's milk as a result of soil ingestion. Sci Total Environ 172:17-20.

*ASTM. 1999. Methods D3352, D3920, D4185. 1999 Annual book of ASTM standards: Water and environmental technology. Vol. 11.02. American Society for Testing and Materials. http://www.astm.org.

*Atkinson G, Ennis M, Pearce FL. 1979. The effect of alkaline earth cations on the release of histamine from rat peritoneal mast cells treated with compound 48/80 and peptide 401. Br J Pharmacol 65:395-402.

*Audi L, Garcia-Ramirez M, Carrascosa A. 1999. Genetic determinants of bone mass. Horm Res 51(3):105-123. (Abstract)

Augustin W, Gellerich F, Wiswedel I, et al. 1979. Inhibition of cation efflux by antioxidants during oscillatory ion transport in mitochondria. FEBS Lett 107(1):151-154.

9. REFERENCES

Avenant-Oldewage A, Marx H. 2000. Manganese, nickel and strontium bioaccumulation in the tissues of the African sharptooth catfish, Clarias gariepinus from the Olifants River. Kruger National Park. Koedoe 43(2):17-33.

*AZ Dept Health Serv. 1999. Health based guidance levels for the ingestion of contaminants in drinking water (HBGL). Arizona Department of Health Services. http://www.hs.state.az.us/edc/oeh/hbgl.htm. Novemeber 15, 1999.

Bacon JR, Bain DC. 1995. Characterization of environmental water samples using strontium and lead stable isotope compositions. Environ Geochem Health 17(1):39-49.

Bader H, Wilkes AB, Jean DH. 1970. The effect of hudroxylamine, mercaptans, divalent metals and chelators on ($Na^+ + K^+$)-ATPase. Biochim Biophys Acta 198:583-593.

*Baes CF, Garten CT, Taylor FG, et al. 1986. Long-term environmental problems of radioactively contaminated land. Environ Int 12:543-553.

Bairakova AK. 1974. Dose and germ cell stage dependence of strontium 89 mutagenic effects in rat males. Strahlentherapie 148(4):394-396.

Balonov MI. 1997. Internal exposure of populations to long-lived radionuclides releases into the environment. Ciba Found Symp 203:120-133.

Banno H, Imaizumi Y, Watanabe M. 1987. Cellular mechanisms of supersensitivity to acetylcholine and potassium ion after ciliary ganglionectomy in the rat iris sphincter muscle. Jpn J Pharmacol 43:153-163.

*Baratta EJ, Ferri ES. 1966. Radionuclides in selected human tissues. Am Ind Hyg Assoc J 438-443.

Bard D, Verger P, Hubert P. 1997. Chernobyl, 10 years after: Health consequences. Epidemiol Rev 19(2):187-204.

*Barnes DG, Dourson M. 1988. Reference dose (RfD): Description and use in health risk assessments. Regul Toxicol Pharmacol 8:471-486.

Barnes DWH, Carr TEF, Evans EP, et al. 1970. ^{90}Sr-induced osteosarcomas in radiation chimaeras. Int J Radiat Biol 18(6):531-537.

*Barnes KW. 1997. Trace metal determinations in fruit, juice, and juice products using an axially viewed plasma. Atom Spectrosc 18(3):84-101.

*Barrie LA, Gregor D, Hargrave B, et al. 1992. Arctic contaminants: sources, occurrence and pathways. Sci Total Environ 122:1-74.

*Barry WH, Marion AM, Harrison DC. 1972. The hemodynamic effects of strontium chloride in the intact dog. Proc Soc Exp Biol Med 141(1):52-58.

*Bartholomay RC, Orr BR, Liszewski MJ, et al. 1995. Hydrologic conditions and distribution of selected radiochemical and chemical constituents in water, Snake River Plain aquifier, Idaho National Engineering Laboratory, Idaho, 1989 through 1991. Water-Resources Investigations Report 95-4175. Idaho Falls, Idaho: U.S. Geological Survey.

Barto R, Sips AJAM, van der Vijgh WJF, et al. 1995. Sensitive method for analysis of strontium in human and animal plasma by graphite furnace atomic absorption spectrophotometry. Clin Chem 41(8):1159-1163.

Bates TH, Smith H. 1966a. Influence of polyphosphates on retention of radioactive strontium in rat and mouse. Nature 212:925-926.

Bates TH, Smith H. 1966b. Influence of sodium saliculate on radioactive strontium retention in rat and mouse. Nature 209:824-825.

*Bauchinger M, Salassidis K, Braselmann H, et al. 1998. FISH-based analysis of stable translocations in a Techa river population. Int J Radiat Biol 73:605-612.

Baud CA, Bang S, Lee HS, et al. 1968. X-ray studies of strontium incorporation into bone mineral in vivo. Calcif Tissue Res 2(Suppl.):6.

*Bauerova K, Koprda V, Harangzo M. 2001. Contribution to the penetration of radionuclides across the skin. Concentration dependence of stronium through the skin in vitro. J Appl Toxicol 21:241-243.

Baverstock KF, Vennart J. 1976. Emergency reference levels for reactor accidents: A re-examination of the windscale reactor accident. Health Phys 30:339-344.

*Baziotis N, Yakoumakis E, Zissimopoulos A, et al. 1998. Strontium-89 chloride in the treatment of bone metastasis from breast cancer. Oncology 55:377-381.

Beddington JR, Mills CA, Beards F, et al. 1989. Long-term changes in strontium-90 concentrations within a freshwater predator-prey system. J Fish Biol 35:679-686.

*Bekerus M. 1970. [Late reaction following radiation with Sr^{90}-derma plates, followed up for 8 and more years]. Strahlentherapie 140(1):105-107. (German)

*Benjamin SA, Boecker BB, Cuddihy RG, et al. 1976a. Nasal carcinomas in beagle dogs after inhalation of relatively soluble forms of beta-emitting radionuclides. Radiat Res 67(3):572-573.

*Benjamin SA, Boecker BB, Cuddihy RG, et al. 1979. Nasal carcinomas in beagles after inhalation of relatively soluble forms of beta-emitting radionuclides. J Natl Cancer Inst 63:133-139.

*Benjamin SA, Brooks AL, McClellan RO. 1976b. Biological effectiveness of ^{239}Pu, ^{144}Ce and ^{90}Sr citrate in producing chromosome damage, bone-related tumours, liver tumours and life shortening in the Chinese hamster. In: Lewis M, ed. Biological and environmental effects of low-level radiation: Proceedings of a symposium on biological effects of low-level radiation pertinent to protection of man and his environment. Vienna: International Atomic Energy Agency, Vol. 2, 143-152.

*Benjamin SA, Hahn FF, Chiffelle TL, et al. 1975. Occurrence of hemangiosarcomas in beagles with internally deposited radionuclides. Cancer Res 35:1745-1755.

*Benjamin SA, Jones RK, Snipes MB, et al. 1974a. Comparative effects of inhaled relatively insoluble forms of ^{90}Y, ^{144}Ce and ^{90}Sr on canine peripheral lymphocyte function. In: Annual reports of the Inhalation Toxicology Research Institute. Albuquerque, NM: Inhalation Toxicology Research Institute, 192-196.

*Benjamin SA, Jones RK, Snipes MB, et al. 1976c. Comparative effects of inhaled relatively insoluble forms of ^{90}Y, ^{144}Ce, and ^{90}Sr on canine peripheral lymphocyte function. In: Radiation and the lymphatic system: Proceedings of the fourteenth annual Hanford biology symposium at Richland, Washington, September 30-October 2, 1974. Springfield, VA: Energy Research and Development Administration, 90-99.

*Benjamin SA, Muggenburg BA, Boecker BB, et al. 1974b. Toxicity of inhaled $^{90}SrCl_2$ in beagle dogs, VIII. In: Annual reports of the Inhalation Toxicology Research Institute. Albuquerque, NM: Inhalation Toxicology Research Institute, 89-92.

Ben-Josef E, Lucas DR, Vasan S, et al. 1995a. Selective accumulation of strontium-89 metastatic deposits in bone: Radio-histological correlation. Nucl Med Commun 16:457-463.

*Ben-Josef E, Maughan RL, Vasan S, et al. 1995b. A direct measurement of strontium-89 activity in bone metastasis. Nucl Med Commun 16:452-456.

Bennett BG. 1972. Fallout ^{90}Sr in diet and human bone. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 457-468.

*Bennett M, Baker EE, Eastcott JW, et al. 1976. Selective elimination of marrow precursors with the bone-seeking isotope ^{89}Sr: Implications for hemopoiesis, lymphopoiesis, viral leukemogenesis and infection. J Reticuloendothel Soc 20(1):71-87.

*Beresford NA, Mayes RW, MacEachern PJ, et al. 1999. The effectiveness of alginates to reduce the transfer of radiostrontium to the milk of dairy goats. J Environ Radioact 44:43-54.

*Berg D, Oberhausen E, Muth H. 1973. [Interaction of ^{47}Ca, ^{85}Sr, ^{133}Ba and ^{226}Ra with serum proteins]. Biophysik 10:309-319. (German)

*Berger GS. 1994. Epidemiology of endometriosis. In: Berger GS, ed. Endometriosis: Advanced management and surgical techniques. New York, NY: Springer-Verlag.

Berger VHJ, Eger W. 1965. Über den mechanismus der strontiumeinlagerung ins knochengewebe. Acta Histochem (Jena) 22:298-308.

Berman MC, King SB. 1990. Stoichiometries of calcium and strontium transport coupled to ATP and acetyl phosphate hydrolysis by skeletal sarcoplasmic reticulum. Biochim Biophys Acta 1029:235-240.

Bernard SR, Nestor CW. 1980. Studies of age-dependent strontium metabolism with application to fallout data. In: International Radiation Protection Society, ed. Radiation protection: A systemic approach to safety: Proceedings of the 5th congress of the International Radiation Protection Society, Jerusalem, March 1980. New York, NY: Pergamon Press, Vol. 2, 1083-1086.

*Best LC, Bone EA, Russell RGG. 1981. Strontium ions induce production of thromboxane B_2 and secretion of 5-hydroxytryptamine in washed human platelets. Biochem Pharmacol 30:635-637.

Betti M, Giannarelli S, Hiernaut T, et al. 1996. Detection of trace radioisotopes in soil, sediment and vegetation by glow discharge mass spectrometry. Fresenius J Anal Chem 355:642-646.

9. REFERENCES

*Bhattacharyya MH, Silbergeld EK, Jeffery E, et al. 1995. Metal-induced osteotoxicities. In: Goyer RA, Klaassen CD, Waalkes MP, eds. Metal toxicology. New York, NY: Academic Press, 465-510.

Bialkowski MM, Wierzbicki JG, Porter AT. 1997. Modeling of internal dose distributions during SR-89 treatment of a patient with bone metastases. Cancer Biother Radiopharm 12(5):355-362.

*Bianchi ML, Ardissino GL, Schmitt CP, et al. 1999. No difference in intestinal strontium absorption after an oral or an intravenous $1,25(OH)_2D_3$ bolus in normal subjects. J Bone Miner Res 14(10):1789-1795.

Bibak A, Sturup S, Haahr V, et al. 1999. Concentrations of 50 major and trace elements in Danish agricultural crops measured by inductively coupled plasma mass spectrometry. 3. potato (*Solanum tuberosum* Folva). J Agric Food Chem 47:2678-2684.

Bibak A, Sturup S, Knudsen L, et al. 1999. Concentrations of 63 elements in cabbage and sprouts in Denmark. Commun Soil Sci Plant Anal 30(17&18):2409-2418.

*Bierke P. 1990. Immune competence in ^{90}Sr-exposed, adult thymectomized and antilymphocyteglobulin-treated CBA mice: II. Reticuloendothelial phagocyte function and in vitro mitogen responsiveness of spleen cells. Acta Oncol 29(5):615-621.

*Bierke P, Nilsson A. 1990. Radiostrontium-induced oncogenesis and the role of immunosuppression: II. Influence of ^{90}Sr dose, adult thymectomy and antilymphocyteglobulin treatment on the development of lympho-reticular and extraskeletal, neoplastic lesions in CBA mice. Acta Oncol 29(1):53-63.

*Bishop M, Harrison GE, Raymond WHA, et al. 1960. Excretion and retention of radioactive strontium in normal men following a single intravenous injection. Int J Radiat Biol 2(2):125-142.

Biskis BO, Finkel MP. 1964. Histopathology of bone in dogs given radiostrontium. Fed Proc 23(2,pt1):393.

Bittel R, Magnaval R. 1977. Microlocalization of artificial radionuclides in radiological protection of the environment. Curr Top Radiat Res Q 12:33-43.

Blair HA. 1972. Radiation dose-time relations for induction of osteosarcoma in mice and dogs and their bearing on maximal permissible burden of ^{90}Sr in man. Health Phys 23:759-765.

Blake GM, Gray JM, Zivanovix MA, et al. 1987a. Strontium-89 radionuclide therapy: A dosimetric study using impulse response function analysis. Br J Radiol 60:685-692.

*Blake GM, Wood JF, Wood PJ, et al. 1989a. ^{89}Sr therapy: Strontium plasma clearance in disseminated prostatic carcinoma. Eur J Nucl Med 15:49-54.

Blake GM, Zivanovic MA, Gray JM. 1987b. Strontium kinetics in metastasized prostatic carcinoma: A comparison with the predictions of impulse response function analysis. Nucl Med Commun 8:909-919.

*Blake GM, Zivanovic MA, Lewington VJ. 1989b. Measurements of the strontium plasma clearance rate in patients receiving ^{89}Sr radionuclide therapy. Eur J Nucl Med 15:780-783.

*Blake GM, Zivanovic MA, McEwan AJ, et al. 1986. Sr-89 therapy: Strontium kinetics in disseminated carcinoma of the prostate. Eur J Nucl Med 12:447-454.

*Blake GM, Zivanovic MA, McEwan AJ, et al. 1987c. ^{89}Sr radionuclide therapy: Dosimetry and haematological toxicity in two patients with metastasising prostatic carcinoma. Eur J Nucl Med 13:41-46.

Blake GM, Zivanovic MA, McEwan AJ, et al. 1987d. Strontium-89 therapy: Strontium kinetics and dosimetry in two patients treated for metastasising osteosarcoma. Br J Radiol 60:253-259.

Blanco Gomis G, Fuente Alonso E, Arias Abrodo P. 1989. Ion-pair extraction and fluorimetric determination of ultratraces of strontium with cryptand 2.2.2 and eosin. Mikrochim Acta III:59-68.

Bland MR, Carr TEF, Loutit JF, et al. 1972. Tumours induced by ^{90}Sr in normal and chimaerical CBA/H mice. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 167-172.

Blincoe C, Bohman VR, Fountain EL. 1969. Fallout concentrations in cattle grazing highly contaminated range. Health Phys 17:559-564.

*Blumsohn A, Morris B, Eastell R. 1994. Stable strontium absorption as a measure of intestinal calcium absorption: Comparison with the double-radiotracer calcium absorption test. Clin Sci 87:363-368.

*BNA. 2001. Environment and Safety Library on the Web States and Territories. Bureau of National Affairs, Inc. Washington, D.C. http//www.esweb.bna.com. May 08, 2001.

Bobovnikova TI, Virchenko YP, Konoplev AV, et al. 1991. Chemical forms of occurrence of long-lived radionuclides and their alteration in soils near the Chernobyl nuclear power station. Sov Soil Sci 23(5):52-57.

*Boecker BB, Chiffelle TL, Hobbs CH, et al. 1969. Toxicity of inhaled $^{90}SrCl_2$ in beagle dogs. III. In: McClellan RO, Rupprecht FC, eds. Annual report of the fission product inhalation program. Albuquerque, NM: Lovelace Foundation for Medical Education and Research, 1-7.

Boecker BB, Hahn FF, Cuddihy RG, et al. 1983. Is the human nasal cavity at risk from inhaled radionuclides? In: Thompson RC, Mahaffey JA, eds. Life-span radiation effects studies in animals: What can they tell us? Proceedings of the twenty-second Hanford life science symposium held at Richland, Washington, September 27-29, 1983. Hanford Life Sciences Symposium 22nd. Springfield, VA: United States Department of Energy, 564-577.

*Boecker BB, Muggenburg BA, Miller SC, et al. 1991. Annual report on long-term dose-response studies of inhaled or injected radionuclides: October 1, 1990 through September 30, 1991. Albuquerque, NM: Lovelace Foundation for Medical Education and Research.

Boegler VF, Kriegel H. 1968. Leukämoide reaktion nach 90-strontium-inkorporation bei ratten. Blut 17(6):345-350.

Bohr DF. 1974. Reactivity of vascular smooth muscle from normal and hypertensive rats: Effect of several cations. Fed Proc 33:127-132.

Boivin G, Deloffre P, Perrat B, et al. 1996. Strontium distribution and interactions with bone mineral in monkey iliac bone after strontium salt (S 12911) administration. J Bone Miner Res 11(9):1302-1311.

9. REFERENCES

Bondar PF. 1984. Influence of soil climate on accumulation by plants of ^{89}Sr from the soil, and prediction of harvest contamination. Sov Soil Sci 16(2):100-112.

Bondar PF. 1987. Some aspects of the evaluation and forecasting of aerial contamination of plants by radioactive substances and chemicals. Sov Soil Sci 18(5):104-114.

*Bone EA, Best LC, Jones PBB, et al. 1980. The effects of strontium and calcium ions on 5-hydroxytryptamine secretion and thromboxane B_2 biosynthesis in washed human platelets. Biochem Soc Trans 8(5):530-531.

*Book SA, Spangler WL, Swartz LA. 1982. Effects of lifetime ingestion of ^{90}Sr in beagle dogs. Radiat Res 90:244-251.

Book SA, Rosenblatt LS, Goldman M. 1983. Lifetime effects of long-term exposures to strontium-90 and radium-226 in beagle dogs. In: Thompson RC, Mahaffey JA, eds. Life-span radiation effects studies in animals: What can they tell us? Proceedings of the twenty-second Hanford life science symposium held at Richland, Washington, September 27-29, 1983. Hanford Life Sciences Symposium 22nd. Springfield, VA: United States Department of Energy, 646-659.

Boonen GJJC, VanSteveninck J, Elferink JGR. 1993. Strontium and barium induce exocytosis in electropermeabilized neutrophils. Biochim Biophys Acta 1175:155-160.

Borisov BK. 1972. Strontium-90 metabolism in the human foetus. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 469-476.

Borisova VV, Zapol'Skaya NA. 1972. Investigation of doses produced by ^{90}Sr taking into account age-dependent biological parameters: An experimental investigation on rats. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 39-48.

*Breen SL, Powe JE, Porter AT. 1992. Dose estimation in strontium-89 radiotherapy of metastatic prostatic carcinoma. J Nucl Med 33:1316-1323.

Brent R, Meistrich M, Paul M. 1993. Ionizing and nonionizing radiations. In: Paul M, ed. Occupational and environmental reproductive hazards: A guide for clinicians. Baltimore, MD: Williams & Wilkins, 165-189.

Brent RL, Beckman DA. 1992. Principles of teratology. In: Evans MI, ed. Reproductive risks and prenatal diagnosis. Norwalk, CT: Appleton & Lange, 43-68.

*Brooks AL, McClellan RO. 1969. Chromosome aberrations and other effects produced by ^{90}Sr-^{90}Y in Chinese hamsters. Int J Radiat Biol 16(6):545-561.

*Brooks AL, Benjamin SA, McClellan RO. 1974. Toxicity of ^{90}Sr-^{90}Y in Chinese hamsters. Radiat Res 57:471-481.

*Bronner F, Pansu D, Stein WD. 1986. An analysis of intestinal calcium transport across the rat intestine. Am J Physiol 250(13):G561-G569.

9. REFERENCES

Bruenger FW, Miller SC, Lloyd RD. 1991. A comparison of the natural survival of beagle dogs injected intravenously with low levels of ^{239}Pu, ^{226}Ra, ^{228}Ra, ^{228}Th, or ^{90}Sr. Radiat Res 126:329-337.

Bruenger FW, Stover BJ, Atherton DR. 1967. The incorporation of various metal ions into in vivo- and in vitro-produced melanin. Radiat Res 32:1-12.

*Brues AM, Auerbach H, Grube D, et al. 1967. Studies on soft-tissue dosage from strontium-90. In: Lenihan JMA, Loutit JF, Martin JH, eds. Strontium metabolism: Proceedings of the international symposium on some aspects of strontium metabolism held at Chapelcross, Glasgow and Strontian, 5-7 May, 1966. New York, NY: Academic Press, 207-212.

*Brues AM, Auerbach H, Grube DD, et al. 1969. Retention of radiostrontium in soft tissues. ANL-7635. 119-120.

Bull S, Stotz S, Munsterer F, et al. 1974. Konzentration und verteilung ^{85}Sr in degenerativ, nekrotisch und entzundlich veranderten femurkopfen. Radiologe 14:383-391.

*Bunde RL, Rosentreter JJ, Liszewski MJ, et al. 1997. Effects of calcium and magnesium on strontium distribution coefficients. Environ Geol 32(3):219-229.

*Bunde RL, Rosentreter JJ, Liszewski MJ. 1998. Rate of strontium sorption and the effects of variable aqueous concentrations of sodium and potassium on strontium distribution coefficients of a surficial sediment at the Idaho National Engineering Laboratory, Idaho. Environ Geol 34(2/3):135-142.

*Bunker DJ, Smith JT, Livens FR, et al. 2000. Determination of radionuclides exchangeability in freshwater systems. Sci Total Environ 263(1-3):171-183.

Bunzl K, Kracke W. 1990. Simultaneous determination of ^{238}Pu, $^{239+240}$Pu, ^{241}Pu, ^{241}Am, ^{242}Cm, ^{244}Cm, ^{89}Sr, and ^{90}Sr in vegetation samples, and application to Chernobyl-fallout contaminated grass. J Radioanal Nucl Chem 138(1):83-91.

*Bunzl K, Schimmack W. 1989. Associations between the fluctuations of the distribution coefficients of Cs, Zn, Sr, Co, Cd, Ce, Ru, Tc and I in the upper two horizons of a podzol forest soil. Chemosphere 18(11/12):2109-2120.

*Burguera M, Burguera JL, Rondón C, et al. 1999. Appraisal of different electrothermal atomic absorption spectrometric methods for the determination of strontium in biological samples. Spectrochim Acta, Part B 54:805-818.

Burt VK, Green JW. 1971. Studies of a calcium-sensitive ATPase in chick heart ventricle cells. Exp Cell Res 65:170-176.

Busselen P. 1971. Potassium chloride contractures in rabbit auricles: Interaction of Sr^{2+} and Ca^{2+}. Arch Int Physiol Biochim 79(4):809.

Butler GC. 1968. Metabolism of radionuclides in workers. Environ Health Ser [Radiol Health] 33:33-44.

Butler GC, Veld A. 1967. Evaluation of radiation exposure from internal deposition of three bone-seeking radionuclides. Health Phys 13(8):916-918.

9. REFERENCES

Cabrera WE, Schrooten I, De Broe ME, et al. 1999. Strontium and bone. J Bone Miner Res 14(5):661-668.

*CA Department of Health Services. 2000. Chemical contaminants in drinking water. California Department of Health Services. http://www.dhs.cahwnet.gov/org_indx.htm.

Calhoun NR, Campbell S, Smith JC. 1970. Accumulation of labeled zinc, strontium, and calcium in bone injuries. J Dent Res 49(5):1083-1085.

*Capar SG, Cunningham WC. 2000. Element and radionuclide concentrations in food: FDA total diet study 1991-1996. J AOAC Int 83(1):157-177.

*Capo RC, Stewart BW, Chadwick OA. 1998. Strontium isotopes as tracers of ecosystem processes: theory and methods. Geoderma 82:197-225.

Carafoli E. 1967. In vivo effect of uncoupling agents on the incorporation of calcium and strontium into mitochondria and other subcellular fractions of rat liver. J Gen Physiol 50:1849-1864.

Carafoli E, Tiozzo R. 1967. Time course of the distribution of in vivo administered $^{89}Sr^{++}$ in rat liver subcellular fractions. Experientia 23(12):1017-1018.

Carafoli E, Rossi CS, Lehninger AL. 1965. Energy-coupling in mitochondria during resting of state 4 respiration. Biochem Biophys Res Commun 19(5):609-614.

*Carini F, Anguissola Scotti I, D'Alessandro PG. 1999. ^{134}Cs and ^{85}Sr in fruit plants following wet aerial deposition. Health Phys 77(5):520-529.

*Carlton WH, Murphy CE, Jannik GT, et al. 1998. Radiostrontium in the Savannah River site environment. U.S. Department of Energy. DE-AC09-96SR18500. WSRC-MS-98-00454, Rev. 1. http://www.srs.gov/general/sci-tech/fulltext/ms9800454.html.

*Carlton WH, Simpkins AA, Jannik GT. 1999. Radionuclides in the Savannah River site environment. Health Phys 77(6):677-685.

*Carmichael KA, Fallon MD, Dalinka M, et al. 1984. Osteomalacia and osteitis fibrosa in a man ingesting aluminum hydroxide antacid. Am J Med 76:1137-1143.

Carmon B, Eliah Y. 1980. A relatively fast assay of Sr-90 by measuring the Cherenkov effect from the ingrowing Y-90. In: Radiation Protection: A systematic approach to safety: Proceedings of the 5th congress of the International Radiation Protection Society, Jerusalem, March 1980. New York, NY: Pergamon Press, Vol. 2, 889-1142.

Carmon B, German U. 1982. Radioassay of low ^{90}Sr activities by early counting of the Cerenkov radiation induced by the ingrowing daughter nuclide ^{90}Y. Health Phys 42(4):529-530.

*Carr TEF, Nolan J. 1968. Inhibition of the absorption of dietary radiostrontium by aluminum phosphate gel and sodium alginate in the rat. Nature 219:500-501.

Carr TEF, Harrison GE, Humphreys ER, et al. 1968. Reduction in the absorption and retention of dietary strontium in man by alginate. Int J Radiat Biol 14(3):225-233.

9. REFERENCES

Carrier GO, Matheny JL, Ahlquist RP. 1975. Adrenergic drug-receptor interaction in the presence of strontium (Sr++) in mammalian myocardium. Arch Int Pharmacodyn 218:11-18.

Carvalho CAM. 1979. Fluxes of Ca^{2+}, Sr^{2+} and Mg^{2+} in synaptosomes. Life Sci 25:73-82.

Carvalho ML, Custodio PJ, Reus U, et al. 2001. Elemental analysis of human amniotic fluid and placenta by total-reflection X-ray fluorescence and energy-dispersive X-ray flourescence: Child weight and maternal age dependence. Spectrochim Acta, Part B 56(11):2175-2180.

Carvalho ML, Ferreira JG, Amorim P, et al. 1997. Study of heavy metals and other elements in macrophyte algae using energy-dispersive x-ray fluorescence. Environ Toxicol Chem 16(4):807-812.

*Casarett GW, Tuttle LW, Baxter RC. 1962. Pathology of imbibed Sr^{90} in rats and monkeys. In: Dougherty TF, Jee WSS, Mays CW, et al., eds. Some aspects of internal irradiation: Proceedings of a symposium held at the Homestead, Heber, Utah, 8-11 May 1961. New York, NY: Pergamon Press, 329-336.

Cawse PA. 1989. The origin, transport and persistence of radionuclides. J Sci Food Agric 49:123-129.

*CDC. 1994. Radionuclide releases to the atmosphere from Hanford operations, 1944-1972: Hanford environmental dose reconstruction project. Richland, WA: Centers for Disease Control and Prevention.

CELDs. 1994. Computer-assisted environmental Legislative database. University of Illinois at Urbana.

*Chan TL, Lippman M. 1980. Experimental measurements and empirical modeling of the regional deposition of inhaled particles in humans. Am Ind Hyg Assoc J 47:399-408.

Chang L-Y, Davidson W, Zhang H, et al. 1998. Performance characteristics for the measurement of Cs and Sr by diffusive gradients in thin films (DGT). Anal Chim Acta 368:243-253.

Chaudhuri TK, Chaudhuri TK. 1972. Altered metabolism of strontium by phosphate. In: International Conference on Strontium Metabolism, ed. Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 289-296.

Chaudhuri TK, Chaudhuri TK, Christie JH. 1972a. Two stage liver and bone scans with single dose of one isotope. Int J Appl Radiat Isot 23(4):204-205.

Chaudhuri TK, Chaudhuri TK, Christie JH. 1972b. Uptake of radiostrontium in lungs and other extraosseous tissues. J Nucl Med 13(11):860.

Chaudhuri TK, Chaudhuri TK, Go RT, et al. 1973. Uptake of ^{85m}Sr by liver metastasis from carcinoma of colon. J Nucl Med 14(5):293-294.

Chaudhuri TK, Chaudhuri TK, Peterson RE, et al. 1971. Effect of phosphate on serum strontium. Proc Soc Exp Biol Med 137(1):1-4.

Chaudhuri TK, Chaudhuri TK, Suzuki Y, et al. 1972c. Splenic accumulation of ^{85m}Sr in a patient with Hodgkin's disease. Radiology 105:617-618.

9. REFERENCES

Cheburkin AK, Shotyk W. 1996. A energy-dispersive miniprobe multielement analyzer (EMMA) for direct analysis of Pb and other trace elements in peats. Fresenius J Anal Chem 354:688-691.

*ChemFinder. 2002. Strontium. Chemfinder.com: Database and internet searching. http://www.chemfinder.com/.

Cherny SN, Chausmer AB, Bellavia JV, et al. 1970. Interactions of thyroxine and thyrocalcitonin in the rat. Endocrinology 86(6):1337-1346.

Cherruault Y, Sarin VB. 1987. A four compartment model to study the kinetics of strontium metabolism in man. Int J Biomed Comput 20:21-26.

Chesser RK, Rodgers BE, Wickliffe JK, et al. 2001. Accumulation of ^{137}cesium and ^{90}strontium from abiotic and biotic sources in rodents at Chornobyl, Ukraine. Environ Toxicol Chem 20(9):1927-1935.

*Chesser RK, Sugg DW, Lomakin MD, et al. 2000. Concentrations and dose rate estimates of ^{134,137}cesium and ^{90}strontium in small mammals at Chornobyl, Ukraine. Environ Toxicol Chem 19(2):305-312.

*Chines A, Pacifici R. 1990. Antacid and sucralfate-induced hypophosphatemic osteomalacia: A case report and review of the literature. Calcif Tissue Int 47:291-295.

Christensen GC, Alstad J, Kvåle E, et al. 1975. Strontium-90 in human bone in Norway 1956-1972. Health Phys 28:677-684.

Christoffersen J, Christoffersen MR, Kolthoff N, et al. 1997. Effects of strontium ions on growth and dissolution of hydroxyapatite and on bone mineral detection. Bone 20(1):47-54.

Chowdhury MJ, Blust R. 2001. A mechanism model for the uptake of waterborne strontium in the common carp (*Cyprinus carpio* L.). Environ Sci Technol 35(4):669-675.

Choudhury MJ, Blust R. 2002. Bioavialability of waterborne strontium to the common carp, *Cyprinus carpio*, in complexing environments. Aquat Toxicol 58:215-227.

Churchill PC, Churchill MC, McDonald FD. 1986. Extracellular strontium substitutes for calcium in in vitro renin secretion. J Pharmacol Exp Ther 236(2):331-333.

*Clarke WJ, Busch RH, Hackett PL, et al. 1972. Strontium-90 effects in swine: A summary to date. AEC Symp Ser 25:242-258.

*Clarke WJ, Palmer RF, Howard EB, et al. 1970. Strontium-90: Effects of chronic ingestion on farrowing performance of miniature swine. Science 169:598-600.

Claver KT, Brey RR, Gesell TF. 1998. Developing a methodology for analysis of ^{90}Sr in milk using 3M empore rad discs. Health Phys 76:S115.

*Clayton E, Wooller KK. 1985. Sample preparation and system calibration for proton-induced x-ray emission analysis of hair from occupationally exposed workers. Anal Chem 57:1075-1079.

Clayton RF. 1966. Health physics problems during the demolition of highly radioactive chemical processing plants. Health Phys 12:1571-1580.

Clayton RF, Smith JW. 1971. Health physics aspects of the decontamination of a high level activity cell line. Health Phys 20:153-165.

Clegg DJ. 1971. Embryotoxicity of chemical contaminants of foods. Food Cosmet Toxicol 9:195-205.

*Clewell HJ III, Andersen ME. 1985. Risk assessment extrapolations and physiological modeling. Toxicol Ind Health 1(4):111-131.

Cochrane E, McCarthy ID. 1991. Rapid effects of parathyroid hormone(1-34) and prostaglandin E_2 on bone blood flow and strontium clearance in the rat *in vivo*. J Endocrinol 131:359-365.

*CO Dept of Public Health and Environ. 1999. Ground water quality classifications and standards. Colorado Department of Public Health & Environment. http://www.cdphe.state.co.us/cdphehom.asp.

Cofield RH, Bassingthwaighte JB, Kelly PJ. 1975. Strontium-85 extraction during transcapillary passage in tibial bone. J Appl Physiol 39(4):596-602.

Coggle JE, Williams JP. 1990. Experimental studies of radiation carcinogenesis in the skin: A review. Int J Radiat Biol 57(4):797-808.

Cohen Y, Brook G, Sobel JD, et al. 1974. ^{85}Sr uptake in lung metastasis of osteogenic sarcoma: A case report. Oncology 30:493-498.

Cohn SH, Gusmano EA. 1967. Kinetics of strontium and calcium skeletal metabolism in the rat. Proc Soc Exp Biol Med 126:79-83.

Cohn SH, Bozzo SR, Jesseph JE, et al. 1966. Strontium and calcium skeletal discrimination determined by compartmental analysis. J Appl Physiol 21:67-72.

*Cole KL, Engstrom DR, Futyma RP, et al. 1990. Past atmospheric deposition of metals in Northern Indiana measured in a peat core from Cowles Bog. Environ Sci Technol 24:543-549.

Cole P, Green LC, Lash TL. 1999. Lifestyle determinants of cancer among Danish mastic asphalt workers. Regul Toxicol Pharmacol 30:1-8.

*Cole VV, Harned BK, Hafkesbring R. 1941. The toxicity of strontium and calcium. J Pharmacol Exp Ther 71:1-5.

*Colomina T, Llobet JM, Domingo JL, et al. 1991. The effects of repeated administration of various chelating agents on the removal of strontium from the mouse. Vet Hum Toxicol 33(2):121-124.

Comar CL, Wasserman RH, Lengemann FW. 1966. Effect of dietary calcium on secretion of strontium into milk. Health Phys 12:1-6.

Coob J, Warwick P, Carpenter RC, et al. 1994. Determination of strontium-90 in water and urine samples using ion chromatography. Analyst 119:1759-1764.

Cooley JL. 1973. Effects of chronic environmental radiation on a natural population of the aquatic snail *Physa heterostropha*. Radiat Res 54:130-140.

9. REFERENCES

*Cooper EL, Rahman MM. 1994. A study of cycling of ^{90}Sr in a natural forest on the Canadian Shield. Sci Total Environ 157:107-113.

Corhay J-L, Bury T, Delavignette J-P, et al. 1995. Nonfibrous mineralogical analysis of bronchoalveolar lavage fluid from blast-furnace workers. Arch Environ Health 50(4):312-319.

Corradino RA. 1972. Strontium inhibition of the vitamin D-induces calcium-binding protein and the intestinal calcium absorptive mechanism. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 277-288.

*Corradino RA, Wasserman RH. 1970. Strontium inhibition of vitamin D_3-induced calcium-binding protein (CaBP) and calcium absorption in chick intestine. Proc Soc Exp Biol Med 133(3):960-963.

*Corradino RA, Ebel JG, Craig PH, et al. 1971a. Calcium absorption and the vitamin D_3-dependent calcium-binding protein: I. Inhibition by dietary strontium. Calcif Tissue Res 7:81-92.

*Corradino RA, Ebel JG, Craig PH, et al. 1971b. Calcium absorption and the vitamin D_3-dependent calcium-binding protein: II. Recovery from dietary strontium inhibition. Calcif Tissue Res 7:93-102.

Côté P, Harrison DC. 1974. Hemodynamic effects of strontium chloride in acute experimental myocardial infarction. Can J Physiol Pharmacol 52:920-929.

Cotman CW, Haycock JW, White WF. 1976. Stimulus-secretion coupling processes in brain: Analysis of noradrenaline and gamma-aminobutyric acid release. J Physiol 254:475-505.

*Cotton FA, Wilkinson G, eds. 1980. Beryllium and the group II elements: Mg, Ca, Sr, Ba, Ra. In: Advanced inorganic chemistry: A comprehensive text. New York, NY: John Wiley & Sons.

Coulon R. 1972. Deposition of ^{90}Sr and contamination of milk, proposition of a model of transfer. In: International Conference on Strontium Metabolism, ed. Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 447-456.

*Couttenye MM, D'Haese PC, Verschoren WJ, et al. 1999. Low bone turnover in patients with renal failure. Kidney Int 56(Suppl. 73):S-70-S-76.

Cowan RL, Hartsook EW, Whelan JB. 1968. Calcium-strontium metabolism in white tailed deer as related to age and antler growth. Proc Soc Exp Biol Med 129(3):733-737.

*Cragle RG, Stone WH, Bacon JA, et al. 1969. Effects of large doses of orally ingested strontium-90 on young cattle. Radiat Res 37:415-422.

Creger CR, Colvin LB. 1971. Strontium and bone development under conditions of suboptimal vitamin D. Calcif Tissue Res 8:83-86.

Creger CR, Colvin LB, Couch JR, et al. 1967. The effect of various dietary calcium levels on the elimination. Health Phys 13:401-404.

Creutzig VH, Creutzig A, Gerdts K-G, et al. 1975. [Comparative investigations of osteotropic isotopes. I. Animal experiments on the uptake of ^{18}F, ^{85}Sr and ^{99m}Tc-EHDP]. 123(2):137-143. (German)

Crist RH, Oberholser K, Schwartz D, et al. 1988. Interactions of metals and protons with algae. Environ Sci Technol 22(7):755-760.

Cross MA, Smith JT, Saxen R, et al. 2002. An analysis of the environmental mobility of radiostrontium from weapons testing and Chernobyl in Finnish river catchments. J Environ Radioact 60:149-163.

*Cuddihy RG, Ozog JA. 1973. Nasal absorption of CsCl, $SrCl_2$, $BaCl_2$ and $CeCl_3$ in Syrian hamsters. Health Phys 25:219-224.

Cukierman S, Krueger BK. 1990. Modulation of sodium channel gating by external divalent cations: Differential effects on opening and closing rates. Pflugers Arch(Eur J Physiol) 416:360-367.

*Cummins CL, Hetrick CS, Martin Dk. 1991. Radioactive releases a t the Savannah River site 1954-1989. Environmental department protection summary. DE92-009983. WSRC-RP-91-684.

*Cunningham WC, Anderson DL, Baratta EJ. 1994. Radionuclides in domestic and imported foods in the United States, 1987-1992. J AOAC Int 77(6):1422-1427.

*Cunningham WC, Stroube WB, Baratta EJ. 1989. Chemical contaminants monitoring: Radionuclides in domestic and imported foods in the United States, 1983-1986. J Assoc Off Anal Chem 72(1):15-18.

Cuthbertson DP, Tilstone WJ. 1968a. The effect of environmental temperature on healing of bone lesions in the rat. I. Effect of environmental temperature on mineral metabolism. Q J Exp Physiol 53:422-427.

Cuthbertson DP, Tilstone WJ. 1968b. The effect of environmental temperature on healing of bone lesions in the rat. II. The effect of bone injury on mineral metabolism at 20º C and 30º C. Q J Exp Physiol 53:428-436.

Daculsi G, Bouler J-M, LeGeros RZ. 1997. Adaptive crystal formation in normal and pathological calcifications in synthetic calcium phosphate and related biomaterials. Int Rev Cytol 172:129-191.

Dahl SG, Allain P, Marie PJ, et al. 2001. Incorporation and distribution of strontium in bone. Bone 28(4):446-453.

Davies CN. 1964. Inhaled radioactive particles and gases. Nature 203:352-355.

Davies DR, Bassingthwaighte JB, Kelly PJ. 1976. Transcapillary exchange of strontium and sucrose in canine tibia. J Appl Physiol 40(1):17-22.

*Davies J. 1979. Lung cancer mortality of workers in chromate pigment manufacture: An epidemiological survey. J Oil Colour Chem Assoc 62:157-163.

*Davies J. 1984. Lung cancer mortality among workers making lead chromate and zinc chromate pigments at three English factories. Br J Ind Med 41:158-169.

Davis J, Cook ND, Pither RJ. 2000. Biologic mechanisms of $^{89}SrCl_2$ incorporation into type I collagen during bone mineralization. J Nucl Med 41:183-188.

9. REFERENCES

Davis WD. 1977. Continuous mass spectrometric determination of concentration of particulate impurities in air by use of surface ionization. Environ Sci Technol 11(6):593-596.

*Dawson EB, Frey MJ, Moore TD, et al. 1978. Relationship of metal metabolism to vascular disease mortality rates in Texas. Am J Clin Nutr 31:1188-1197.

De Agostini A, Mascaro L, Pizzocaro C, et al. 1993. ^{85}Sr contaminant as a reliable tracer of ^{89}Sr for monitoring urinary radioactivity in patients treated with ^{89}Sr for bone metastasis. J Nucl Biol Med 37:38-44.

Dean JM. 1968. Cycling of Sr^{90} in molting crayfish. Comp Biochem Physiol 25:113-116.

DeFiore JC, Nilsson BER. 1969. Uptake of ^{85}Sr in osteoarthrosis of the spine in man. Acta Radiol Diagn 8:321-328.

Degteva MO, Kozheurov VP. 1994. Age-dependent model for strontium retention in human bone. Radiat Prot Dosim 53(1-4):229-233.

Degteva MO, Kozheurov VP, Tolstykh EI. 1998. Retrospective dosimetry related to chronic environmental exposure. Radiat Prot Dosim 79(1-4):155-160.

Degteva MO, Kozheurov VP, Tolstykh EI, et al. 2000. The techa river dosimetry system: methods for the reconstruction of internal dose. Health Phys 79(1):24-35.

Degteva MO, Kozheurov VP, Vorobiova MI. 1994. General approach to dose reconstruction in the population exposed as a result of the release of radioactive wastes into the Techa river. Sci Total Environ 142:49-61.

*de la Sierra A, Hannaert P, Ollivier J-P, et al. 1990. Kinetic study of the Ca^{2+} pump in erythrocytes from essential hypertensive patients. J Hypertens 8:285-293.

Dell'Antone P, Frigeri L, Azzone GF. 1973. The effects of electrolytes on the interaction of cationic dyes with energized mitochondrial fragments. Eur J Biochem 34:448-454.

Della Rosa RJ, Peterson G, Gielow F. 1966. Strontium-90 in beagle hair. Nature 5050:777-779.

*Demayo A. 1986. Elements in sea water. In: Weast RD, ed. CRC Handbook of Chemistry and Physics. Boca Raton, FL: CRC Press, Inc. FL:F-148.

*de Oliveira EM, Suzuki MF, do Nascimento A, et al. 2001. Evaulation of the effect of ^{90}Sr beta-radiation on human blood cells by chromosome aberration and single cell gel electrophoresis (comet assay) analysis. Mutat Res 476:109-121.

*De Rooij DG, Rönnbäck C. 1989. The effect of ^{90}Sr given to pregnant mice on spermatogenesis in the male offspring: A comparison with the effect on the ovaries in the female offspring. Int J Radiat Biol 56(2):151-159.

*D'Haese PC, De Broe ME. 1996. Adequacy of dialysis: Trace elements in dialysis fluids. Nephrol Dial Transplant 11(Suppl. 2):92-97.

9. REFERENCES

*D'Haese PC, Couttenye MM, Lamberts LV, et al. 1999. Aluminum, iron, lead, cadmium, copper, zinc, chromium, magnesium, strontium, and calcium content in bone of end-stage renal failure patients. Clin Chem 45(9):1548-1556.

*D'Haese PC, Schrooten I, Goodman WG, et al. 2000. Increased bone strontium levels in hemodialysis patients with osteomalacia. Kidney Int 57:1107-1114.

*D'Haese PC, Van Landeghem GF, Lamberts LV, et al. 1996. Measurement of strontium in serum, urine, bone, and soft tissues by Zeeman atomic absorption spectrometry. Clin Chem 43(1):121-128.

*Dietz ML, Horwitz EP, Nelson DM, et al. 1991. An improved method for determining ^{89}Sr and ^{90}Sr in urine. Health Phys 61(6):871-877.

DiPietro ES, Phillips DL, Paschal DC, et al. 1989. Determination of trace elements in human hair. Biol Trace Elem Res 22:83-100.

*Doberenz AR, Weber CW, Reid BL. 1969. Effect of high dietary strontium levels on bone and egg shell calcium and strontium. Calcif Tissue Res 4:180-184.

*DOE. 1984. Strontium-90 in the US diet, 1982. New York, NY: Environmental Measurements Laboratory, U.S. Department of Energy. DE85002012.

*DOE. 1991. Radioactive releases at the Savannah River site 1954-1989 (U). Washington, DC: U.S. Department of Energy. NTIS/DE92009983. 82-97; 219-254.

*DOE. 1992. Chemical contaminants on DOE lands and selection of contaminant mixtures for subsurface science research. Washington, DC: U.S. Department of Energy. DE92-014826.

*DOE. 1993. Occupational radiation protection. U.S. Department of Energy. Code of Federal Regulations. 10 CFR 835.

*DOE. 1995. Radionuclide concentrations in terrestrial vegetation and soil on and around the Hanford site, 1983 through 1993. Richland, WA: U.S. Department of Energy. DE-AC06-76RLO1830.

*DOE. 1996a. Closing the circle on the splitting of the atom: The environmental legacy of nuclear weapons production in the United States and what the department of energy is doing about it. Washington, DC: Office of Environmental Management, U.S. Department of Energy. DOE/EM-0266.

*DOE. 1996b. Selected radionuclides important to low-level radioactive waste management: National low-level waste management program. U.S. Department of Energy. DOE/LLW-238.

*DOE. 1996c. High-level waste inventory, characteristics, generation, and facility assessment for treatment, storage, and disposal alternatives considered in the U.S. Department of Energy environmental management programmatic environmental impact statement. Argonne, IL: U.S. Department of Energy. ANL/EAD/TM-17.

*DOE. 1996d. Worldwide deposition of strontium-90 through 1990. New York, NY: Environmental Measurements Laboratory, U.S. Department of Energy. EML-579.

*DOE. 1996e. Strontium-90 adsorption-desorption properties and sediment characterization at the 100N-area. Richland, WA: U.S. Department of Energy. DE-AC06-76RLO 1830.

*DOE. 1998a. Subpart N-accidents and emergencies. US Department of Energy. Code of Federal Regulations. 10 CFR 835 Sub N.

*DOE. 1998b. Occupational radiation protection; final rule. U.S. Department of Energy. Federal Register. 63 FR 59662. November 4, 1998.

DOE. 2000a. Location of laboratories and national laboratories. Laboratory site map. U.S. Department of Energy. http://www.doe.gov/people/labsmap.htm.

*DOE. 2000b. General provisions. Department of Energy. 10 CFR 835, App. A. http://frwebgate5access.gpo.gov/.

*DOE. 2001a. Individual monitoring. U.S. Department of Energy. Code of Federal Regulations. 10 CFR 835.402. http://frwebgate.access.gpo.gov/. May 11, 2001.

*DOE. 2001b. Limits for members of the public entering a controlled area. U.S. Department of Energy. Code of Federal Regulations. 10 CFR 835.208. http://frwebgate.access.gpo.gov/. May 11, 2001.

*DOE. 2001c. Limits for the embryo/fetus. U.S. Department of Energy. Code of Federal Regulations. 10 CFR 835.206. http://frwebgate.access.gpo.gov/. May 11, 2001.

*DOE. 2001d. Occupational dose limits for general employees. U.S. Department of Energy. Code of Federal Regulations. 10 CFR 835.202. http://frwebgate.access.gpo.gov/. May 11, 2001.

*DOE. 2001e. Occupational dose limits for minors. U.S. Department of Energy. Code of Federal Regulations. 10 CFR 835.207. http://frwebgate.access.gpo.gov/. May 11, 2001.

Donaldson SKB, Kerrick WGL. 1975. Characterization of the effects of Mg^{2+} on Ca^{2+}- and Sr^{2+}-activated tension generation of skinned skeletal muscle fibers. J Gen Physiol 66:427-444.

*DOT. 1995. Carriage by public highway. Class 7 (radioactive) material. U.S. Department of Transportation. Code of Federal Regulations. 49 CFR 177.842.

*DOT. 1996. Radiation protection program. U.S. Department of Transportation, Washington, D.C. 49 CFR 172.803.Subpart I.

*DOT. 1997. General requirements for shipments and packaging. Class 7 (radioactive) materials. U.S. Department of Transportation. Code of Federal Regulations. 49 CFR 173, Subpart I.

*DOT. 1998. Hazardous materials; withdrawal of radiation protection program requirement; final rule. U.S. Department of Transportation. Federal Register. 63 FR 48566. September 10, 1998.

*DOT. 2001a. List of hazardous substances and reportable quantities. U.S. Department of Transportation. 49 CFR 172.101 Appendix A. http://63.141.231.97/cgi-bin/. May 10, 2001.

*DOT. 2001b. Activity values for radionuclides. U.S. Department of Transportation. 49 CFR 173.435 Appendix A. http://63.141.231.97/cgi-bin/om. May 10, 2001.

*DOT. 2001c. Carriage by public highway. U.S. Department of Transportation. Code of Federal Regulations. 49 CFR 177.842. http://63.141.97/cgi-bin/. May 09, 2001.

*DOT. 2001d. General requirements for shipments and packaging. U.S. Department of Transportation. Code of Federal Regulations. 49 CFR 173, Subpart I. http://63.141.97/cgi-bin/. May 10, 2001.

*DOT. 2001e. Radiation level limitations. U.S. Department of Transportation. Code of Federal Regulations. 49 CFR 173.441. http://63.141.97/cgi-bin/. May 08, 2001.

*Dougherty JH, Taylor GN, Mays C. 1972. Strontium-90 toxicity in adult beagles after acute exposure. AEC Symp Ser 25:259-276.

*Downey HF, Stewart WE, Cragie RG. 1964. Depletion of strontium from calves by hemodialysis. Trans Am Soc Artif Intern Organs 10:350-352.

*Downie ED, Macpherson S, Ramsden EN, et al. 1959. The effect of daily feeding of ^{90}Sr to rabbits. Br J Cancer 13:408-423.

Duce RA, Hoffman GL, Zoller WH. 1975. Atmospheric trace metals at remote northern and southern hemisphere sites: Pollution or natural? Science 187:59-61.

*Duncan EL, Brown MA, Sunsheimer J, et al. 1999. Suggestive linkage of the parathyroid receptor type 1 to osteoporosis. J Bone Miner Res 14(12):1993-1999.

*Dungworth DL, Goldman M, Switzer JW, et al. 1969. Development of a myeloproliferative disorder in beagles continuously exposed to ^{90}Sr. Blood 34(5):610-632.

Durbin PW, Lynch J, Murray S. 1970. Average milk and mineral intakes (calcium, phosphorus, sodium and potassium) of infants in the United States from 1954 to 1968; Implication for estimating annual intakes of radionuclides. Health Phys 19:187-222.

*Dzubay TG, Stevens RK. 1975. Ambient air analysis with dichotomous sampler and x-ray fluorescence spectrometer. Environ Sci Technol 9(7):663-668.

Eagling EM, Lovell HG, Pickles VR. 1972. Interaction of prostaglandin E_1 and calcium in the guinea-pig myometrium. Br J Pharmacol 44:510-516.

Eakins JD, Gomm PJ. 1966. A new method for the determination of radiostrontium in urine. Health Phys 12:1557-1563.

*Eary LE, Rai D, Mattigod SV, et al. 1990. Geochemical factors controlling the mobilization of inorganic constituents from fossil fuel combustion residues: II. Review of the minor elements. J Environ Qual 19:202-214.

Ebel JG, Comar CL. 1968. Effect of dietary magnesium on strontium-calcium discrimination and incorporation into bone of rats. J Nutr 96:403-408.

Edwards C, Lorkovic H, Weber A. 1966. The effect of the replacement of calcium by strontium on excitation-concentration coupling in frog skeletal muscle. J Physiol 186:295-306.

Eisenberg E. 1966. Effects of androgens, estrogens and corticoids on strontium kinetics in man. J Clin Endocrinol 26:566-572.

9. REFERENCES

Eisenberg E. 1970. Effect of intravenous phosphate on serum strontium and calcium. N Engl J Med 282(16):889-892.

*Eisenbud M, ed. 1987. Environmental radioactivity: From natural, industrial, and military sources. New York, NY: Academic Press, Inc.

*Eisenbud M, Gesell T, eds. 1997. Environmental radioactivity from natural, industrial, and military sources. 4th ed. San Diego, CA: Academic Press, 426-428.

El Alfy S, Abdel-Rassoul AA. 1993. Trace metal pollutants in El Manzala lakes by inductively coupled plasma spectroscopy. Water Res 27(7):1253-1256.

El-Hodhdod MA, Abdelkarim AH, Samaan MN. 2000. Does serum strontium carry a relationship to rickets in Egyptian infants? J Pediatr Gastroenterol Nutr 31:S90-S91.

*Elias Z, Poirot O, Baruthio F, et al. 1991. Role of solubilized chromium in the induction of morphological transformation of Syrian hamster embryo (SHE) cells by particulate chromium (VI) compounds. Carcinogenesis 12(10):1811-1816.

*Elias Z, Poirot O, Pezerat H, et al. 1989. Cytotoxic and neoplastic transforming effects of industrial hexavalent chromium pigments in Syrian hamster embryo cells. Carcinogenesis 10(11):2043-2052.

*Ellenhorn MJ, Schonwald S, Ordog G, et al. 1997. Ellenhorn's medical toxicology: Diagnosis and treatment of human poisoning. 2nd ed. Baltimore, MD: Williams & Wilkins, 1682-1723.

El Solh N, Rousselet F, Girard ML. 1972. A study on protein-strontium bonds. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 255-272.

El-Yazigi A, Kanaan I, Martin CR, et al. 1990. Cerebrospinal fluid content of manganese, platinum, and strontium in patients with cerebral tumors, leukemia, and other noncerebral neoplasms. Oncology 47(5):385-388.

*Emmanuel FXS, Vaughan ATM, Catty D. 1981. Mice treated with strontium 90: An animal model deficient in NK cells. Br J Cancer 44:160-165.

*EMMI. 2000a. Metals in water by nebulization and ICP-AES - Method 200.15. Environmental Monitoring Methods Index. U.S. Environmental Protection Agency.

*EMMI. 2000b. Strontium-89 and strontium-90 in water - Method 008. Environmental Monitoring Methods Index. U.S. Environmental Protection Agency.

*EMMI. 2000c. Strontium in high level samples - Method RP501. Environmental Monitoring Methods Index. U.S. Environmental Protection Agency.

*EMMI. 2000d. Strontium-90 in soil, water and filter- Method RP520. Environmental Monitoring Methods Index. U.S. Environmental Protection Agency.

Engfeldt B, Reinholt FP, Svensson O, et al. 1986. The parathyroid gland in metal rickets. Calcif Tissue Int 39(Suppl.):A104.

9. REFERENCES

*EPA. 1976a. Maximum contaminant levels for beta particle and photon-radioactivity from man-made radionuclides in community water systems. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 141.16.

*EPA. 1976b. Monitoring frequency for radioactivity in community water systems. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 141.26.

EPA. 1980. Prescribed procedures for measurement of radioactivity in drinking water. Cincinnati, OH: U.S. Environmental Protection Agency, Environmental Monitoring and Support Laboratory. EPA-600/4-80-032.

*EPA. 1981. Data base for influent heavy metals in publicly owned treatment works. Cincinnati, OH: Municipal Environmental Research Laboratory. U.S. Environmental Protection Agency. EPA-600/S2-81-220.

*EPA. 1987. Radiation protection guidance to federal agencies for occupational exposure. U.S. Environmental Protection Agency. 52 FR 2822.

*EPA. 1988. Recommendations for and documentation of biological values for use in risk assessment. U.S. Environmental Protection Agency. Office of Research and Development, Cincinnati, OH. PB88-179874.

*EPA. 1989a. Compliance procedures methods for determining compliance with subpart I [40 CFR 61]. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 61, Appendix E.

*EPA. 1989b. Methods for estimating radionuclide emissions. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 61, Appendix D.

*EPA. 1989c. National emission standards for emissions of radionuclides other than radon from Department of Energy facilities. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 61, Subpart H.

*EPA. 1990. Interim methods for development of inhalation reference concentrations. Washington, DC: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Office of Research and Development, Environmental Criteria and Assessment Office. EPA 600/8-90/066A.

*EPA. 1993a. Environmental radiation protection standards for management and disposal of spent nuclear fuel, high-level and transuranic radioactive wastes. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 191.

*EPA. 1993b. Standards for management of uranium byproduct material pursuant to section 84 of the Atomic Energy act of 1954, as amended. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 192, Subpart D.

*EPA. 1995a. Determination of background concentrations of inorganics in soils and sediments at hazardous waste sites. Washington, DC: Office of Solid Waste and Emergency Response. U.S. Environmental Protection Agency. EPA 540/S-96/500.

*EPA. 1995b. Standards for cleanup of land and buildings contaminated with residual radioactive materials from inactive uranium processing sites. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 192, Subpart B.

*EPA. 1995c. Implementation. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 192, Subpart C.

*EPA 1995d. Standards for the control of residual radioactive materials from inactive uranium processing sites. Standards. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 192, Subpart A.

*EPA 1995e. Environmental radiation data. Office of Radiation and Indoor Air. Washington, DC. U.S. Environmental Protection Agency. Report 84, Table 13. http://www.epa.gov/narel/erd84w.htm#Table13. December 21, 2003.

*EPA. 1996a. Drinking water regulations and health advisories. Office of Water. US Environmental Protection Agency. EPA 822-B-96-002.

*EPA. 1996b. National emission standards for radionuclide emissions from federal facilities other than nuclear regulatory commission licensees and not covered by subpart H. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 61, Subpart I.

*EPA. 1996c. Test methods. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 61, Appendix B.

*EPA. 1997a. National primary drinking water regulations: Analytical methods for radionuclides; final rule and proposed rule. U.S. Environmental Protection Agency. Federal Register. 62 FR 10168. March 5, 1997.

*EPA. 1997b. Health effects assessment summary tables. FY-1997 update. Office of Research and Development, Office of Emergency and Remedial Response. Washington, DC: U.S. Environmental Protection Agency. EPA/540/R-97/036. NTIS PB 97-921199.

*EPA. 1997c. Special report on environmental endocrine disruption: An effects assessment and analysis. Washington, DC: U.S. Environmental Protection Agency, Risk Assessment Forum. EPA/630/R-96/012.

*EPA. 1998a. Land disposal restrictions phase IV: final rule promulgating treatment standards for metal wastes and mineral processing wastes; mineral processing secondary materials and bevill exclusion issues; treatment standards for hazardous soils, and exclusion of recycled wood preserving wastewaters. U.S. Environmental Protection Agency. Federal Register. 63 FR 28566. May 26, 1998.

*EPA. 1998b. Class V injection wells underground injection control regulations, revisions; proposed rule. U.S. Environmental Protection Agency. Federal Register. 63 FR 40586. July 29, 1998.

*EPA. 1998c. Subpart C-Environmental standards for ground-water protection. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 191 SubC.

*EPA. 1999a. Designation of hazardous substances. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 302.4.

*EPA. 1999b. Maximum contaminant levels for beta particle and photon radioactivity from man-made radionuclides in community water systems. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 141.16.

*EPA. 1999c. Monitoring frequency for radioactivity in community water systems. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 141.26.

*EPA. 1999d. Cancer risk coefficients for environmental exposure to radionuclides. U.S. Environmental Protection Agency. Code of Federal Regulations. 402-R-99-001.

*EPA. 2000a. Environmental radiation data, Report 84, October - December 1995: U.S. Environmental Protection Agency, Office of Radiation and Indoor Air. http://www.epa.gov/narel/erd84w.htm.

*EPA. 2000b. Environmental radiation data, Report 91, July - September 1997. U.S. Environmental Protection Agency, Office of Radiation and Indoor Air. http://www.epa.gov/narel/erd91.pdf.

EPA. 2000c. National drinking water contaminant occurrence query user's guide. National contaminant occurrence database. U.S. Environmental Protection Agency. http://www.epa.gov/ncodwork/html/ncod/ncod_userguide.html.

*EPA. 2000d. Drinking water standards and health advisories. Washington, DC: U.S. Environmental Protection Agency. Office of Water. EPA-822-B-00-001. http://www.epa.gov/ost/drinking/standards/dwstandards.pdf.

*EPA. 2000e. Federal Guidance Report No. 13. Cancer risk coefficients for environmental exposure to radionuclides, CD Supplement [CD-ROM]. EPA 402/C-99-001.

*EPA. 2001a. Designation of hazardous substances. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 302.4. http://ecfrback.access.gpo.gov/.

*EPA. 2001b. NPDES permit application testing requirements. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 122, App. D. http://ecfrback.access.gpo.gov/.

*EPA. 2001c. Release limits for containment requirements. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 191, App. A. http://ecfrback.access.gpo.gov/.

*EPA. 2001d. Compliance procedures methods for determining compliance with subpart I. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 61, App. E. http://ecfrback.access.gpo.gov/.

*EPA. 2001e. Designation of hazardous substances. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 302.4. http://ecfrback.access.gpo.gov/otcgi/cfr/.

*EPA. 2001f. Maximum containment levels for beta particle and photon radioactivity from man-made radionuclides in community water systems. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 141.16. http://ecfrback.access.gpo.gov/.

*EPA. 2001g. Analytical methods for radioactivity. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 141.25. http://ecfrback.access.gpo.gov/.

*EPA. 2001h. Monitoring frequency for radioactivity in community water systems. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 141.26. http://ecfrback.access.gpo.gov/.

*EPA. 2001i. Environmental radiation protection standards for management and disposal of spent nuclear fuel, high-level and transuranic radioactive wastes. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 191, Subpart A, B, and C. http://www4.law.cornell.edu/cfr/40p191.htm. May 11, 2001.

*EPA. 2001j. Hazardous waste injection restrictions. Waste specific prohibitions–newly listed and identified wastes. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 148.18. http://www.access.gpo.gov.html. May 11, 2001.

*EPA. 2001k. Health and environmental protection standards for uranium and thourium mill tailings. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 192, Subpart A, B, C, and D. http://www4.law.cornell.edu/cfr/40p192.htm. May 11, 2001.

*EPA. 2001l. Land disposal restrictions. LDR effective dates of injected prohibited hazardous waste. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 268, Appendix VIII. http://www.access.gpo.gov/nara/cfr/cfrhtml_00/Title_40/40tab_00.html. May 11, 2001.

*EPA. 2001m. Methods for estimating radionuclide emissions. U.S. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 61, Appendix D. http://www.epa.gov/epahome/cfr40.html. May 08, 2001.

*EPA. 2001n. Underground injection control regulations for Class V injection wells. U.S. Environmental Protection Agency. Federal Register. 63 FR 40586. http://frwebgate5.access.gpo.gov/. May 11, 2001.

*EPA. 2002a. Strontium and Srontium-90. Environmental Protection Agency. Federal Register. http://www.epa.gov.ncod/

*EPA. 2002b. National drinking water contaminant occurrence query user's guide. National contaminant occurrence database. U.S. Environmental Protection Agency. http://www.epa.gov/ncodwork/html/ncod/ncod_userguide.html.

Ercegovich CD, Vallejo RP, Gettig RR, et al. 1981. Development of a radioimmunoassay for parathion. J Agric Food Chem 29:559-563.

Erickson BE. 2002. A simple way to remediate strontium? Environ Sci Technol 36(1):20A-21A.

Escanero JF, Cordova A. 1991. Effects of glucagon on serum calcium, magnesium and strontium levels in rats. Miner Electrolyte Metab 17:190-193.

Escanero J, Carre M, Miravet L. 1976. [Effects of different metabolites of vitamin D3 and of calcium concentration on the intestinal absorption of strontium]. C R Seances Soc Biol Fil 170(1):47-53. (French)

*Etoh H, Taguchi YH, Tabachnick J. 1977. Cytokinetics of regeneration in β-irradiated guinea-pig epidermis. Radiat Res 71:109-118.

*Evans GJ, Tan PV. 1998. The fate of elements in residential composters. Arch Environ Contam Toxicol 34:323-329.

*Fatayerji D, Mawer EB, Eastell R. 2000. The role of insulin-like growth factor I in age-related changes in calcium. J Clin Endocrinol Metab 85(12):4657-4662.

*FDA. 1997. Ionizing radiation for the treatment of food. U.S. Department of Health and Human Services. U.S. Food and Drug Administration. Code of Federal Regulations. 21 CFR 179.26.

*FDA. 1998. Accidental radioactive contamination of human food and animal feeds: Recommendations for state and local agencies. U.S. Department of Health and Human Services. U.S. Food and Drug Administration. Center for Devices and Radiological Health. Rockville, MD 20850. August 13, 1998.

*FDA. 1999. Sources of radiation used for inspection of food, for inspection of packaged food, and for controlling food processing. U.S. Food and Drug Administration. Code of Federal Regulations. 21 CFR 179.21.

*FDA. 2000. Irradiation in the production, processing and handling of food. U.S. Food and Drug Administration. Code of Federal Regulations. 21 CFR 179.21. http://www.access.gpo.gov/nara/cfr/waisidx_00/21cfr179_00.html.

*Federman JH, Sachter JJ. 1997. Status asthmaticus in a paramedic following exposure to a roadside flare: A case report. J Emerg Med 15(1):87-89.

*FEDRIP. 2002. Dialog Information Systems, Inc., Palo Alto, CA: Federal Research in Progress.

Felt TP, Harrison JD, Leggett RW. 1998. A model for the transfer of calcium and strontium to the fetus. Radiat Prot Dosim 79(1-4):311-315.

Feng X, Melander AP, Klaue B. 2000. Contribution of municipal waste incineration to trace metal deposition on the vicinity. Water Air Soil Pollut 119:295-316.

*Ferenbaugh JK, Fresque PR, Ebinger MH, et al. 2002. Radionuclides in soil and water near a low-level disposal site and potential ecological and human health impacts. Environ Monit Assess 74:243-254.

Ferrendelli JA, Rubin EH, Kinscherf DA. 1976. Influence of divalent cations on regulation of cyclic GMP and cyclic AMP levels in brain tissue. J Neurochem 26:741-748.

Finkel MP. 1947. The transmission of radio-strontium and plutonium from mother to offspring in laboratory animals. Physiol Zool 20:405-421.

*Finkel MP, Biskis BO. 1969. Pathologic consequences of radiostrontium administered to fetal and infant dogs. AEC Symp Ser 17:543-566.

*Finkel MP, Bergstrand PJ, Biskis BO. 1960. The consequences of the continuous ingestion of Sr^{90} by mice. Radiology 74:458-467.

*Finkel MP, Biskis BO, Greco I, et al. 1972. Strontium-90 toxicity in dogs: Status of Argonne study on influence of age and dosage pattern. AEC Symp Ser 52:285-312.

Finston RA, Woodard HQ, Laughlin JS. 1966. Effects of external irradiation on mineral metabolism in the bones of adult dogs. Clin Orthop Relat Res 46:183-201.

9. REFERENCES

Firschein HE. 1970. Collagen and mineral accretion rates in bone during vitamin A deficiency. Am J Physiol 219(5):1183-1187.

Firschein HE, Alcock NW. 1969. Rate of removal of collagen and mineral from bone and cartilage. Metabolism 18(2):115-119.

Firusian N. 1974. Kinetik des radiostrontium. Nucl Med Commun 13(2):127-138.

*Fission Product Inhalation Project. 1967a. Toxicity of inhaled ^{90}Sr in beagle dogs. In: Fission product inhalation program annual report 1966-1967. Albuquerque, NM: Lovelace Foundation for Medical Education and Research.

*Fission Product Inhalation Project. 1967b. Toxicity of inhaled ^{90}Sr in rats. In: Fission product inhalation program annual report 1966-1967. Albuquerque, NM: Lovelace Foundation for Medical Education and Research.

*FL DEP. 2000. Water resource management. Florida Department of Environmental Protection. http://www.dep.state.fl.us/water/wf/dw/dw_contm_radio.htm.

Fleschner CR, Kraus-Friedmann N. 1986. The effect of Mg^{2+} on hepatic microsomal Ca^{2+} $^{2+}$ transport. Eur J Biochem 154:313-320.

*Fomon SJ. 1966. Body composition of the infant: Part I: The male "reference infant". In: Falkner F, ed. Human development. Philadelphia, PA: WB Saunders, 239-246.

*Fomon SJ, Haschke F, Ziegler EE, et al. 1982. Body composition of reference children from birth to age 10 years. Am J Clin Nutr 35:1169-1175.

*Forbes GB, Reina JC. 1972. Effect of age on gastrointestinal absorption (Fe, Sr, Pb) in the rat. J Nutr 102:647-652.

Forbes GB, Zalenski D. 1971. Uptake and elution of radiosodium in bone powder: Comparison with ^{47}Ca and ^{85}Sr. Calcif Tissue Res 8:172-176.

Forbes M, Mitchell HH. 1957. Accumulation of dietary boron and strontium in young and adult albino rats. AMA Arch Ind Health 16:489-492.

*Foreman JC. 1977. Spontaneous histamine secretion from mast cells in the presence of strontium. J Physiol 271:215-232.

*Foreman JC, Mongar JL. 1972a. Activation of anaphylactic histamine release by calcium and strontium ions. Br J Pharmacol 44(2):326.

*Foreman JC, Mongar JL. 1972b. The role of the alkaline earth ions in anaphylactic histamine secretion. J Physiol 224:753-769.

*Foreman JC, Hallett MB, Monger JL. 1977. Movement of strontium ions into mast cells and its relationship to the secretory response. J Physiol 271:233-251.

Forlani F, Arnoldi A, Pagani S. 1992. Development of an enzyme-linked immunosorbent assay for triazole fungicides. J Agric Food Chem 40:328-331.

Forsberg S, Rosen K, Brechignac. 2001. Chemical availability of ^{137}Cs and ^{90}Sr in undisturbed lysimeter soild maintained under controlled and close-to-real conditions. J Environ Radioact 54:253-265.

*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(2):373-383.

Foulkes EC. 1985. Interactions between metals in rat jejunum: implications on the nature of cadmium uptake. Toxicology 37:117-125.

*Fresquez PR, Foxx TS, Naranjo L. 1996a. Uptake of strontium by Chamisa (*Chrysothamnus nauseosus*) shrub plants growing over a former liquid waste disposal site at Los Alamos National Laboratory: Proceedings of the HSRC/WERC joint conference on the environment. Los Alamos, NM: Los Alamos National Laboratory.

*Fresquez PR, Mullen MA, Ferenbaugh JK, et al. 1996b. Radionuclides and radioactivity in soils within and around Los Alamos National Laboratory, 1974 through 1994: Concentrations, trends, and dose comparisons. Los Alamos, NM: Los Alamos National Laboratory.

*Friday GP. 1996. Radiological bioconcentration factors for aquatic terrestrial and wetland ecosystems at the savannah river site. Aiken, SC: U.S. Department of Energy. DE-AC09-89SR18035. WSRC-TR-96-0231.

Friedland JA, Brdlik OB, Methfessel AH, et al. 1969. Reduction of radiostrontium uptake in the rat. Radiat Res 38:340-348.

Friedman M, Hirschfeld Z. 1982. EDTA enhancement of strontium uptake by intact human enamel. J Oral Rehabil 9:327-333.

*Friedman PA, Gesek FA. 1995. Cellular calcium transport in renal epithelia: Measurement, mechanisms and regulation. Physiol Rev 75:429-471.

Fugimori T, Jencks WP. 1992. The kinetics for the phosphoryl transfer steps of the sarcoplasmic reticulum calcium ATPase are the same with strontium and with calcium bound to the transport sites. J Biol Chem 267(26):18466-18474.

Fujiki H, Mori M, Tanooka H. 1982. Delayed induction of ornithine decarboxylase in mouse skin after irradiation with beta-rays. Cancer Lett 15:15-17.

Fujimori T, Jencks WP. 1992. Binding of two Sr^{2+} ions changes the chemical specificities reticulum calcium ATPase through a stepwise mechanism. J Biol Chem 267(26):18475-18487.

Fujita M, Iwamoto J, Kondo M, et al. 1969a. Correlation between ingestion, accumulation and excretion of fallout ^{90}Sr in man on a long-term scale. Health Phys 17:41-50.

Fujita M, Iwanoto J, Kondo M. 1969b. Variation of strontium-calcium observed ratio (urine/diet) in man. Health Phys 16:441-447.

*Fukushi Y, Ozawa T, Wakui M, et al. 1995a. Sr^{2+} can pass through Ca^{2+} entry pathway activated by Ca^{2+} depletion, but can be hardly taken up by the Ca^{2+} stores in the rat salivary acinar cells. Tohoku J Exp Med 176:83-97.

9. REFERENCES

*Fukushi Y, Suga S, Kamimura N, et al. 1995b. Stimulated Ca^{2+} entry activates Cl^- currents after releasing Ca^{2+} from the intracellular store in submandibular gland cells of the rat. Jpn J Physiol 45:1071-1085.

*Furr AK, Parkinson TF, Hinrichs RA, et al. 1977. National survey of elements and radioactivity in fly ashes absorption of elements by cabbage grown in fly ash-soil mixtures. Environ Sci Technol 11(13):1194-1201.

*Gachályi A, Naményi J, Szegedi I, et al. 1988. Mobilization of ^{85}Sr by flavone derivatives (Morin and Iproflavone) in normal and pregnant rats. Radiobiol Radiother 29(4):513-517.

Garder K, Skulberg O. 1964. Sorption phenomena of radionuclides to clay particles in river water. Int J Air Wat Poll 8:229-241.

Garner RJ, Morley F. 1967. Agricultural implications of a release of fission products from a criticality incident. Health Phys 13:465-475.

Garnier A, Lanzola E, Karhausen L. 1972. Variability of ^{90}Sr bone burdens. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 489-504.

*Gastberger M, Steinhäusler F, Gerzabek MH, et al. 2000. ^{90}Sr and ^{137}Cs in environmental samples from dolon near the semipalatinsk nuclear test site. Health Phys 79(3):257-265.

Gastberger M, Steinhäusler F, Gerzabek MH, et al. 2001. Fallout strontium and caesium transfer from vegetation to cow milk at two lowland and two alpine pastures. J Environ Radioact 54:267-273.

Gatti LV, Mozeto AA, Artaxo P. 1999. Trace elements in lake sediments measured by the PIXE technique. Nucl Instrum Meth Phys Res B 150:298-305.

Gedalia I. 1975. Strontium uptake by the developing femur bone and deciduous dentition. J Dent Res 54:B125-B130.

*Gehr P. 1994. Anatomy and morphology of the respiratory tract. In: Human respiratory tract model for radiological protection. ICRP Publication 66. International Commission on Radiological Protection. Oxford: Pergamon Press, 121-166.

*Gennari L, Becherini L, Masi L, et al. 1997. Vitamin D receptor genotypes and intestinal calcium absorption in postmenopausal women. Calcif Tissue Int 61:460-463.

*George GA, Mehdi EI, Toma NA. 1979. Internal deposition of radiostrontium and its removal. In: Biological Implications of Radionuclides Released from Nuclear Industries. Proceedings of an International Symposium on Biological Implications. Vol. 2:53-64.

Gerritse RG, Vriesema R, Dalengerg JW, et al. 1982. Effect of sewage sludge on trace element mobility in soils. J Environ Qual 11(3):359-364.

*Ghosh S, Talukder G, Sharma A. 1990. Clastogenic activity of strontium chloride on bone marrow cells in vivo. Biol Trace Elem Res 25:51-56.

9. REFERENCES

Giang N, Shiraishi K, Sinh N, et al. 2001. Estimation of dietary ^{232}Th, ^{238}U, cesium, and strontium intakes in Vietnamese people from different geographical regions. Health Phys 80(6):605-611.

Gibbons RA, Sanson BF, Sellwood R. 1972. The passage of calcium and strontium across the gut of the anaesthetized goat. J Physiol 222:397-406.

*Gidlund M, Bierke P, Örn A, et al. 1990. Impact of ^{90}Sr on mouse natural killer cells and their regulation by alpha interferon and interleukin 2. Scand J Immunol 31:575-582.

*Gillett NA, Muggenburg BA, Boecker BB, et al. 1987a. Single inhalation exposure to $^{90}SrCl_2$ in the beagle dog: Hematological effects. Radiat Res 110:267-288.

*Gillett NA, Muggenburg BA, Boecker BB, et al. 1987b. Single inhalation exposure to $^{90}SrCl_2$ in the beagle dog: Late biological effects. J Natl Cancer Inst 79:359-376.

Gillett NA, Pool R, Taylor G, et al. 1986. Strontium-90 induced bone tumors in beagle dogs: Effects of route exposure and dose rate. Health Phys 56(Suppl. 1):S26.

*Giwercman A, Carlsen E, Keiding N, et al. 1993. Evidence for increasing incidence of abnormalities of the human testis: A review. Environ Health Perspect Suppl 101(2):65-71.

*Glowiak B, Pacyna J. 1978. Radionuclide movement in an ecological chain. Ecotoxicol Environ Saf 1:447-455.

Goblet C, Mounier Y. 1987. Activation of skinned muscle fiber by calcium and strontium ions. Can J Physiol Pharmacol 65:642-647.

Goldberg J, Sacks R. 1982. Direct determination of metallic elements in solid, powder samples with electrically vaporized thin film atomic emission spectrometry. Anal Chem 54:2179-2186.

Goldman M, Longhurst WM, Della Rosa RJ, et al. 1965. The comparative metabolism of strontium, calcium and cesium in deer and sheep. Health Phys 11:1415-1422.

Goldman M, Pool R, Momeni MH, et al. 1972. Quantitation of ^{90}Sr toxicity in dogs. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 17-30.

Goldman M, Rosenblatt LS, Book SA. 1983. Lifetime radiation effects research in animals: An overview of the status and philosophy of studies at University of California-Davis Laboratory for energy-related health research. In: Thompson RC, Mahaffey JA, eds. Life-span radiation effects studies in animals: What can they tell us? Proceedings of the twenty-second Hanford life science symposium held at Richland, Washington, September 27-29, 1983. Hanford Life Sciences Symposium 22nd. Springfield, VA: United States Department of Energy, 53-65.

*Goncalves PP, Meireles SM, Neves P, et al. 1999. Ionic sensitivity of the Ca^{2+}/H^{+} antiport in synaptic vesicles of sheep brain cortex. Mol Brain Res 67:283-291.

Gong JK, Burgeww E, Bacalao P. 1966. Accretion and exchange of strontium-85 in trabecular and cortical bones. Radiat Res 28:753-765.

9. REFERENCES

*Gong YF, Huang ZJ, Qiang MY et al. 1991. Suppression of radioactive strontium absorption by sodium alginate in animals and human subjects. Biomed Environ Sci 4:273-282.

*Gonzalez MD, Vassalle M. 1990. Strontium induces oscillatory potentials in sheep cardiac Purkinje fibers. Int J Cardiol 27:87-99.

*Gonzalez-Reimers E, Rodriguez-Moreno F, Martinez-Riera A, et al. 1999. Relative and combined effects of ethanol and protein deficiency on strontium and barium bone content and fecal and urinary excretion. Biol Trace Elem Res 68:41-49.

Gould JM, Sternglass EJ. 1994. Nuclear fallout, low birth weight, and immune deficiency. Int J Health Serv 24(2):311-335.

*Gould JM, Sternglass EJ, Sherman JD, et al. 2000. Strontium-90 decidous teeth as a factor in early childhood cancer. Int J Health Serv. 30(3):515-539.

*Grahek Z, Zecervic N, Lulic S. 1999. Possibility of rapid determination of low-level ^{90}Sr activity by combination of extraction chromatography separation and Cherenkov counting. Anal Chim Acta 399:237-247.

Graustein WC, Armstrong RL. 1983. The use of strontium-87/strontium-86 ratios to measure atmospheric transport into forested watersheds. Science 219:289-292.

*Green MO, Brannen AL. 1995. Hyperbaric oxygen therapy for Beta-radiation - induced scleral necrosis. Ophthalmology 102(7):1038-1041.

Green N. 2001. The effect of storage and processing on radionuclide content of fruit. J Environ Radioact 52:281-290.

Greenawalt JW, Carafoli E. 1966. Electron microscope studies on the active accumulation of Sr^{++} by rat-liver mitochondria. J Cell Biol 29(1):37-61.

Greenberg EJ, Chu FCH, Dwyer AJ, et al. 1972. Effects of radiation therapy on bone lesions as measured by ^{47}Ca and ^{85}Sr local kinetics. J Nucl Med 13(10):747-751.

*Gregoire G, Loirand G, Pacaud P. 1993. Ca^{2+} and Sr^{2+} entry induced Ca^{2+} release from the intracellular Ca^{2+} store in smooth muscle cells of rat portal vein. J Physiol 474:483-500.

Gridgeman NT. 1971. Methods of assay of the relative toxicity of certain bone-seeking radionuclides. Radiat Res 48:291-302.

*Griffith WC, Boecker BB, Hahn FF, et al. 1992. Effect of dose protraction on the incidence of lung carcinomas in beagle dogs with internally deposited (beta)-emitting radionuclides. Albuquerque, NM: Lovelace Biomedical and Environmental Research Institute. Inhalation Toxicology Research Institute. DE92004258.

*Gross M, Kumar R. 1990. Physiology and biochemistry of vitamin D-dependent calcium binding proteins. Am J Physiol 259:F195-209.

Grubb BR, Bentley PJ. 1984. The biology of strontium: Interactions with the mammalian crystalline lens. Exp Eye Res 39:107-112.

Gruden N. 1984. The effect of lactose and iron on strontium absorption. Experientia 40(9):941-942.

Gruden N, Stantic M, Buben M. 1974. Influence of lead on calcium and strontium transfer through the duodenal wall in rats. Environ Res 8:203-206.

Grundt TJ, Usowicz MM, Henderson G. 1996. Ca^{2+} entry following store depletion in SH-SY5Y neuroblastoma cells. 36:93-100.

*Grynpas MD, Hamilton E, Cheung R, et al. 1996. Strontium increases vertebral bone volume in rats at a low dose that does not induce detectable mineralization defect. Bone 18(3):253-259.

Grzegorzewski K, Komschlies KL, Mori M, et al. 1994. Administration of recombinant human interleukin-7 to mice induces the exportation of myeloid progenitor cells from the bone marrow to peripheral sites. Blood 83(2):377-385.

Guimaraes-Motta H, Sande-Lemos MP, Mrid LD. 1984. Energy interconversion in sarcoplasmic reticulum vesicles in the presence of Ca^{2+} and Sr^{2+} gradients. J Biol Chem 259(14):8699-8705.

*Gulson BL, Mizon KJ, Korsch MJ, et al. 2001. Dietary intakes of selected elements from longitudinal 6-day duplicate diets for pregnant and nonpregnant subjuects and elemental concentrations of breast milk and infant formula. Environ Res A87:160-174.

Guogang J, Testa C, Desideri D, et al. 1998. Sequential separation and determination of plutonium, americium-241 and strontium-90 in soils and sediments. J Radioanal Nucl Chem 230(1-2):21-27.

Gusmano EA, Concannon JN, Bozzo SR, et al. 1968. Evaluation of the parameters of strontium metabolism in the rat as a function of age. Radiat Res 33:540-553.

Gutteridge DH, Robinson CJ, Joplin GF. 1968. Delayed strontium absorption in post-menopausal osteoporosis and osteomalacia. Clin Sci 34:351-363.

*Guzelian PS, Henry CJ, Olin SS, eds. 1992. Similarities and differences between children and adults: Implications for risk assessment. Washington, DC: International Life Sciences Institute Press.

Hackett PL, Thompson RC. 1966. Strontium and calcium excretion in the rat. In: Thompson RC, Swezea EG, eds. Pacific Northwest Laboratory annual report for 1965 in the biological sciences. Richland, WA: Pacific Northwest Laboratory, 28-31.

*Haddad LM, Shannon MW, Winchester JF, eds. 1998. Clinical management of poisoning and drug overdose. 3rd ed. Philadelphia, PA: W.B. Saunders Company, 413-425.

*Hahn FF, Boecker BB, Cuddihy RG, et al. 1983a. Influence of radiation dose patterns on lung tumor incidence in dogs that inhaled beta emitters: A preliminary report. Radiat Res 96:505-517.

*Hahn FF, Gillett NA, Boecker BB, et al. 1991. Comparison of bone lesions induced by inhaled $^{90}SrCl_2$ or $^{238}PuO_2$. Albuquerque, NM: Lovelace Biomedical and Environmental Research Institute. NTIS/DE91017509.

9. REFERENCES

Hahn FF, Muggenburg BA, Boecker BB, et al. 1983b. Insights into radionuclide-induced lung cancer in people from life-span studies in beagle dogs. In: Thompson RC, Mahaffey JA, eds. Life-span radiation effects studies in animals: What can they tell us? Proceedings of the twenty-second Hanford life science symposium held at Richland, Washington, September 27-29, 1983. Hanford Life Sciences Symposium 22nd. Springfield, VA: United States Department of Energy, 521-534.

Hahn GS. 1999. Strontium is a potent and selective inhibitor of sensory irritation. Dermatol Surg 25:689-694.

Hakem N, Al Mahamid I, Apps J, et al. 1997. Sorption of cesium and strontium on Savanah river soils impregnated with colloidal silica. Conf Proc-Int Containment Technol Conf.

Hall JC, Deschamps RJA, Krieg KK. 1989. Immunoassays for the detection of 2,4-D and picloram in river water and urine. J Agric Food Chem 37:981-984.

*Hall SC, Wells, J. 1988. Micronuclei in human lymphocytes as a biological dosemeter: preliminary data following beta irradiation *in vitro*. J Radiol Prot. 8(2):97-102.

*Haller O, Wigzell H. 1977. Suppression of natural killer cell activity with radioactive strontium: Effector cells are marrow dependent. J Immunol 118(4):1503-1506.

*Hällgren R, Svensson K, Johansson E, et al. 1984. Elevated granulocyte strontium in inflammatory arthritides is related to the inflammatory activity. J Lab Clin Med 104(6):893-900.

*Hamilton TF, Millies-Lacrox JC, Hong GH. 1996. ^{137}Cs (Sr) and Pu isotopes in the Pacific Ocean: Sources & trends. Livermore, CA: Lawrence Livermore National Laboratory.

*Hamlet R, Heryet JC, Hopewell JW, et al. 1986. III.3 Late changes in pig skin after irradiation from beta-emitting sources of different energy. Br J Radiol 19(Suppl.):51-54.

Hammermeister AM, Naeth MA, Chanasyk DS. 1998. Implications of fly ash application to soil for plant growth and feed quality. Environ Technol 19:143-152.

Hannaert-Merah Z, Combettes L, Coquil J-F, et al. 1995. Characterization of the co-agonist effects of strontium and calcium on myo-inositol trisphosphate-dependent ion fluxes in cerebellar microsomes. Cell Calcium 18:390-399.

Hanson WC. 1968. Fallout radionuclides in northern Alaskan ecosystems. Arch Environ Health 17:639-648.

Hanson WC, Thomas JM. 1982. Prediction of ^{90}Sr body burdens and radiation dose in Anaktuvuk pass Alaskan Eskimos due to fallout. Health Phys 43(3):323-333.

Hardy EP, Rivera J. 1968. Transfer of fallout strontium-90 to cows' milk. J Dairy Sci 51(8):1210-1214.

Harrison GE, Carr TEF, Sutton A, et al. 1966a. Plasma concentration and excretion of calcium-47, strontium-85, barium-133, and radium-223 following successive intravenous doses to a healthy man. Nature 209:526-527.

*Harrison GE, Carr TEF, Sutton A. 1967a. Distribution of radioactive calcium, strontium, barium and radium following intravenous injection into a healthy man. Int J Radiat Biol 13(3):235-247.

*Harrison GE, Howells GR, Pollard J, et al. 1966b. Effect of dietary phosphorus supplementation on the uptake of radioactive strontium in rats. Br J Nutr 21:561-569.

Harrison GE, Howells GR, Pollard J. 1967b. Comparative uptake and elution of ^{45}Ca, ^{85}Sr, ^{133}Ba, Ra in bone powder. Calcif Tissue Res 1:105-113.

*Harrison GE, Lumsden E, Raymond WHA, et al. 1959. On the metabolism of skeletal fixation of strontium I. II. Arch Biochem Biophys 80:97-113.

*Harrison GE, Raymond WHA, Tretheway HC. 1955. The metabolism of strontium in man. Clin Sci 14:681-695.

*Harrison GE, Sutton A, Shepherd H, et al. 1965. Strontium balance in breast-fed babies. Brit J Nutr 19:111-117.

*Harrison J, McNeill KG, Janiga A. 1966c. The effect of sodium alginate on the absorption of strontium and calcium in human subjects. Can Med Assoc J 95:532-534.

Harrison JE, McNeill KG, Elaguppillai V. 1972. Strontium and calcium kinetics at the bone level. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 379-388.

*Hart H, Spencer H. 1967. Rate of initial entry of Ca^{47} and Sr^{85} from the intestine into the vascular space. Proc Soc Exp Biol Med 126:365-371.

*Hartsook EW, Hershberger TV. 1973. Strontium-calcium discrimination during placental transfer and fetal uptake in rats: Effect of gestation duration. Proc Soc Exp Biol Med 143(2):343-349.

Hartsook EW, Cowan RL, Chandler PT, et al. 1969. Effect of dietary protein source and corn oil and cellulose levels in strontium-calcium discrimination in growing rats. J Nutr 97:95-103.

*Hayes KF, Traina SJ. 1998. Metal ion speciation and its significance in ecosystem health. In: Soil chemistry and ecosystem health. Soil Science Society of America, Special Publication no. 52 . Madison, WI: Soil Science Society of America, 46-83.

*HazDat. 2003. Strontium. ATSDR's hazardous substance release and health effects database. Agency for Toxic Substances and Disease Registry. http://www.atsdr.cdc.gov/hazdat.html.

Hazzard DG. 1969. Percent cesium-134 and strontium-85 in milk, urine, and feces of goats on normal and verxite-containing diets. J Dairy Sci 52(7):990-994.

Heine K, Wiechen A. 1980. Studies of the transfer factors of Sr^{90} and Cs^{137} in the food-chain soil-plant-milk. In: Radiation protection: A systemic approach to safety: Proceedings of the 5th congress of the International Radiation Protection Society, Jerusalem, March 1980. New York, NY: Pergamon Press, Vol. 2, 1099-1102.

*Helal AA, Aly HF, Imam DM, et al. 1998a. Effect of some metal ions on the complexation of strontium with humic acid. J Radioanal Nucl Chem 227(1-2):49-53.

*Helal AA, Imam DM, Khalifa SM, et al. 1998b. Effect of some environmental ligands and fertilizers on humic acid complexation with strontium. J Radioanal Nucl Chem 232(1-2):159-161.

Hems G, Mole RH. 1966. The relative toxicities of radium 226, plutonium 239 and strontium 90 for bone tumour induction. Br J Radiol 39:719-726.

Henkart P, Henkart M, Millard P, et al. 1985. The role of cytoplasmic granules in NK cell cytotoxicity. In: Herberman RB, Callewaert DM, eds. Mechanisms of cytotoxicity by NK cells. New York, NY: Academic Press, 305-322.

Henquin J-C. 1980. Specificity of divalent cation requirement for insulin release: Effects of strontium. Pflugers Arch(Eur J Physiol) 383:123-129.

Henricson B, Nilsson A. 1965. Effect of radiostrontium on oocytes and follicles of adult mice. Acta Radiol Ther Phys Biol 3:296-304.

Henshaw DL. 1996. Chernobyl 10 years on: Thyroid cancer may be the only measurable health effect. Br Med J 312(7038):1052-1053.

*Herring LC, Keefer DH. 1971a. II. Comparison of stable and radioactive strontium deposition in urinary calculi and human diet. Arch Environ Health 22:251-258.

Herring LC, Keefer DH. 1971b. A radiologic study of inorganic urinary calculi: I. Comparison of stable and radioactive strontium deposition in urinary calculi and human bone. Arch Environ Health 22:239-250.

Hert J, Mertl F, Babicky A. 1971. Reaction of bone to mechanical stimuli incorporation of ^{45}Ca and ^{35}S into rabbit tibia subjected to intermittent stress. Physiol Bohemoslov 20(6):575-581.

Hesp R, Ramsbottom B. 1965. Radiobiology: Effect of sodium alginate in inhibiting uptake of radiostrontium by the human body. Nature 5017:1341-1342.

*Hibbins SG. 1997. Strontium and strontium compounds. In: Kroschwitz JI, Howe-Grant M, eds. Kirk-Othmer encyclopedia of chemical technology. New York, NY: John Wiley & Sons, Vol. 22, 947-955.

*HI Dept Health. 1999. Environmental health: Safe drinking water rules. Hawaii Department of Health. http://www.hawaii.gov/heath/rules/emd/dwrule.html.

Hilpert K, Waidmann E. 1986. Multi-element determination in environmental samples by mass spectrometric isotope dilution analysis using thermal ionization: Part I: Pine needles. Fresenius Z Anal Chem 325:141-145.

*Hirose K, Takatani S, Aoyama M. 1993. Wet deposition of radionuclides derives from the Chernobyl accident. J Atmos Chem 17:16-71.

*Hobbs CH, Snipes MB, Barnes JE, et al. 1972. Toxicity of inhaled ^{90}Sr fused clay in dogs: Early effects. Radiat Res 51(2):503-504.

Hodgkinson A, Nordin BEC, Hambleton J, et al. 1967. Radiostrontium absorption in man: Suppression by calcium and by sodium alginate. Can Med Assoc J 97:1139-1143.

*Hoel DG, Davis DL, Miller AB, et al. 1992. Trends in cancer mortality in 15 industrialized countries, 1969-1986. J Natl Cancer Inst 84(5):313-320.

*Hole DJ, Gillis CR, Sumner D. 1993. Childhood cancer in birth cohorts with known levels of strontium-90. Health Rep 5(1):39-43.

Holguín JA. 1986. Cooperative effects of Ca^{2+} and Sr^{2+} on sarcoplasmic reticulum adenosine triphosphatase. Arch Biochem Biophys 251(1):9-16.

Holmuhamedov EL, Teplova VV, Chukhlova EA, et al. 1995. Strontium excitability of the inner mitochondrial membrane: Regenerative strontium-induced strontium release. Biochem Mol Biol Int 36(1):39-49.

Holopainen T, Rekonen A. 1966. Uptake of radioactive strontium (^{85}Sr) in joints damaged by rheumatoid arthritis measured by external counting of radiation. Acta Rheumatol Scand 12:102-111.

Holynska B, Olko M, Ostachowicz B, et al. 1998. Performance of total reflection and grazing emission x-ray fluorescence spectrometry for the determination of trace metals in drinking water in relation to other analytical techniques. Fresenius J Anal Chem 362:294-298.

Hong G-H, Lee S-H, Kim S-H, et al. 1999. Sedimentary fluxes of 90Sr, 137Cs, 239, 240Pu, and 210Pb in the East Sea (Sea of Japan). Sci Total Environ 237/238:225-240.

*Hopewell JW, Coggle JE, Wells J, et al. 1986. III.2. The acute effects of different energy beta-emitters on pig and mouse skin. Br J Radiol 19(Suppl.):47-51.

*Hopewell JW, Hamlet R, Peel D. 1985. The response of pig skin to single doses of irradiation from strontium-90 sources of differing surface area. Br J Radiol 58:778-780.

*Hopkins BJ. 1967. The retention of strontium-90 transferred through milk (and placenta) in rat offspring. Health Phys 13:973-976.

*Hopkins BJ, Casarett GW. 1972. Some pathogenic aspects of gross pathological changes in ^{90}Sr-treated bone of newborn rats. Int J Radiat Biol 21(5):405-416.

*Hopkins BJ, Casarett GW, Baxter RC, et al. 1966. A roentgenographic study of terminal pathological changes in skeletons of strontium-90 treated rats. Radiat Res 29:39-49.

*Hopkins BJ, Casarett GW, Tuttle LW, et al. 1967. Strontium-90 and intrauterine development in the rat. J Embryol Exp Morphol 17(2):583-591.

*Horwitz EP, Dietz ML, Fisher DE. 1991. Separation and preconcentration of strontium from biological, environmental, and nuclear waste samples by extraction chromatography using a crown ether. Anal Chem 63:522-525.

*Hoshino H, Tanooka H. 1975. Interval effect of β-irradiation and subsequent 4-nitroquinoline 1-oxide painting on skin tumor induction in mice. Cancer Res 35:3663-3666.

*Howard EB. 1970. Experimental induction of porcine leukemia. In: Dutcher RM, ed. Comparative leukemia research 1969. New York, NY: Karger, 430-439.

*Howard EB, Clarke WJ. 1970. Induction of hematopoietic neoplasms in miniature swine by chronic feeding of strontium-90. J Natl Cancer Inst 44(1):21-38.

*HSDB. 2000. Strontium. Hazardous Substances Data Bank. National Library of Medicine, National Toxicology Information Program, Bethesda, MD. http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~BAArea4Ke:1:FULL.

*HSDB. 2002. Strontium. Hazardous Substances Data Bank. National Library of Medicine, National Toxicology Information Program, Bethesda, MD. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.

Hueper WC. 1961. Environmental carcinogenesis and cancers. Cancer Res 21:842-857.

Hult M, Fessler A. 1998. Sr/Ca mass ratio determination in bones using fast neutron activation analysis. Appl Radiat Isot 49(9-11):1319-1323.

Hulth AG, Nilsson BE. 1969. Effect of actinomycin-D on bone mineral metabolism in rats. Calcif Tissue Res 3:194-197.

Humphreys ER, Howells GR. 1972. Promotion of excretion of injected ^{85}Sr, ^{133}Ba and ^{244}Ra from the rat by injected derivatives of sodium alginate. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 315-324.

Humphreys ER, Van Puymbroeck S, Vanderborght O. 1972. Inhibition of intestinal absorption of simultaneously administered ^{47}Ca, ^{85}Sr, ^{133}Ba and ^{226}Ra by different sodium alginates. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 309-314.

*IARC. 1990. Chromium and chromium compounds. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. International Agency fro Research on Cancer. Lyon, France. Vol.49, pp.49-256.

*IARC. 2001. Ionizing radiation, part 2: Some internally deposited radionuclides. In: IARC monographs on the evaluation of carcinogen risks to humans. International Agency for Research on Cancer. Lyon, France. Vol 78.

*IARC. 2002a. Chromium and chromium compounds: Chromium[IV](group 1), metallic chromium and chromium[III] compounds (group3). International Agency for Research on Cancer. http://www.cie.iarc.fr/htdocs/monographs/vol149/chromium.html. October 23, 2002.

*IARC. 2002b. Some internally deposited radionuclides (generally Group 1). International Agency for Research on Cancer. http://www.cie.iarc.fr/htdocs/monographs/col178-radionuclides.html. October 23, 2002.

*ICRP. 1990. 1990 Recommendations of the International Commission on Radiological Protection, ICRP Publication 60. Oxford: Pergamon Press.

*ICRP. 1993. Age-dependent doses to members of the public from intake of radionuclides: Part 2 Ingestion dose coefficients. International Commission on Radiological Protection. Publication No. 67. Pergamon Press, Oxford. 95-120.

*ICRP. 1994a. Human respiratory tract model for radiological protection. International Commission on Radiological Protection. Publication No. 66. Pergamon Press, Oxford.

*ICRP. 1994b. Dose coefficients for intakes of radionuclides by workers. International Commission on Radiological Protection. Annals of the ICRP. Vol. 24(4). ICRP publication 68.

*ICRP. 1996. Age-dependent doses to members of the public from intake of radionuclides. Part 5. International Commission on Radiological Protection. Pergamon Press, Oxford. Publication No. 72.

*ICRP. 1995. Age-dependent doses to members of the public from intake of radionuclides: Part 4 inhalation dose coefficients. Publication No. 71. Pergamon Press, Oxford.

*ID Department of Health Welfare. 2000. Ground water quality rules. Idaho Department of Health and Welfare. http://www2.state.id.us/adm/adminrules/rules/idapa16/16index.htm.

*Iiyinskikh NN, Iiyinskikh IN, Shakirov NN, et al. 1999. Chromosome aberrations in the radiation-exposed residents around Mayak nuclear facility in the Chelyabinsk region, Russia. Environ Toxicol 14(4):414-423.

*IL Environmental Protection Agency. 1999. Water quality standards. Illinois Environmental Protection Agency. http:www.epa.state.il.us/regulations.html.

*Ilyin LA, Ivannikov AT, Parfenov YD, et al. 1975. Strontium absorption through damaged and undamaged human skin. Health Phys 29:75-80.

*IN General Assembly. 2000. Title 327 water pollution control board. Indiana Administrative Code. Indiana General Assembly. http://www.state.in.us/legislative/iac/title327.html.

*Inoue Y, Saijoh K, Katsuyama H, et al. 1988. Effects of heavy metal cations on second messenger systems in the brains of mice. In: Sumino K, ed. Environmental and occupational chemical hazards, No. 8. Asia-Pacific Symposium on Environmental and Occupational Toxicology, Singapore, October 4-7, 1987. Kobe, Japan: Kobe University School of Medicine.

IRIS. 2000. Strontium. Integrated Risk Information System. U.S. Environmental Protection Agency. http://www.epa.gov/iris/subst/0550.htm.

*IRIS. 2002. Strontium. Integrated Risk Information System. U.S. Environmental Protection Agency. http://www.epa.gov/ngispgm3/iris/subst/0550.htm.

*Iskander FY. 1986. Cigarette ash as a possible source of environmental contamination. Environ Pollut Ser B 11:291-301.

*Ito T, Nagao K, Kawamura Y, et al. 1976. Studies on the leukemogenic and immunologic effects of radiostrontium (^{90}Sr) and x rays in mice. In: Radiation and the lymphatic system: Proceedings of the fourteenth annual Hanford biology symposium at Richland, Washington, September 30-October 2, 1974. Springfield, VA: Energy Research and Development Administration, 209-217.

Ivanov SN, Shagalova ED. 1972. Strontium in the environment. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 437-446.

*Iyengar GV, Kollmer WE, Bowen HJM. 1978. The elemental composition of human tissues and body fluids: A compilation of values for adults. Weinheim, NY: Verlag Chemie.

Jacobs RL, Shapiro FD, Ray RD. 1972. In vitro study of mobilization and uptake of bone mineral. Clin Orthop Relat Res 82:214-220.

Jacobsen N, Jonsen J. 1975. Strontium, lead and nickel incorporated into mouse calvaria in vitro. Pathol Eur 10:115-121.

*Jacobsen N, Alfheim I, Jonsen J. 1978. Nickel and strontium distribution in some mouse tissues passage through placenta and mammary glands. Res Commun Chem Pathol Pharmacol 20(3):571-584.

*James AC. 1978. Lung deposition of sub-micron aerosols calculated as a function of age and breathing rate. In: National Radiological Protection Board Annual Research and Development Report. Harwell, United Kingdom: National Radiological Protection Board, 71-75.

*James AC, Stahlhofen W, Rudolf G, et al. 1994. Deposition of inhaled particles. In: ICRP Publication 66. Oxford: Pergamon Press, 231-299.

*Järplid B. 1973. Radiostrontium induced early changes in the haematopoietic tissues. Acta Radiol Ther Phys Biol 12:145-154.

Järplid B. 1974. Combined effect of roentgen irradiation and radiostrontium on the haematopoietic tissue and the development of lymphoma in mice. Acta Radiol Ther Phys Biol 13:217-231.

Jasinski WK, Watras J, Gwiazdowska BA, et al. 1971. Retention of strontium^{85} in rats contaminated in utero and fed with the contaminated milk. Radiobiol Radiother 12(3):325-328.

Jeffree RA, Sarkich SJ, Twining JR. 2001. Element concentrations in the flesh and osteoderms of esturine crocodiles (*Crocodylus porosus*) from the alligator rivers region, Northern Australia: biotic and geographic effects. Arch Environ Contam Toxicol 40:236-245.

Jethi RK, Mackey MG, Meredith PD, et al. 1972. Studies of the mechanism of biological calcification. 3. The interaction of strontium with a calcifiable matrix from beef tendon. Calcif Tissue Res 9(4):310-324.

*Jia G, Triuzi C, Marzano N, et al. 1999. Plutonium, 241Am, ^{90}Sr, and ^{137}Cs concentrations in some Antarctic matrices. Biol Trace Elem Res 71-72:349-357.

Jiang M-S, Fletcher JE, Smith LA. 1989. Factors influencing the hemolysis of human erythrocytes by cardiotoxins from *Naja naja kaiuthia* and *Naja naja atra* venoms and a phopholipase A_2 with cardiotoxin-like activities from *Bungarus fasciatus* venom. Toxicol 27(2):247-257.

*Johanson CE. 1980. Permeability and vascularity of the developing brain: Cerebellum vs cerebral cortex. Brain Res 190:3-16.

Johnson AR, Armstrong AR, Singer L. 1970. The exchangeability of calcium and strontium of bone *in vitro*. Calcif Tissue Res 6:103-112.

9. REFERENCES

*Johnson AR, Armstrong WD, Singer L. 1968. The incorporation and removal of large amounts of strontium by physiologic mechanisms in mineralized tissues. Calcif Tissue Res 2(3):242-252.

Johnson JR, Dunford DW, Kramer GH. 1983. Summary of a strontium-89 contamination case. Radiat Prot Dosim 5(4):247-249.

Jones P, Foulkes M, Paull B. 1994. Determination of barium and strontium in calcium-containing matrices using high-performance chelation ion chromatography. J Chromatogr A 673:173-179.

Jones P, Williams T, Ebdon L. 1990. Development of a novel multi-element detection system for trace metal determination based on chemiluminescence after separation by ion chromatography. Anal Chim Acta 237:291-298.

*Jones RK, Boecker BB, Hobbs CH, et al. 1972. Hematologic effects of inhaled ^{90}Y, ^{91}Y, ^{144}Ce or ^{90}Sr fused clay in beagle dogs. Radiat Res 51(2):470-471.

*Jones RK, Boecker BB, Pickrell JA, et al. 1976. Influence of radiation-dose pattern from inhaled beta-gamma-emitting radionuclides on canine peripheral lymphocytes. In: Radiation and the lymphatic system: Proceedings of the fourteenth annual Hanford biology symposium at Richland, Washington, September 30-October 2, 1974. Springfield, VA: Energy Research and Development Administration, 83-99.

Jones S, Robbins J, Brown DA. 1992. Neurotransmitter modulation of calcium channels is dependent on the charge carrier used in the recording of currents. Neurosci Lett 145:153-156.

Jonsen J, Storeng R, Jacobsen N. 1980. Heavy metal toxicity to mouse embryos cultivated in vitro. J Dent Res 59(Special Issue B):948.

Jowsey J, Balasubramaniam P. 1972. Effect of phosphate supplements on soft-tissue calcification and bone turnover. Clin Sci 42:289-299.

Kahn B, Jones IR, Porter CR, et al. 1965. Transfer of radiostrontium from cows' feed to milk. J Dairy Sci 48:1023-1030.

*Kahn B, Straub CP, Robbins PJ, et al. 1969a. Part 1: Long-term study in the home; Diet and results. Pediatrics 43(4):652-667.

Kahn B, Straub CP, Robbins PJ, et al. 1969b. Part 3: Intake, excretion, and retention of stable strontium. Pediatrics 43(4):687-705.

Kahn B, Straub CP, Robbins PJ, et al. 1969c. Part 4: Intake, excretion, and retention of strontium-90. Pediatrics 43(4):706-731.

Kahn B, Straub CP, Robbins PJ, et al. 1969d. Strontium, calcium, and phosphorous retention. Pediatrics 43(4):733-756.

Kahn DS, Nakhani JS, Skoryna SC. 1963. Studies of the late effects of internal irradiation by radioactive strontium in the rat. Laval Med 34(1):169-183.

9. REFERENCES

Kal'chenko VA, Budashkina EB, Khvostova VV. 1973. Content of Sr^{90}, Ca, and strontium units in the grain of wheat hybrids obtained by crossing *Triticum aestivum x Triticum dicoccum*. Sov Genet 7(8):1018-1021.

*Kan MK. 1995. Palliation of bone pain in patients with metastatic cancer using strontium-89 (Metastron). Cancer Nurs 18(4):286-291.

*Kanematsu N, Hara M, Kada T. 1980. Rec assay and mutagenicity studies on metal compounds. Mutat Res 77:109-116.

*Kano K, Horikawa M, Utsunomiya T, et al. 1993. Lung cancer mortality among a cohort of male chromate pigment workers in Japan. Int J Epidemiol 22(1):16-22.

Karaki H, Urakawa N. 1972. Increase in ^{85}Sr uptake by elevated concentration of K in guinea pig *Taenia coli*. Jpn J Pharmacol 22:437-439.

Karaki H, Nakagawa H, Urakawa N. 1986. Strontium uptake during the different modes of contraction in the smooth muscle of rabbit aorta, rat aorta and guinea-pig taenia coli. Arch Int Pharmacodyn 282:93-107.

*Karbach U, Rummel W. 1987. Strontium transport in the rat colon. Naunyn-Schmiedebergs Arch Pharmacol 335:91-96.

Kargacin B, Kostial K. 1985. Reduction of ^{85}Sr, ^{137}Cs, ^{131}I and ^{141}Ce retention in rats by simultaneous oral administration of calcium alginate, ferrihexacyanoferrate(II), KI and Zn-DTPA. Health Phys 49(5):859-864.

Kargacin B, Landeka M. 1990. Effect of glucocorticoids on metal retention in rats. Bull Environ Contam Toxicol 45:655-661.

*Kashparov VA, Lundin SM, Khomutinin YV, et al. 2001. Soil contamination with ^{90}Sr in the near zone of the Chernobyl accident. J Environ Radioact 56:285-298.

Kerrick WGL, Zot HG, Hoar PE, et al. 1985. Evidence that the Sr^{2+} activation properties of cardiac troponin C are altered when substituted into skinned muscle fibers. J Biol Chem 260(29):15687-15693.

*Keslev D, Van Puymbroeck S, Van Der Borght O. 1972. Effect of aluminum phosphate gel on whole-body retention of simultaneously administered ^{226}Ra, ^{85}Sr and ^{47}Ca in mice. Experientia 28(5):524-525.

Khairallah PA, Vadaparampil GJ, Page IH. 1965. Effect of ions on angiotensin interaction with smooth muscle. Arch Int Pharmacodyn 158(1):155-164.

Kidman B, Tutt ML, Vaughan JM. 1951. The retention of radioactive strontium and yttrium (Sr^{89}, Sr^{90} and Y^{90}) in pregnant and lactating rabbits and their off-spring. J Pathol Bacterial 63:253-268.

Kinoshita A, Braga FJ, Graeff CF, et al. 2001. ESR dosimetry of ^{89}Sr and ^{153}Sm in bone. Appl Radiol 54(2):269-274.

Kirkeby OJ, Berg-Larsen T. 1991. Regional blood flow and strontium-85 incorporation rate in the rat hindlimb skeleton. J Orthop Res 9:862-868.

Knight WM, Bohman VR, Lesperance AL, et al. 1967. Strontium retention in the bovine. J Anim Sci 26(4):839-844.

Knivvsland Y, Skretting A, Bruland OS. 2001. Radionuclide therapy with bone-seeking compounds: Monte Carlo calculations of dose-volume histograms for bone marrow in trabecular bone. Phys Med Biol 46(4):1149-1161.

Knizhnikov VA, Petukhova EV, Varkhudarov RM. 1972. ^{90}Sr intake in food by the population of the Soviet Union 1963-1971. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 477-482.

Knobel LL, Cecil LD, Wenger SJ, et al. 1992. Comparison of the effects of filtration and preservation methods on analysis for strontium-90 in ground water. Environ Monit Assess 20:67-80.

Ko WH, Pediani JD, Bovell DL, et al. 1995. Sr^{2+} can become incorporated into an agonist-sensitive, cytoplasmic Ca^{2}+ store in a cell line derived from the equine sweat gland epithelium. Experientia 51:804-808.

Kobayashi E, Sugihira N, Suzuki KT. 1990. Renal handling and discrimination of calcium and strontium in the chronically cadmium-poisoned population. Trace Elem Med 7:114-117.

Kobayashi E, Sugihira N, Suzuki KT. 1991. Biological discrimination between calcium and strontium in kidneys and bone of young and adult rats. Biol Trace Elem Res 28:187-194.

*Kodaira K, Tsumura A, Kobayashi H. 1973. Uptake of radioactive strontium and cesium in rice plants: (1) Accumulation of Sr and Cs in rice grains through roots. J Radiat Res 14:31-39.

Kohama K, Saida K, Hirata M, et al. 1986. Superprecipitation is a model for in vitro contraction superior to ATPase activity. Jpn J Pharmacol 42:253-260.

Kohara K, Ogura A, Akagawa K, et al. 2001. Increase in nunber of functional release sites by cyclic AMP-dependent protein kinase in cultured neurons isolated from hippocampal dentate gyrus. Neurosci Res 41:79-88.

Kolar J, Babicky A, Bibr B, et al. 1968. Metabolic studies with bone-seekers in diseased joints. Calcif Tissue Res 2(Suppl.):34,34A,34B.

Kolhardt M, Haastert HP, Krause H. 1973. Evidence of non-specificity of the Ca channel in mammalian myocardial fibre membranes: Substitutions of Ca by Sr, Ba or Mg as charge carriers. Pflugers Arch(Eur J Physiol) 342:125-136.

Kollenkirchen U. 1995. Measurement of bone resorption by strontium excretion in prelabelled rats. Bone 17(4):455S-460S.

Kollmer WE, Kriegel H. 1965. Das biologische verhalten von radiostrontium bei ratten im verlauf der laktation. Int J Radiat Biol 9(4):369-381.

Komarneni S, Scheetz BE. 1981. Hydrothermal interactions of basalts with Cs and Sr of spent fuel elements. 43:1967-1975.

9. REFERENCES

*Komori M, Nishio K, Kitada M, et al. 1990. Fetus-specific expression of a form of cytochrome P-450 in human livers. Biochemistry 29:4430-4433.

*Kossenko MM. 1996. Cancer mortality among Techa River residents and their offspring. Health Phys 71(1):77-82.

*Kossenko MM, Degteva MO, Vyushkova OV, et al. 1997. Issues in the comparison of risk estimates for the population in the Techa River region and atomic bomb survivors. Radiat Res 148:54-63.

*Kossenko MM, Hoffman DA, Thomas TL. 2000. Stochastic effects of environmental radiation exposure in populations living near the Mayak Industrial Association: Preliminary report on study of cancer morbidity. Health Phys 79(1):55-62.

*Kossenko MM, Izhevsky PV, Degteva MO, et al. 1994. Pregnancy outcome and early heath status of children born to the Techa River population. Sci Total Environ 142:91-100.

*Kossenko MM, Preston DL, Krestinina LY, et al. 2002. Studies on the extended Techna cohort: Cancer risk estimation. Radiat Environ Biophys 41(1):45-48.

Kossmna SE, Weiss MA. 2000. Acute myelogenous leukemia after exposure to strontium-89 for the treatment of adenocarcinoma of the prostate. Cancer 88(3):620-624.

Kostial K, Durakovic A, Simonovic I, et al. 1969a. The effect of some dietary additives on calcium and strontium absorption in suckling and lactating rats. Int J Radiat Biol 15(6):563-570.

*Kostial K, Gruden N, Durakovic A. 1969b. Intestinal absorption of calcium-47 and strontium-85 in lactating rats. Calcif Tissue Res 4(1):13-19.

Kostial K, Gruden N, Durakovic A, et al. 1972. Reduction in strontium absorption in pregnant, lactating and suckling rats. Acta Radiol 11(3):277-287.

*Kostial K, Kargacin B, Landeka M. 1984. Influence of dietary ingredients on the body retention of strontium, cadmium and mercury in suckling rats. Toxicol Lett 23(2):163-168.

Kostial K, Kargacin B, Rabar I, et al. 1981a. Simultaneous reduction of radioactive strontium, caesium and iodine retention by single treatment in rats. Sci Total Environ 22:1-10.

Kostial K, Kargacin B, Simonovic I. 1987. Reduced radiostrontium absorption in a human subject treated with composite treatment for mixed fission product contamination. Health Phys 52(3):371-372.

Kostial K, Maljkovic T, Kadic M, et al. 1967. Reduction of the absorption and retention of strontium in rats. Nature 215:182.

*Kostial K, Maljkovic T, Paulic N, et al. 1979. The effect of THPC, a new cyclic analogue of BAETA on radiostrontium removal in rats. Health Phys 37:181.

Kostial K, Simonovic I, Rabar I, et al. 1980a. Influence of human foods and rat diet on radiostrontium bioavailability in rats. Period Biol 82(2):229-234.

*Kostial K, Simonovic I, Rabar I, et al. 1981b. Effect of rat's diet on ^{85}Sr, ^{115m}Cd, and ^{203}Hg absorption in suckling rats. Environ Res 25(2):281-285.

Kostial K, Vnucec M, Tominac C, et al. 1980b. A method for a simultaneous decrease of strontium, caesium and iodine retention after oral exposure in rats. Int J Radiat Biol 37(3):347-350.

Kostial K, Vojvodic S, Comar CL. 1965. Effects of dietary levels of phosphorus and calcium on the comparative behaviour of strontium and calcium. Nature 208:1110-1111.

Kowalewski K, Rodin AE. 1964. Strontium-89-induced bone tumour in the rat. Can J Surg 7:204-215.

*Kozheurov VP. 1994. SICH-9.1 - A unique whole-body counting system for measuring Sr-90 via bremsstrahlung. The main results from a long-term investigation of the Techa River population. Sci Total Environ 142:37-48.

*Krachler M, Scharfetter H, Wirnsberger GH. 2000. Kinetics of the metal cations magnesium, calcium, copper, zinc, strontium, barium, and lead in chronic hemodialysis patients. Clin Nephrol 54(1):35-44.

*Kramer GH, Davies JM. 1982. Isolation of strontium-90, yttrium-90, promethium-147, and cerium-144 from wet ashed urine by calcium oxalate coprecipitation and sequential solvent extraction. Anal Chem 54:1428-1431.

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.

*Kraybill HF. 1983. Assessment of human exposure and health risk to environmental contaminants in the atmosphere and water with special reference to cancer. J Environ Sci Health C 1(2):175-232.

Krieger HL, Martin ER, Frishkorn GW. 1976. Sequential radiochemical analysis for ruthenium, strontium and cesium in environmental air. Health Phys 30:465-470.

Krishnamurthy GT, Krishnamurthy. 2000. Radionuclides for metastatic bone pain palliation: a need for rational re-evaluation in the new millennium. J Nucl Med 41(4):688-691.

*Krishnan K, Andersen ME. 1994. Physiologically based pharmacokinetic modeling in toxicology. In: Hayes AW, ed. Principles and methods of toxicology. 3rd ed. New York, NY: Raven Press, Ltd., 149-188.

*Krishnan K, Andersen ME, Clewell HJ III, et al. 1994. Physiologically based pharmacokinetic modeling of chemical mixtures. In: Yang RSH, ed. Toxicology of chemical mixtures: Case studies, mechanisms, and novel approaches. San Diego, CA: Academic Press, 399-437.

*Kroes R, den Tonkelaar EM, Minderhoud A, et al. 1977. Short-term toxicity of strontium chloride in rats. Toxicology 7(1):11-21.

Krusemark LL, Boomgaardt J, Harmon BG, et al. 1974. Distribution of injected ^{85}Sr in tissues and bones of growing pigs. J Anim Sci 39(2):331-334.

Krushevska A, Barnes RM. 1994. Inductively coupled plasma atomic emission spectrometric determination of aluminium, barium, silicon, strontium and titanium in food after sample fusion. Analyst 119:131-134.

9. REFERENCES

*KS Dept Health & Environ. 1999. Water pollution control. Kansas Department of Health and Environment. Wysiwig://29/http://www.kdhe.state.ks.us/regs/index.html.

Kshirsagar SG. 1975. The effect of stable strontium on the alkaline phosphatase activity of rat tissues -- *In vitro* studies. Biochem Pharmacol 24:13-20.

*Kshirsagar SG. 1976. Effect of stable strontium on the tissue alkaline and acid phosphatase activities of rat: Feeding studies. J Nutr 106(10):1475-1483.

*Kshirsagar SG. 1977. Radiostrontium distribution measured in vitro between bound and free forms in the soft tissues of rat. Int J Radiat Biol 32(6):561-569.

*Kshirsagar S, Vaughan J, Williamson M. 1965. The occurrence of squamous carcinoma and osteosarcoma in young rabbits injected with ^{90}Sr(50-100 μc/kg). Br J Cancer 19(4):777-786.

*Kulev YD, Polikarpov GG, Pridodey EV, et al. 1994. Strontium-90 concentrations in human teeth in south Ukraine, 5 years after the Chernobyl accident. Sci Total Environ 155:215-219.

Kulp JL, Schulert AR, Hodges EJ. 1959. Strontium-90 in man III: The annual increase of this isotope and its pattern of world-wide distribution in man are defined. Science 129(3358):1249-1255.

Kumar S, Singh S, Garg ML, et al. 1989. Elemental analysis of environmental samples using energy dispersive x-ray fluorescence technique. Indian J Environ Health 31(1):8-16.

Kumar V, Bennett M. 1981. The biology of marrow dependent cells in mice. In: Waters H, ed. The handbook of cancer immunology. New York, NY: Garland STPM Press, Vol. 6, 145-160.

Kurzel RB, Cetrulo CL. 1981. The effect of environmental pollutants on human reproduction, including birth defects. Environ Sci Technol 15(6):626-640.

Lagged E, Akron K, Fonyó A. 1979. The inhibitor-sensitivity and pathways of P_i uptake during calcium and strontium accumulation in liver mitochondria. FEBS Lett 107(1):205-208.

Lamberts HB, Van Andel JG. 1965. The deposition of radioactive Ba and Sr in the aortic wall. Proc K Ned Akad Wet C 68(4):311-319.

*Lansdown ABG, Longland RC, Grasso P. 1972. Reduced foetal calcium without skeletal malformations in rats following high maternal doses of a strontium salt. Experientia 28(5):558-560.

LaPuma PT, Bolch WE. 1999. The impact of recirculating industrial air on aircraft painting operations. Appl Occup Environ Hyg 14(10):682-690.

Larsson S-E, Lorentzon R, Boquist L. 1977. The effect of immunotherapy with BCG on the development of radiostrontium (^{90}Sr)-induced osteosarcoma. Acta Pathol Microbiol Scand Sect A 85:433-446.

*Lassey KR. 1979. The transfer of radiostrontium and radiocesium from soil to diet: Models consistent with fallout analyses. Health Phys 37:557-573.

Latch C, Hoffmann E, Sole J. 1994. Studies on the determination of the metal content of airborne particulate by furnace atomization non-thermal excitation spectrometry. J Anal Atom Spectrum 9:685-689.

*Lavinia E, Kumar V, Bennett M. 1981. Hybrid resistance to EL-4 lymphoma cells. Scand J Immunol 13:563-571.

Ledin M, Pedersen K, Allard B. 1997. Effects of pH and ionic strength on the adsorption of Cs, Sr, Eu, Zn, Cd and Hg by *Pseudomonas putida*. Water Air Soil Pollut 93:367-381.

*Lee CK, Aeppli DM, Unger J, et al. 1996. Strontium-89 chloride (metastron) for palliative treatment of bony metastasis: The University of Minnesota experience. Am J Clin Oncol 19(2):102-107.

*Lee RE, von Lehmden DJ. 1973. Trace metal pollution in the environment. J Air Pollut Control Assoc 23(10):853-857.

*Leeder JS, Kearns GL. 1997. Pharmcogenetics in pediatrics: Implications for practice. Pediatr Clin North Am 44(1):55-77.

Leeuwenkamp OR, van der Vijgh WJH, Hüsken BCP, et al. 1989. Quantification of strontium in plasma and urine with flameless atomic absorption spectrometry. Clin Chem 35(9):1911-1914.

*Leeuwenkamp OR, van der Vijgh WJF, Hüsken BCP, et al. 1990. Human pharmacokinetics of orally administered strontium. Calcif Tissue Int 47:136-141.

*Leggett RW. 1992. A generic age-specific biokinetic model for calcium-like elements. Radiat Prot Dosim 41(2/4):183-198.

Leggett RW, Eckerman KF, Williams LR. 1982. Strontium-90 in bone: A case study in age-dependent dosimetric modeling. Health Phys 43(3):307-322.

Le Grand L. 1972. Contamination by osteotropic β emitters - An evaluation of the doses in bone marrow and endosteum - Effect of age. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 49-66.

*Leininger JR, Riley MGI. 1990. Bones, joints, and synovia. In: Boorman GA, Eustis SL, Elwell MR, et al. eds. Pathology of the Fischer rat: Reference and atlas. New York, NY: Academic Press, Inc, 209-226.

*Lembrechts J. 1993. A review of literature on the effectiveness of chemical amendments in reducing the soil-to-plant transfer of radiostrontium and radiocesium. Sci Total Environ 137:81-98.

Lemon GJ, Davies DR, Hughes SPF, et al. 1980. Transcapillary exchange and retention of fluoride, strontium, EDTA, sucrose, and antipyrine in bone. Calcif Tissue Int 31:173-181.

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

*LeRoy GV, Rust JH, Hasterlik RJ. 1966. The consequences of ingestion by man of real and simulated fallout. Health Phys 12:449-473.

9. REFERENCES

*Leung H-W. 1993. Physiologically-based pharmacokinetic modeling. In: Ballentine B, Marro T, Turner P, eds. General and applied toxicology. Vol. 1. New York, NY: Stockton Press, 153-164.

Levis AG, Majone F. 1981. Cytotoxic and clastogenic effects of soluble and insoluble compounds containing hexavalent and trivalent chromium. Br J Cancer 44:219-235.

Levy EM, Bennett M, Kumar V, et al. 1980. Adoptive transfer of spleen cells from mice treated with radioactive strontium: Suppressor cells, natural killer cells, and "hybrid resistance" in recipient mice. J Immunol 124(2):611-618.

*Levy EM, Kumar V, Bennett M. 1981. Natural killer activity and suppressor cells in irradiates mice repopulated with a mixture of cells from normal and ^{89}Sr-treated donors. J Immunol 127(4):1428-1432.

*Levy LS, Martin PA, Bidstrup PL. 1986. Investigation of the potential carcinogenicity of a range of chromium containing materials on rat lung. Br J Ind Med 43:243-256.

Lewis FV, Dobrota M, Taylor MG. 1999. Metal toxicity in two rodent species and redox potential evaluation of quantitative structure-activity relationships. Environ Toxicol Chem 18(10):2199-2204.

*Li C, Davletov BA, Südhof TC. 1995. Distinct Ca^{2+} and Sr^{2+} binding properties of synaptotagmins: Definition of candidate Ca^{2+} sensors for the fast and slow components of neurotransmitter release. J Biol Chem 270(42):24898-24902.

Li L, Kruszewski FH, Punnonen K, et al. 1993. Strontium induces marine keratinocyte differentiation in vitro in the presence of serum and calcium. J Cell Physiol 154:643-653.

*Lide DR. 1995. Physical constants of inorganic compounds. In: CRC handbook of chemistry and physics. 76th ed. Boca Raton, FL: CRC Press, 4-37 to 4-98.

*Lide DR. 2000. CRC handbook of chemistry and physics: A ready-reference book of chemical and physical data. 81st ed. Boca Raton, FL: CRC Press.

Light JM, Stacey GK. 1972. Effect of fluoride-containing compounds on the skeletal retention of ^{90}Sr and ^{45}Ca in the rat. J Dent Res 51(4):909-917.

*Light JM, Stacey GK, Mahler JC. 1970a. Effect of dietary sodium alginate on radiostrontium absorption and retention in rats. J Dent Res 49(2):442-453.

Light JM, Stacey GK, Mahler JC. 1970b. The effects of sodium alginate and other untested polymers on radiostrontium retention in the rat. Proc Soc Exp Biol Med 133:1259-1269.

Linner E, Rosengren B. 1969. Complications following eye treatment with ^{90}Sr applicator. Acta Ophthalmol 47:202-207.

*Lisk DJ. 1988. Environmental implications of incineration of municipal solid waste and ash disposal. Sci Total Environ 74:39-66.

Litvak J, Oberhausen E, Rask J, et al. 1967. Strontium-85 kinetics in hypoparathyroidism at different levels of calcium intake. J Nucl Med 8:60-69.

*Livingston, AL. 1978. Forage plant estrogens. J Toxicol Environ Health 4:301-324.

*Llobet JM, Colomina MT, Domingo JL, et al. 1991a. Effect of chelating agents on tissue distribution and excretion of strontium following semichronic strontium ingestion. Res Commun Chem Pathol Pharmacol 71(2):243-246.

*Llobet JM, Colomina MT, Domingo JL, et al. 1991b. Evaluation of the effects of chelation therapy with time following strontium exposure to mice. Arch Environ Contam Toxicol 21:612-620.

*Llobet JM, Colomina MT, Domingo JL, et al. 1992a. Influence of several antidotal treatments on the distribution and excretion of strontium. J Environ Sci Health Part A A27(4):1103-1114.

*Llobet JM, Colomina MT, Domingo JL, et al. 1992b. Lack of effectiveness of several chelators in removing internally deposited strontium from mice following repeated parental strontium administration. Vet Hum Toxicol 34(1):7-9.

*Llobet JM, Colomina MT, Domingo JL, et al. 1993. Evaluation of potential strontium chelators in an actinal-water system. Health Phys 65(5):541-544.

*Lloyd E. 1968. Relative binding of strontium and calcium in protein and non-protein fractions of serum in the rabbit. Nature 217:355-356.

Lloyd RD. 1990. Does the growth rate of a radionuclide-induced osteosarcoma depend of the skeletal dose rate during the growth period? Health Phys 58(1):73-76.

*Lloyd RD, Angus W, Taylor GN, et al. 1995. Soft tissue tumors among beagles injected with ^{90}Sr, ^{228}Ra, ^{228}Th. Health Phys 69(2):272-277.

Lloyd RD, Miller SC, Taylor GN, et al. 1994a. Relative effectiveness of ^{239}Pu and some other internal emitters for bone cancer induction in beagles. Health Phys 67(4):346-353.

Lloyd RD, Miller SC, Taylor GN. 2001. Does longevity in beagles injected with bone-seeking radionuclides depend upon radiation dose in the absence of known radiation effects? Health Phys 81(4):456-459.

*Lloyd RD, Taylor GN, Angus W, et al. 1994b. Eye tumors and other lesions among beagles give ^{90}Sr or ^{226}Ra. Health Phys 66(3):346-349.

Lloyd RD, Taylor GN, Miller SC. 2000. Does body size contribute to sensitivity of bone tumor induction by radionuclide exposure? Health Phys 79(2):199-202.

*Loeb LA, Sirover MA, Weymouth LA, et al. 1977. Infidelity of DNA synthesis as related to mutagenesis and carcinogenesis. J Toxicol Environ Health 2:1297-1304.

*Loeser D, Konwiser AL. 1930. A study of the toxicity of strontium and comparison with other cations employed in therapeutics. J Lab Clin Med 15:35-41.

Loutit JF. 1965. Diurnal variation in urinary excretion of calcium and strontium. Proc R Soc London, Ser B 162:458-472.

Loutit JF. 1967. Strontium-90 and leukemia. Sci Basis Med 1967:340-355.

Loutit JF. 1968. What is the turnover of bone mineral? Calcif Tissue Res 2:111-114.

*Loutit JF. 1976. Vasoformative non-osteogenic (agio) sarcomas of bone-marrow stroma due to strontium-90. Int J Radiat Biol 30(4):359-383.

Loutit JF, Vaughan JM. 1971. Correspondence: The radiosensitive tissues in bone. Br J Radiol 44:815.

*Luevano E, Kumar V, Bennett M. 1981. Hybrid resistance to EL-4 lymphoma cells. Scand J Immunol 13:563-571.

*Lüning KG, Fraulein H, Nelson A, et al. 1963a. Genetic effects of strontium-90 injected into male mice. Nature 197(4864):304-305.

*Lüning KG, Fraulein H, Nelson A, et al. 1963b. Genetic effects of strontium-90 on immature germ-cells in mice. Nature 199(4890):303-304.

Lust JA, Kumar V, Burton RC, et al. 1981. Heterogeneity of natural killer cells in the mouse. J Exp Med 154:306-317.

Lykhtarev IA, Krasnostchekova GP. 1972. Mathematical model of endocrine regulation of calcium-strontium metabolism and its experimental study. In: International Conference on Strontium Metabolism, ed. Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 229-238.

MacDonald NS, Braden L, James E, et al. 1967. Short term tissue distribution of several radionuclides useful in bone scanning. Proc Soc Exp Biol Med 124(1):69-73.

*MacDonald NS, Figaro WG, Crist MR. 1965. Short-term retention of strontium-85 and estimation of initial strontium-90 burdens in humans. Health Phys 11:1187-1194.

MacDonald NS, Nusbaum RE, Stearns R, et al. 1951. The skeletal deposition of non-radioactive strontium. J Biol Chem 188:137-143.

Mackay WA, Strange L, Walker MI, et al. 1994. A study of plutonium and americium concentrations in sea spray on the southern Scottish coast. Sci Total Environ 144:73-86.

*Madeddu L, Saito I, Hsiao TH, et al. 1985. Leptinotoxin-h action in synaptosomes and neurosecretory cells: Stimulation of neurotransmitter release. J Neurochem 45:1719-1730.

Magna PJ, Baratta EJ, Leonard IE. 1966. Strontium-90 in human hair and blood. Health Phys 12:1493-1496.

*Mahara Y. 1993. Heavy metals in the environment: Storage and migration of fallout strontium-90 and cesium-137 for over 40 years in the surface soil of Nagasaki. J Environ Qual 22:722-730.

*Malek MA, Hinton TG, Webb SB. 2002. A comparison of 90Sr and 137Cs uptake in plants via three pathways at two Chernobyl-contaminated sites. J Environ Radioact 58:129-141.

Maltby B, Lemon GJ, Bassingthwaighte JB, et al. 1982. Exchange of potassium and strontium in adult bone. Am J Physiol 242:H705-H712.

Marcus AH, Becker A. 1980. Alkaline earth metabolism: The ICRP model reformulated as a semi-markov model. Health Phys 38:825-832.

Marcus CS. 1972. Use of ^{87m}Sr and semiconductor radiation detectors for *in vivo* physiological studies. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 79-90.

Marcus CS, Vos O. 1967. Two-component radiation effect on strontium^{85} absorption by the rat ileum *in situ*. Proc Soc Exp Biol Med 121(3):885-888.

*Marcus CS, Wasserman RH. 1965. Comparison of intestinal discrimination between calcium 47, strontium 85, and barium 133. Am J Physiol 209:973-977.

*Marei AN, Borisov BK, Petukhova EV. 1976. The content of ^{90}Sr in the bone tissue of the population of the Soviet Union (1959-1971) (The basic laws of its accumulation and distribution). J Hyg Epidemiol Microbiol Immunol 20(3):257-265.

*Marie PJ, Hott M. 1986. Short-term effects of fluoride and strontium on bone formation and resorption in the mouse. Metabolism 35(6):547-551.

Marie PJ, Ammann P, Boivin G, et al. 2001. Mechanisms of action and theraputic potential of strontium in bone. Calcif Tissue Int 69:121-129.

*Marie PJ, Gaba MT, Hot M, et al. 1985. Effects of low doses of stable strontium on bone metabolism in rats. Miner Electrolyte Metab 11(1):5-13.

Markham OD, Hafford DK, Autenrieth RE. 1980. Strontium-90 concentrations in pronghorn antelope bones near a nuclear fuel reprocessing plant. Health Phys 38:811-816.

*MARLAP. 2001. Multi-Agency Radiological Laboratory Analytical Protocols Manual (MARLAP) Draft. U.S. Environmental Protection Agency. PB2001-106745. http://www.eml.doe.gov/marlap/. November 21, 2002.

Marois P, Marois M. 1971. [Action of tetracycline on tooth and bone. (General review and experimental study in rats)]. Biol Med (Paris) 60(3):293-362. (French)

Marshall JH. 1964. Theory of alkaline earth metabolism: The power function makes possible a simple but comprehensive model of skeletal systems. J Theor Biol 6:386-412.

Marshall JH. 1972. Alkaline earth metabolism in adult man: A condensation. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 207-228.

*MARSSIM. 1997. Multi-agency radiation survey and site investigation manual. Nuclear Regulatory Commission, Energy Department, Environmental Protection Agency, and Defense Department. NUREG 1575, EPA 402 R 97 016.

Mart E. 1980. Immune T lymphocyte to tumor cell adhesion: Magnesium sufficient, calcium insufficient. J Cell Biol 84:584-598.

9. REFERENCES

Martin WE, Turner FB. 1966. Transfer of ^{89}Sr from plants to rabbits in a fallout field. Health Phys 12:621-631.

*Matsumoto A. 1976. Effect of strontium on the epiphyseal cartilage plate of rat tibiae -- Histological and radiographic studies. Jpn J Pharmacol 26:675-681.

Matsumoto A. 1988. Effect of strontium chloride on bone resorption induced by prostaglandin E_2 in cultured bone. Arch Toxicol 62:240-241.

*Mayr U, Busch A, Schneider S. 1992. Validation of two in vitro test systems for estrogenic activities with zearalenone, Phytoestrogens and cereal extracts. Toxicology 74:135-149.

Mays CW, Dougherty TF. 1972. Progress in the beagle studies at the University of Utah. Health Phys 22:793-801.

Mays CW, Lloyd RD. 1966. ^{90}Sr and ^{89}Sr dose estimates for the fetus and infant. Health Phys 12:1225-1236.

Mays CW, Lloyd RD. 1972. Predicted toxicity of ^{90}Sr in humans. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 181-206.

Mays CW, Jee WSS, Lloyd RD, et al., eds. 1969. Delayed effects of bone-seeking radionuclides. Salt Lake City, UT: University of Utah Press.

Maxilla GF, Tyrannid L, Caen G, et al. 1966. Effects of thyrocalcitonin on bone and renal excretion of calcium 45 and strontium 85 in the rat. Foliar Endocrinol 19(1):7-13.

Mazzucotelli A, Raver P. 1993. Study of interferences in the spectrochemical behavior of strontium, related to its determination in the shell of marine organisms. Annals di Camacho 83:105-115.

McAughey JJ, Samuel AM, Baxter PJ, et al. 1988. Biological monitoring of occupational exposure in the chromate pigment production industry. Sci Total Environ 71:317-322.

McBride MB, Richards BK, Steenhuis T, et al. 1997. Mobility and solubility of toxic metals and nutrients in soil fifteen years after sludge application. Soil Sci 162(7):487-500.

McBride MB, Richards BK, Steenhuis T, et al. 1999. Long-term leaching of trace elements in a heavily sludge-amended silty clay loam soil. Soil Sci 164(9):613-623.

McCarthy ID, Hughes SPF. 1986. Inhibition of bone cell metabolism increases strontium-85 uptake. Calcif Tissue Int 39:386-389.

McCarthy ID, Hughes SPF. 1989. Multiple tracer studies of bone uptake of ^{99m}Tc-M.P. and ^{85}Sr. Am J Physiol 256:H1261-H1265.

*McClellan RO, Benjamin SA, Boecker BB, et al. 1973. Neoplasms in dogs that inhaled $^{90}SrCl_2$. AEC Symp Ser 29:215-232.

*McClellan RO, Boecker BB, Hahn FF, et al. 1983a. Lovelace TRI studies on the toxicity of inhaled radionuclides in beagle dogs. In: Thompson RC, Mahaffey JA, eds. Life-span radiation effects studies

in animals: What can they tell us? Proceedings of the twenty-second Hanford life science symposium held at Richland, Washington, September 27-29, 1983. Hanford Life Sciences Symposium 22nd. Springfield, VA: United States Department of Energy, 74-96.

McClellan RO, Boecker B, Hahn FF. 1983b. Toxicity of inhaled $^{90}SrCl_2$. In: Brewers JJ, Barendsen GW, Kan HB, et al., eds. Somatic and genetic effects. Amsterdam: Margins Nijhoff Publishers, C7-05-C7-06.

*McClellan RO, Kerr ME, Bustard LK. 1963. Reproductive performance of female miniature swine ingesting strontium-90 daily. Nature 197:670-671.

*McCormack JG, Osbaldeston NJ. 1990. The use of the Ca^{2+}-sensitive intra mitochondrial dehydrogenate and entrapped Furr-2 to study Sr^{2+} and Ba^{2+} transport across the inner membrane of mammalian mitochondria. Eur J Biochem 192:239-244.

McCredie D, Rosenberg E. 1972. Strontium kinetic studies in children with bone disorders. Aust Paediat 69:79-86.

*McLachlan EM. 1977. The effects of strontium and barium ions at synapses in sympathetic ganglia. J Physiol 267:497-518.

McQueen CM, Smith DA. 1972. The relative uptake of ^{45}Ca and ^{85}Sr into bone. In:. Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 403-412.

*MDEQ. 2000. Safe drinking water act. Michigan Department of Environmental Quality. http://www.deq.state.mi.us/dept/envregs.html.

Mellen PF, Lust JA, Bennett M, et al. 1982. Analysis of low natural killer cell activity in ^{89}Sr-treated mice. Eur J Immunol 12:442-445.

Menczel J, Mor E. 1972. The effect of thyrocalcitonin (TCT) on calcium binding protein (CABP) and strontium binding protein (SRBP). In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 273-276.

Merck. 1989. The Merck index: An encyclopedia of chemicals, drugs, and biologicals. 11th ed. Rahway, NJ: Merck and Company, Inc, 1394-1395.

*Merluzzi VJ, Levy EM, Kumar V, et al. 1978. *In vitro* activation of suppressor cells from spleens of mice treated with radioactive strontium. J Immunol 121(3):505-512.

*Mermier P, Hasselbach W. 1976. Comparison between strontium and calcium uptake by the fragmented sarcoplasmic reticulum. Eur J Biochem 69:79-86.

*Merriam GR. 1955. Late effects of beta radiation on the eye. AMA Arch Ophth 53:708-717.

*Meunier PJ, Roux C, Seeman E, et al. 2004. The effects of strontium ranelate on the risk of vertebral fracture in women with postmenopausal osteoporosis. N Engl J Med 350(5):459-468.

9. REFERENCES

*Meunier PJ, Slosman, DO, Delmas PD, et al. 2002. Strontium ranelate: dose-dependent effects in established postmenopausal vertebral osteoporosis—a 2-year randomized placebo controlled trial. J Clin Endocrinol Metab 87(5):2060-2066.

Mewhinney JA, Griffith WC, Hahn FF, et al. 1983. Incidence of bone cancer in beagles after inhalation of $^{90}SrCl_2$ or $^{238}PuO_2$: Implications for estimation of risk to humans. In: Thompson RC, Mahaffey JA, eds. Life-span radiation effects studies in animals: What can they tell us? Proceedings of the twenty-second Hanford life science symposium held at Richland, Washington, September 27-29, 1983. Hanford Life Sciences Symposium 22nd. Springfield, VA: United States Department of Energy, 535-554.

Milin L, Anderson JJB. 1968. Whole-body retention of strontium-85 in swine given sodium alginate or barium and sodium sulfates. J Nutr 97:181-184.

*Miller DL, Schedl HP. 1976. Effects of experimental diabetes on intestinal strontium absorption in the rat. Proc Soc Exp Biol Med 152:589-592.

*Mill AJ, Wells J, Hall SC, et al. 1996. Micronucleus induction in human lymphocytes: comparitive effects of X-rays, alpha particles, beta particles and neutrons and implications for biological dosimetry. Radiat Res 145(5):575-585.

*Milsom S, Ibbertson K, Hannan S, et al. 1987. Simple test of intestinal calcium absorption measured by stable strontium. Br Med J 295:231-234.

*Miro M, Gomez E, Estela JM, et al. 2002. Sequential injection ^{90}Sr determination in environmental samples using a wetting-flim extraction method. Anal Chem 74:826-833.

Mitchel RE, Gragtmans NJ, Morrison DP. 1990. Beta-radiation-induced resistance to MNNG initiation of papiloma but not carcinoma formation in mouse skin. Radiat Res 121:180-186.

Mitchell CE, Longwell BB. 1970. The effects of adrenocorticotrophin hormone and metyrapone on the excretion of urinary steroids by beagle dogs burdened with strontium-90. Radiat Res 41:78-88.

Mittleman R, Chausmer A, Bellavia J, et al. 1967. Thyrocalcitonin activity in hypercalcemia produced by calcium salts, parathyroid hormone and vitamin D. Endocrinology 81:599-604.

Möbius S, Ramamonjisoa T-L, Jongisook W, et al. 1995. Ion chromatography and liquid scintillation counting couples to determine α- and β-emitters. Sci Total Environ 173/174:231-235.

Moghissi AA, Mayes MG, Carter MW. 1972. Radiobioassay program of the institutional total diet sampling network: IV. Evaluation of the ^{90}Sr data for children. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 505-512.

Mohammed J, Chowdhury J, Blust R. 2001. Effect of temperature on the uptake of waterborne strontium in the common carp, Cyprinus carpio (L). Aquat Toxicol 54:151-160.

Moisecu DG, Thieleczek R. 1978. Calcium and strontium concentration changes within skinned muscle preparations following a change in the external bathing solution. J Physiol 275:241-262.

Molchanova IV, Karavaeva EN, Kulikov NV. 1973. Influence of soil moisture content on strontium-90 uptake by plants. Sov J Ecol 3(3):257-259.

Mole RH. 1963. Bone tumour production in mice by strontium-90: Further experimental support for a two-event hypothesis. Br J Cancer 17(3):524-531.

Mole RH, Ward AH. 1970. Yttrium-90 in gonads of monkeys containing strontium-90. Nature 226:175.

Moloukhia MK, Abdel-Fattah AT. 1980. Equilibrium treatment for radiostrontium uptake by human and animal bones. Isot Radiat Res 12(1):35-42.

*Momčilovič B, Gruden N. 1981. The effect of dietary fibre on ^{85}Sr and ^{47}Ca absorption in infant rats. Experientia 37(5):498-499.

*Momeni MH, Williams JR, Jow N, et al. 1976. Dose rates, dose and time effects of ^{90}Sr + ^{90}Y and ^{226}Ra on beagle skeleton. Health Phys 30:381-390.

Moon J. 1994. The role of vitamin D in toxic metal absorption: A review. J Am Coll Nutr 13(6):559-569.

Moore W, Elder RL. 1965. Effect of alginic acid and the movement of strontium-85 and calcium-45 across surviving ileal segments. Nature 206:841-842.

Moraes MEA, Aronson JK, Grahame-Smith DG. 1991a. The effect of nifedipine on the disposition of strontium gluconate used as a kinetic marker for calcium in healthy volunteers. Br J Clin Pharmacol 32:441-445.

Moraes MEA, Aronson JK, Grahame-Smith DG. 1991b. Intravenous strontium gluconate as a kinetic marker for calcium in healthy volunteers. Br J Clin Pharmacol 31:423-427.

Morgan JE, Richards SPG, Morgan AJ. 2001. Stable strontium accumulation by earthworms: a paradigm for radiostrontium interactions with its cationic analogue, calcium. Environ Toxicol Chem 20(6):1236-1243.

Morohashi T, Sano T, Harai K, et al. 1995. Effects of strontium on calcium metabolism in rats II. Strontium prevents the increased rate of bone turnover in ovariectomized rats. Jpn J Pharmacol 68:153-159.

*Morohashi T, Sano T, Yamada S. 1994. Effects of strontium on calcium metabolism in rats: I. A distinction between the pharmacological and toxic doses. Jpn J Pharmacol 64:155-162.

Morrison SJ, Cahn LS. 1991. Mineralogical residence of alpha-emitting contamination and implications for mobilization from uranium mill tailings. J Contam Hydrol 8:1-21.

Morse BS, Giuliani D, Giuliani ER. 1974. Effect of radiation on bone formation: A functional assessment. Radiat Res 60:307-313.

*Morselli PL, Franco-Morselli R, Bossi L. 1980. Clinical pharmacokinetics in newborns and infants: Age-related differences and therapeutic implications. Clin Pharmacokin 5:485-527.

*Mortimer D. 1986. Comparison of the fertilizing ability of human spermatozoa preincubation in calcium- and strontium-containing media. J Exp Zool 237:21-24.

9. REFERENCES

*Mortimer D, Curtis EF, Dravland JE. 1986. The use of strontium-substituted media for capacitating human spermatozoa: an improved sperm preparation method for the zona-free hamster egg penetration test. Fertil Steril 46(1):97-103.

*Moskalev JI, Buldakov LA, Lyaginskaya AM, et al. 1969. Experimental study of radionuclide transfer through the placenta and their biological action on the fetus. AEC Symp Ser 17:153-160.

Moskalev YI, Buldakov LA. 1968. The kinetics of accumulation and elimination of orally administered strontium-90. Health Phys 15:229-235.

Moskalev YI, Strel'tsova VN, Kalistratova VS. 1972. The combined effects of ^{131}J and ^{90}Sr in experimental animals. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 155-166.

Muck K, Sinojmeri M, Whilidal H, et al. 2001. The long-term decrease of ^{90}Sr availability in the environment and its transfer to man after a nuclear fallout. Radiat Prot Dosim 94(3):251-259.

Muggenburg BA, Boecker BB, Hahn FF, et al. 1983. The risk of liver tumors in dogs and man from radioactive aerosols. In: Thompson RC, Mahaffey JA, eds. Life-span radiation effects studies in animals: What can they tell us? Proceedings of the twenty-second Hanford life science symposium held at Richland, Washington, September 27-29, 1983. Hanford Life Sciences Symposium 22nd. Springfield, VA: U.S. Department of Energy, 556-563.

*Muggenburg BA, Hahn FF, Boecker BB, et al. 1979. Toxicity of inhaled $^{90}SrCl_2$ in beagle dogs, XIII. In: Annual reports of the Inhalation Toxicology Research Institute. Albuquerque, NM: Inhalation Toxicology Research Institute, 57-61.

*Muggenburg BA, Rebar AH, Benjamin SA, et al. 1977. Toxicity of inhaled $^{90}SrCl_2$ in beagle dogs, XI. In: Annual reports of the Inhalation Toxicology Research Institute. Albuquerque, NM: Inhalation Toxicology Research Institute, 62-65.

*Muggenburg BA, Rebar AH, Boecker BB, et al. 1978. Toxicity of inhaled $^{90}SrCl_2$ in beagle dogs. XII. In: McClellan RO, ed. Annual report of the inhalation toxicology research institute. Albuquerque: Lovelace Biomedical and Environmental Research Institute.

*Müller J, Thomas J. 1968. The course in time of the strontium retention in man. Health Phys 14:285-292.

Müller J, David A, Rejskova M, et al. 1961. Chronic occupational exposure to strontium-90 and radium-226. Lancet:129-131.

*Müller J, Klener V, Tuscany R, et al. 1966. Study of internal contamination with strontium-90 and radium-226 in man in relation to clinical findings. Health Phys 12:993-1006.

Muller WA. 1967. Radiobiology: Gonad dose in male mice after incorporation of strontium-90. Nature 214:931-933.

Muller WA. 1972. ^{90}Y distribution in male mice after injection of ^{90}Sr, and consequences for dose burden of bone, soft tissue, and gonads. In: Second international conference on strontium metabolism,

Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 137-144.

*Müller WH. 1970. Sr-85 decorporation with a cryptating agent. Naturwissenschaften 57(5):248.

*Mumma RO, Raupach DC, Waldman JP, et al. 1984. National survey of elements and other constituents in municipal sewage sludges. Arch Environ Contam Toxicol 13:75-83.

*Muñiz CS, Marchante-Gayón JM, Alonso JIG, et al. 1999. Multi-elemental trace analysis of human serum by double-focusing ICP-MS. J Anal Atom Spectrom 14:193-198.

*Murray RL. 1994. Understanding radioactive waste. 4th ed. Columbus, OH: Battelle Press, 58-193.

*Mutschke U, Pribilla O. 1967. Detection of radionuclides of biological interest in human bones and tissues. Prog Chem Toxicol 3:244-303.

Nakai GS, Guganig ME, Kelley RO, et al. 1971. Cytoplasmic DNA in ^{90}Sr-induced rat chloro leukemia. Rev Eur Etud Clin Biol XVI:560-563.

Nakaji S, Fukuda S, Sakamoto J, et al. 2001. Relationship between mineral and trace element concentration in drinking water and gastric cancer mortality in Japan. Nutr Cancer 40(2):99-102.

*Naményi J, Gachalyi A, Varga LP. 1986. Decorporation of ^{85}Sr by radioadsorbents from the lungs of rats with bronchial disorders. Health Phys 51(4):539-544.

Narayan K, Cliff WJ. 1981. Use of rabbit ear chamber and strontium-90 source to study radiation pathology *in vivo*. Microvasc Res 21:384-389.

Narayan K, Cliff WJ. 1982. Morphology of irradiated microvasculature: A combined in vivo and electron-microscopic study. Am J Pathol 106:47-62.

*NAS/NRC. 1989. Report of the oversight committee. In: Biologic markers in reproductive toxicology. Washington, DC: National Academy of Sciences, National Research Council, National Academy Press.

*Navarro T, López MA. 1998. Accidental contamination with ^{90}Sr: A case study. Radiat Prot Dosim 79(1-4):67-70.

*NCRP. 1984. Radiological assessment: Predicting the transport, bioaccumulation, and uptake by man of radionuclides released to the environment. NCRP Report No. 76. Bethesda, MD: National Council on Radiation Protection and Measurements.

*NCRP. 1987a. Ionizing radiation exposure of the population of the United States. National Council on Radiation Protection and Measurements. NCRP Report No. 93, 1-69.

*NCRP. 1987b. Public radiation exposure from nuclear power generation in the United States. National Council on Radiation Protection and Measurements. Report No. 92. Bethesda, MD.

*NCRP. 1991. Some aspects of strontium radiobiology. Bathesda, MD: National Council on Radiation Protection and Measurements. NCRP Report No. 110.

9. REFERENCES

*NCRP. 1993. Limitation of exposure to ionizing radiation. National Council on Radiation Protection and Measurements. Report No. 116.

*Neighbor PA, Huberman HS, Kress Y. 1982. Human large granular lymphocytes and natural killing: Ultrastructural studies of strontium-induced degranulation. Eur J Immunol 12:588-595.

*Neufeld EB, Boskey AL. 1994. Strontium alters the complexed acidic phospholipid content of mineralizing tissues. Bone 15(4):425-430.

Neumann GK. 1974. Diaplazentarer ubertritt von strontium-90 bei der ratte. Naturwissenschaften 61:221-222.

Nevissi AE. 1992. Measurement of actinides and long-lived radionuclides in large coral samples. J Radioanal Nucl Chem 156(2):243-251.

*Newton D, Harrison GE, Rundo J, et al. 1990. Metabolism of Ca and Sr in late adult life. Health Phys 59(4):433-442.

Nieuwinhuis BJWM, Weijers CAGM, Borst-Pauwels GWFH. 1981. Uptake and accumulation of Mn^{2+} and Sr^{2+} in *Saccharomyces cerevisiae*. Biochim Biophys Acta 649:83-88.

*Niggli E. 1989. Strontium-induced creep currents associated with tonic concentrations in cardiac in cardiac myocytes isolated from guinea-pigs. J Physiol 414:549-568.

*Nilsson A. 1970. Pathologic effects of different doses of radiostrontium in mice. Acta Radiol Ther Phys Biol 9(6):528-544.

*Nilsson A. 1971. Pathologic effects of different doses of radiostrontium in mice: Development and incidence of leukemia. Acta Radiol Ther Phys Biol 10(1):115-128.

*Nilsson A. 1972. Strontium-90-induced malignancies in mice. AEC Symp Ser 25:207-241.

*Nilsson A, Henricson B. 1969. The effect of ^{90}Sr on the ovaries of the fetal mouse. AEC Symp Ser 17:313-324.

Nilsson A, Rönnbäck C. 1972. Influence of oestrogenic hormones on carcinogenesis and toxicity of radiostrontium. Acta Radiol Ther Phys Biol 12:209-228.

Nilsson A, Rönnbäck C. 1973. Carcinogenic effect in bone of radiostrontium and estrogenic hormones. AEC Symp Ser 29:154-158.

*Nilsson A, Rönnbäck C. 1988. Influence of low temperature on the excretion of radiocesium and radioruthenium compared with radiostrontium. Acta Oncol 27(3):289-292.

*Nilsson A, Bierke P, Haraldsson I, et al. 1980a. Induction of pituitary tumours by combination of oestrogenic hormones and ^{90}Sr. Acta Radiol Oncol 19(5):373-385.

*Nilsson A, Bierke P, Walinder G, et al. 1980b. Age and dose related carcinogenicity of ^{90}Sr. Acta Radiol Oncol 19(3):223-228.

Nilsson BE. 1969. Uptake of ^{47}Ca and ^{85}Sr in the tibia and the femur in rats. Calcif Tissue Res 3:96-99.

*Nilsson BE, Book SA. 1987. Occurrence and distribution of bone tumors in beagle dogs exposed to ^{90}Sr. Acta Oncol 26(2):133-138.

Nilsson BE, Saville PD. 1968. Relations between femur density and strontium-85 uptake in bipedal rats. Acta Orthop Scand 39:433-438.

*Nilsson BE, Morgan JP, Book SA. 1985. Investigations of ^{90}Sr in dogs: I. Pathogenesis of radiation-induced bone tumors. Acta Radiol Oncol 24(1):95-111.

*NIOSH. 1994. Elements in blood or tissue. Method 8005, issue 2. In: NIOSH manual of analytical methods. 4th ed. Cincinnati, OH: U.S. Department of Health and Human Services. National Institute for Occupational Safety and Health.

*NIOSH. 2000. Online pocket guide to chemical hazards. http://www.cdc.gov/niosh/npg/npg.html.

*Nishimura Y, Nakai A, Yoshimasu T, et al. 2000. Long-term results of fractional strontium-90 radiation therapy for pterygia. Int J Radiat Oncol Biol Phys 1(46):137-141.

*NOES. 1983. National Occupational Exposure Survey (NOES). Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health.

Nordin BEC, Smith DA, Shimmins J, et al. 1967. The effect of dietary calcium on the absorption and retention of radiostrontium. Clin Sci 32:39-48.

Nordio S, Donath A, Macagno F, et al. 1971. Chronic hypomagnesemia with magnesium-dependent hypocalcemia. Acta Paediatr Scand 60:449-455.

*NRC. 1993. National Research Council. Pesticides in the diets of infants and children. Washington, DC: National Academy Press.

Ochs S, Jersild RA, Breen T, et al. 1986. The maintenance of axoplasmic transport by strontium and its localization in nerve fibers. J Neurobiol 17(1):55-61.

*O'Connor BH, Kerrigan GC, Taylor KR, et al. 1980. Levels and temporal trends of trace element concentrations in vertebral bone. Arch Environ Health 35(1):21-28.

*O'Day PA, Newville M, Neuhoff PS, et al. 2000. X-ray absorption spectroscopy of strontium(II) coordination. J Colloid Interface Sci 222:184-197.

*Oghiso Y, Kubota Y, Takahashi S, et al. 1988. Effect of ^{89}Sr-induced monocytopenia on splenic and pulmonary alveolar macrophage populations in a normal steady state. J Radiat Res 29:189-202.

*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 7:917-927.

Olsen I. 1979. ^{90}Sr in maternal, fetal and embryonic tissues of mice, evaluated by whole-body auto-radiography. J Dent Res 58(special issue D):2293.

9. REFERENCES

*Olsen I, Jonsen J. 1979. ^{90}Sr in placentas, embryos and foetuses of mice, evaluated by whole-body autoradiography. Acta Pharmacol Toxicol (Copenh) 44:22-27.

*Olson EJ. 1979. Inhibition of active strontium transport from erythrocyte ghosts by internal calcium: Evidence for a specificity controlling site. J Membr Biol 48:265-284.

*Olson EJ, Cazort RJ. 1969. Active calcium and strontium transport in human erythrocyte ghosts. J Gen Physiol 53(3):311-322.

*Omdahl JL, DeLuca HF. 1971. Strontium induced rickets: Metabolic basis. Science 174:949-951.

*Omdahl JL, DeLuca HF. 1972. Rachitogenic activity of dietary strontium. J Biol Chem 247(17):5520-5526.

Omdahl JL, Hunsaker LA, Aschenbrenner VA. 1977. Control of kidney 25-hydroxy vitamin D_3 metabolism: Strontium and the involvement of parathyroid hormone. Arch Biochem Biophys 184:172-178.

*Ondov JM, Choquette CE, Zoller WH, et al. 1989. Atmospheric behavior of trace elements on particles emitted from a coal-fired power plant. Atmos Environ 23(10):2193-2204.

*Onyskowova Z, Josífko M. 1985. Strontium-85 in the fetuses of pregnant rats and mice. J Hyg Epidemiol Microbiol Immunol 29(1):1-7.

*Ootsuyama A, Tanooka H. 1986. Unscheduled DNA synthesis after β-irradiation of mouse skin in situ. Mutat Res 166:183-185.

*Ootsuyama A, Tanooka H. 1988. One hundred percent tumor induction in mouse skin after repeated β irradiation in a limited dose range. Radiat Res 115:488-494.

*Ootsuyama A, Tanooka H. 1989. Induction of osteosarcomas in mouse lumbar vertebrae by repeated external β-irradiation. Cancer Res 49:1562-1564.

Orlowski S, Champeil P. 1993. Strontium binding to sarcoplasmic reticulum Ca^{2+}-ATPase: Spectroscopic differentiation of the substeps involved. FEBS Lett 328(3):296-300.

*Ortega A, Gómez M, Domingo JL, et al. 1989. The removal of strontium from the mouse by chelating agents. Arch Environ Contam Toxicol 18:612-616.

Osanov DP, Panova VP, Arefieva SS. 1971. Evalutation of age influence on accumulation and elimination rate of radioactive strontium. Health Phys 21:205-210.

*OSHA. 1996a. Toxic and hazardous substances. Ionizing radiation. U.S. Department of Labor. Occupational Safety and Health Administration. Code of Federal Regulations. 29 CFR 1910.1096.

*OSHA. 1996b. Safety and health regulations for construction. Ionizing radiation. U.S. Department of Labor. Occupational Safety and Health Administration. Code of Federal Regulations. 29 CFR 1926.53.

*OSHA. 1999a. Air contaminants. Occupational Safety and Health Administration. Code of Federal Regulations. 29 CFR 1910.1000.

9. REFERENCES

*OSHA. 1999b. Air contaminants. Occupational Safety and Health Administration. Code of Federal Regulations. 29 CFR 1915.1000.

*OSHA. 1999c. Gases, vapors, fumes, dusts, and mists. Occupational Safety and Health Administration. Code of Federal Regulations. 29 CFR 1926.55.

*OSHA. 2000. Ionizing radiation. Occupational Safety and Health Administration. Code of Federal Regulations. 29CFR1910.1096. http://frwebgate.access.gpo.gov/

*OSHA. 2001. Safety and health regulations for construction. Ionizing radiation. Occupational Safety and Health Administration. U.S. Department of Labor. Code of Federal Regulations. 29 CFR 1926.53. http://www.osha-slc.gov/OshStd_data/1926_0053.html. Mary 08, 2001.

Ostadalova I, Ostadal B. 1992. Effect of isoproterenol on ^{85}Sr accumulation in the myocardium of the rat during postnatal ontogeny. Physiol Res 41:471-473.

*OSW. 1992. Strontium (atomic absorption, direct aspiration). Method 7780. In: Test methods for evaluating solid waste, physical/chemical methods, SW-846. 3rd ed. Washington, DC: Office of Solid Waste, U.S. Environmental Protection Agency. Vol. IA, Chap. 3, Sec. 3.3.

*Outridge PM, Hughes RJ, Evans RD. 1996. Determination of trace metals in teeth and bones by solution nebulization ICP-MS. Atom Spectrosc 17(1):1-8.

Overton TR, Snyder RE, Hangartner TN, et al. 1992. Changes in the linear attenuation coefficient of canine appendicular bone following intravenous infusion of strontium lactate, measured using gamma-ray computed tomography. Calcif Tissue Int 50:350-356.

*Owen GM, Brozek J. 1966. Influence of age, sex and nutrition on body composition during childhood and adolescence. In: Falkner F, ed. Human development. Philadelphia, PA: WB Saunders, 222-238.

Oyvin IA, Uklonskaya LI, Gaponiuk PJ. 1967. The participation of kinins in the pathogenesis of early disturbances in the skin capillary permeability in local β-ray irradiation. Experientia 23(7):555-556.

*Özgür S, Sümner H, Kocoglu G. 1996. Rickets and soil strontium. Arch Dis Child 75:524-526.

Palatay JL, Ragan HA, Clarke WJ, et al. 1966. Effects of strontium-90 in miniature swine - sixth progress report. In: Thompson RC, Swezea EG, eds. Pacific Northwest Laboratory annual report for 1965 in the biological sciences. Richland, WA: Pacific Northwest Laboratory, 24-28.

Palmer HE, Karagianes MT. 1976. Use of ^{85}Sr as an indicator of bone mineral replacement in dogs after disuse demineralization. Aviat Space Environ Med 47(1):17-19.

*Palmer RF, Thompson RC. 1961. Discrimination in intestinal absorption of strontium and calcium. Proc Soc Exp Biol Med 108:296-300.

Palmer RF, Thompson RC. 1964. Strontium-calcium interrelationships in the growing rat. Am J Physiol 207(3):561-566.

Palmer RF, Thomas JM, Watson CR, et al. 1970. Some aspects of dosimetry in miniature swine chronically ingesting ^{90}Sr. Health Phys 19:775-783.

9. REFERENCES

*Palmer RF, Thompson RC, Kornberg HA. 1958. Effect of calcium on deposition of strontium-90 and calcium-45 in rats. Science 127:1505-1506.

*Palmer RF, Watson CR, Beamer JL. 1969. Radiation dose to fetuses of miniature swine ingesting ^{90}Sr. AEC Symp Ser 17:89-96.

Panteleev LI, Rasin IM, Sarapultsev IA. 1972. Animal-man extrapolation of strontium-90 accumulative regularities. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 239-246.

Pany JE. 1966. Die wirking von calciumsalzen auf die resorption con Ca und Sr dunndarm. Naturwissenschaften 53(18):480.

Papatheofanis FJ. 2000. Decreased serum E-selectin concentration after ^{89}Sr-chloride therapy for metastatic prostate cancer bone pain. J Nucl Med 41:1021-1024.

Papavasiliou C, Kostamis P, Angelakis P, et al. 1971. Localization of ^{87m}Sr in extra-osseous tumors. J Nucl Med 12(5):265-268.

*Papworth DG, Patrick G. 1970. The kinetics of influx of calcium and strontium into rat intestine in vitro. J Physiol 210:999-1020.

*Papworth DG, Vennart J. 1984. The uptake and turnover of ^{90}Sr in the human skeleton. Phys Med Biol 29(9):1045-1061.

*Parkman RH, Charnock JM, Livens FR, et al. 1998. A study of the interaction of strontium ions in aqueous solution with the surfaces of calcite and kaolinite. Geochim Cosmochim Acta 62(9):1481-1492.

Parks NJ. 1985. Dynamics of lifespan strontium-90 distribution in beagles with uniformly labelled skeletons acquired by radionuclide ingestion from *in utero* to adulthood. EUR 9250:107-115.

Parks NJ. 1991. Radionuclide distribution dynamics in skeletons of beagles fed ^{90}Sr: Correlation with injected ^{226}Ra and ^{239}Pu. Health Phys 60(3):343-351.

Patrick G. 1967. Inhibition of strontium and calcium uptake by rat duodenal slices: Comparison of polyuronides and related substances. Nature 216:815-816.

Patrick G, Carr TEF, Humphreys ER. 1967. Inhibition by alginates of strontium absorption studied *in vivo* and *in vitro*. Int J Radiat Biol 12(5):427-434.

Patten BC, Iverson RL. 1966. Radiobiology: Photosynthesis and uptake of strontium-85 in freshwater plankton. Nature 211(5044):96-97.

Paul TM, Skoryna SC, Waldron-Edward D. 1966. Studies on the inhibition of intestinal absorption of radioactive strontium: V. The effect of administration of calcium alginate. Can Med Assoc J 95:957-960.

Payton PH, Hild SB, Oertti CU, et al. 1977. Strontium-90 in the western Gulf of Mexico. Health Phys 33(2):143-145.

*Peel DM, Hopewell JW, Wells J, et al. 1984. Nonstochastic effects of different energy beta emitters on pig skin. Radiat Res 99:372-382.

Pérez-Jordán MY, Salvador A, de la Guardia M. 1998. Determination of Sr, K, Mg and Na in human teeth by atomic spectrometry using a microwave-assisted digestion in a closed flow system. Anal Lett 31(5):867-877.

*Perry KD. 1999. Effects of outdoor pyrotechnic displays on the regional air quality of western Washington State. J Air Waste Manage Assoc 49:146-155.

Peters CJ, Walser M. 1966. Transport of cations by rabbit gall bladder: Evidence suggesting a common cation pump. Am J Physiol 210:677-683.

*Petkau A, Pleskach SD. 1972. A case of accidental aspiration of $^{90}SrCl_2$. Health Phys 22:87-90.
Pezzi L. 1984. Effect of ruthenium red on the Ca^{2+} and Sr^{2+} efflux from rat liver mitochondria: Influence of nupercaine. Biosci Rep 4:231-237.

Pfeiffer DR, Kauffman RF, Lardy HA. 1978. Effects of N-ethylmaleimide on the limited uptake of Ca^{2+}, Mn^{2+}, and Sr^{2+} by rat liver mitochrondria. J Biol Chem 253(12):4165-4171.

*Pfleger H, Wolf HU. 1975. Activation of membrane-bound high-affinity calcium ion-sensitive adenosine triphosphatase of human erythrocytes by bivalent metal ions. Biochem J 147:359-361.

*Phalen RF, Oldham HJ, Beaucage CB, et al. 1985. Postnatal enlargement of human tracheobronchial airways and implications for particle deposition. Anat Rec 212:368-380.

Pietrzak-Flis Z, Grabowski D. 1972. Long-term study of the urinary strontium-90 and calcium in children. Health Phys 23:215-221.

*Piette M, Desmet B, Dams R. 1994. Determination of strontium in human whole blood by ICP-AES. Sci Total Environ 141:269-273.

*Piffanelli A, Dafermou A, Giganti M, et al. 2001. Radionuclide therapy for painful bone metastases. An Italian multicentre observational study. 45(1):100-107.

Pinchouk VG, Serkiz YI, Goldshmid BJ, et al. 1990. Peculiarities of spontaneous carcinogenesis in rats under the continuous influence of low intensity ionizing radiation. Anticancer Res 10(5 pt B):1386.

*Pivnick EK, Kerr NC, Kaufman RA, et al. 1995. Rickets secondary to phosphate depletion. Clin Pediatr 34:73-74.

Plishker GA. 1984. Effects of cadmium and zinc on calcium uptake in human red blood cells. Am J Physiol 247(16):C143-C149.

*Poggi M, Aterini S, Nicastro L, et al. 1999. Lack of association between body weight, bone mineral density and vitamin D receptor gene polymorphism in normal and osteoporotic women. Disease Markers 15(4):221-227.

Polachek I, Krejci I, Rudinger J. 1967. The action of oxytocin and synthetic analogues on the isolated mammary-gland myoepithelium of the lactating rat; effect of some ions. J Endocrinol 38:13-24.

9. REFERENCES

Poll B, Beddoe AH, Aspden PJ, et al. 1972. Thermoluminescence dosimetry of beta emitters in bone. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 67-78.

*Pool RR, Williams RJR, Goldman M. 1972. Strontium-90 toxicity in adult beagles after continuous ingestion. AEC Symp Ser 25:277-284.

Pool RR, Williams JR, Goldman M, et al. 1973a. Comparison of bone-tumor sites in beagles continually fed ^{90}Sr or injected with ^{226}Ra as a means of scaling risk to humans. AEC Symp Ser 29:475-486.

*Pool RR, Williams R, Goldman M. 1973b. Induction of tumors involving bone in beagles fed toxic levels of strontium 90. Am J Roentgenol Radium Ther Nucl Med 18(4):900-908.

Porter VL, Marcus CS, Stahl SS. 1975. Use of solid state miniature detectors for study of alkaline earth metabolism in rat oral bone. Int J Nucl Med Biol 2:5-12.

*Porzig H. 1973. Calcium-calcium and calcium-strontium exchange across the membrane of human red cell ghosts. J Membr Biol 11:21-46.

Pott F. 1994. Asbestos use and carcinogenicity in Germany and a comparison with animal studies. Ann Occup Hyg 38(4):589-600.

*Prange A, Böddeker H, Michaelis W. 1989. Multi-element determination of trace elements in whole blood and blood serum by TXRF. Fresenius Z Anal Chem 335:914-918.

Puhakainen M, Riekkinen I, Heikkinen T, et al. 2001. Effect of chemical pollution on forms of ^{137}Cs, ^{90}Sr and ^{239,240}Pu in Arctic soul studied by sequential extraction. J Environ Radioact 52:17-29.

*Pujol Li, Sanchez-Cabeza JA. 2000. Natural and artifical radioactivity in surface waters of the Ebro River basin (Northeast Spain). J Environ Radioact 51:181-210.

Qian G, Wu MB, Wu G, et al. 1998. Strontium ion-selective electrodes based on the diamides with pyridine ring as ionophores. Talanta 47:1149-1155.

*Que Hee SS, Finelli VN, Fricke FL, et al. 1982. Metal content of stack emissions, coal and fly ash from some eastern and western power plants in the U.S.A. as obtained by ICP-AES. Int J Environ Anal Chem 13:1-18.

Que Hee SS, Igwe OJ, Boyle JR. 1988. Elemental alterations during the exposure of 1,2-dichloroethane (EDC), disulfiram (DSF), and EDC-DSF to male sprague-dawley rats. Biol Trace Elem Res 18:9-28.

Raabe OG, Parks NJ. 1993. Skeletal uptake and lifetime retention of ^{90}Sr and ^{226}Ra in beagle dogs. Radiat Res 133:204-218.

*Raabe OG, Book SA, Parks NJ, et al. 1981a. Lifetime studies of ^{226}Ra and ^{90}Sr toxicity in beagles -- A statis report. Radiat Res 86:515-528.

*Raabe OG, Book SA, Parks NJ. 1983. Lifetime bone cancer dose-response relationships in beagles and people from skeletal burdens of ^{226}Ra and ^{90}Sr. Health Phys 44(Suppl. 1):33-48.

9. REFERENCES

*Raabe OG, Culbertson MR, White RG, et al. 1994. Comparative toxicity of strontium-90 and radium-226 in beagle dogs. U.S. Department of Energy. Davis, CA: University of California. DOE DE-FG03-89ER60914/92. NTIS/DE94006408.

*Raabe OG, Parks NJ, Book SA. 1981b. Dose-response relationships for bone tumors in beagles exposed to ^{226}Ra and ^{90}Sr. Health Phys 40:863-880.

*Ragan HA, Hackett PL, McClanahan BJ, et al. 1973. Pathologic effects of chronic ^{90}Sr ingestion in miniature swine. In: Harrison LT, ed. Research animals in medicine, [National conference on research animals in medicine], Washington, D.C. Jan. 28-30, 1972. Washington, DC: U.S.Department of Health, Education, and Welfare, 919-929.

Ragna HA, Buschbom RL, Clarke WL, et al. 1972. Late effects of chronic ^{90}Sr ingestion in miniature swine. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 145-154.

*Randall K, Coggle JE. 1995. Expression of transforming growth factor-β1 in mouse skin during the acute phase of radiation damage. Int J Radiat Biol 68(3):301-309.

*Randall K, Coggle JE. 1996. Long-term expression of transforming growth factor TGFβ1 in mouse skin after localized β-irradiation. Int J Radiat Biol 70(3):351-360.

*Rasgado-Flores H, Sanchez-Armass S, Blaustein MP, et al. 1987. Strontium, barium, and manganese metabolism in isolated presynaptic nerve terminals. Am J Physiol 252(21):C604-C610.

Rashed MN, Awadallah RM. 1998. Trace elements in faba bean (*Vicia faba* L) plant and soil as determined by atomic absorption spectroscopy and ion selective electrode. J Sci Food Agric 77:18-24.

Ravaglia G, Forti P, Maioli F, et al. 1994. Calcium regulating hormones in healthy elderly men: Relation to intestinal calcium absorption. Boll Soc Ital Biol Sper 70(12):323-328.

*Raven KP, Loeppert RH. 1997. Heavy metals in the environment: Trace element composition of fertilizers and soil amendments. J Environ Qual. 26:551-557.

*Ray RD, Stedman DE, Wolff NK. 1956. Bone Metabolism: III. The effect of various diets on the mobilization of strontium from the rat skeleton. J Bone Jt Surg Am 38A:637-654.

*Reddi OS. 1971. Long term genetic effects of strontium-90 in mice. Indian J Med Res 59(11):1754-1757.

Reeve J, Arlot ME, Chavassieux PM, et al. 1987. The assessment of bone formation and bone resorption in osteoporosis: A comparison between tetracycline-based iliac histomorphometry and whole body ^{85}Sr kinetics. J Bone Miner Res 2(6):479-489.

Reeve J, Wootton R, Edouard C, et al. 1988. Skeletal blood flow, iliac histomorphometry, and strontium kinetics in osteoporosis: A relationship between blood flow and corrected apposition rate. J Clin Endocrinol Metab 66(5):1124-1131.

9. REFERENCES

*Reginster JY, Deroisy R, Dougados M, et al. 2002. Prevention of early postmenopausal bone loss by strontium ranelate: the randomized, two-year, double-masked, dose-ranging, placebo-controlled PREVOS trial. Osteoporosis Int 13:925-931.

*Reginster JY. 2002. Strontium ranelate in osteoporosis. Curr Pharmaceut Design 8(21):1917-1928. [Abstract]

*Reginster JY. 2003. Strontium ranelate—a new paradigm in the treatment of osteoporosis. Bus Briefing: Eur Pharmacother 2003. http://www.bbriefing.com/pdf/26/ept032_r_25_reginster.pdf.

*Reid IR, Pybus J, Lim TMT, et al. 1986. The assessment of intestinal calcium absorption using stable strontium. Calcif Tissue Int 38:303-305.

*Reif AE, Triest WE. 1982. Effects of strontium-90 plus external irradiation in C57Bl/6J mice. Health Phys 43(6):891-904.

*Reinholt FP, Engfeldt B, Heinegard D, et al. 1985. Proteoglycans and glycosaminoglycans of normal and strontium rachitic epiphyseal cartilage. Coll Relat Res 5:41-53.

*Reinholt FP, Hjerpe A, Jansson K, et al. 1984. Stereological studies on the epiphyseal growth plate in strontium-induced rickets. J Bone Jt Surg Am 66-A(8):1274-1280.

Remagen W, Heitz P, Weidmann D, et al. 1975. Comparative kinetics of 45 Ca and 89 Sr in chronic uremic syndrome in the rat. Res Exp Med 165:271-284.

*Richard S, Potreau D, Charnet P, et al. 1989. Are Ba2+ and Sr2+ ions transported by the Na+-Ca2+ exchanger in frog atrial cells? J Mol Cell Cardiol 21:865-875.

Risica S, Grisanti G, Tancredi F, et al. 1994. A study on some stable elements and radionuclides in human milk. Models Chem 131(5):651-660.

Robillard J, Loyau G, Couette JE, et al. 1972. A study of retention of strontium-85 by a method of integration of profile scan: Variations in miscellaneous bony diseases. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 357-368.

Romanov SA, Vasilenko EK, Khokhyankov VF, et al. 2002. Studies on the Mayak nuclear workers: Dosimetry. Radiat Environ Biophys 41(1):23-28.

Romanyukha AA, Mitch MG, Lin Z, et al. 2002. Mapping the distribution of ^{90}Sr in teeth with a photosimulable phosphor imaging detector. Radiat Res 157:341-349.

Romanyukha AA, Seltzer SM, Desrosiers M, et al. 2001. Correction factors in the EPR dose reconstruction for residents of the middle and lower techa riverside. Health Phys 81(5):554-566.

*Rönnbäck C. 1979. Effect of ^{90}Sr on ovaries of foetal mice depending on time for administration during pregnancy. Acta Radiol Oncol 18:225-234.

*Rönnbäck C. 1980. Effect of different ^{90}Sr doses on the microscopic structure of foetal mouse ovaries. Acta Radiol Oncol 19(2):145-152.

9. REFERENCES

*Rönnbäck C. 1981a. Disturbances of fertility in female mice ^{90}Sr-contaminated as foetuses. Acta Radiol Oncol 20(5):337-343.

*Rönnbäck C. 1981b. Influence of ^{90}Sr-contaminated milk on the ovaries of foetal and young mice. Acta Radiol Oncol 20(2):131-135.

*Rönnbäck C. 1986. Strontium retention in mouse foetuses at different intervals after contamination of the dam. Acta Radiol Oncol 25(2):155-159.

Rönnbäck C, Nilsson A. 1975. Influence of estrogen on the excretion of strontium-90 and -85 in mice. Acta Radiol Ther Phys Biol 14(5):85-96.

*Rönnbäck C, Nilsson A. 1982. Neoplasms in ovaries of CBA mice ^{90}Sr-treated as foetuses. Acta Radiol Oncol 21(2):121-128.

*Rönnbäck C, Nelson A, Nilsson A. 1968. Influence of laktation on retention of radiostrontium in mice. Acta Radiol Ther Phys Biol 7(5):330-336.

Roomans GM, Theuvenet APR, Van Den Berg PR. 1979. Kinetics of Ca^{2+} and Sr^{2+} uptake by yeast effects of pH, cations and phosphate. Biochim Biophys Acta 551:187-196.

Root AW, Bongiovanni AM, Eberlein WR, et al. 1966. Measurement of the kinetics of calcium metabolism in children and adolescents utilizing nonradioactive strontium. J Clin Endocrinol 26:537-544.

Rosenthal HL, Cochran OA. 1972. Binding of ^{85}Sr to homogenate and subcellular fractions of rabbit tissues. Proc Soc Exp Biol Med 141(3):850-856.

Rosenthal HL, Harbor NC. 1965. The absorption, retention, and distribution of strontium 90 from naturally contaminated food by female rabbits. J Dent Res 44(5):935-939.

Rosenthal HL, Austin SA, Gilster JE, et al. 1967. Accumulation of strontium-90 into human fetal teeth and bone. Proc Soc Exp Biol Med 125(2):493-495.

Rosenthal HL, Cochran OA, Eves MM. 1972. Strontium content of mammalian bone, diet and excreta. Environ Res 5:182-191.

Rosner G, Hötzl H, Winkler R. 1990. Simultaneous radiochemical determination of plutonium, strontium, uranium, and iron nuclides and application to atmospheric deposition and aerosol samples. Fresenius J Anal Chem 338:606-609.

*Rossipal E, Krachler M, Li F, et al. 2000. Investigation of transport of trace elements across barriers in humans: studies of placental and mammary transfer. Acta Paediatr Suppl 89:1190-1195.

Roth P, Giussani A, Werner E. 1998. Kinetics of gastrointestinal absorption. Radiat Prot Dosim 79(1-4):279-282.

*Roushdy HM, Moloukhia MK, Abdel-Fattah AT. 1980. Inhibition of radiostrontium deposition in calcium-deficient mammalian bones using certain chemical treatment. Isot Radiat Res 12(2):93-101.

9. REFERENCES

*Roushdy HM, Moloukhia MK, Abdel-Fattah AT. 1981. Effect of dietary calcium level on the rate of deposition of radiostrontium in rat bones. Isot Radiat Res 13(1):19-26.

*Roy M, Becquemin H-H, Bertholon J-F, et al. 1994. Respiratory physiology. In: Human respiratory tract model for radiological protection. ICRP Publication 66. International Commission on Radiological Protection. Oxford: Pergamon Press, 167-201.

Rozing J, Buuraman WA, Benner R. 1976. B lymphocyte differentiation in lethally irradiated and reconstituted mice. Cell Immunol 24:79-89.

Rumpel E, Behrends JC. 1999. Sr^{2+}-dependent asynchronous evoked transmission at rat striatal inhibitory synapses *in vitro*. J Physiol 514(2):447-458.

*Rundo J, Lillegraven AL. 1966. Uptake and retention of radioactive strontium in normal subjects. Br J Radiol 39:676-685.

*Rundo J, Williams K. 1961. A case of accidental inhalation of $^{90}SrCO_3$. Br J Radiol 34(407):734-740.

*Rushton MA. 1963. Oral effects of injected strontium 90. J Dent Res 42(1):340-342.

Rutherford PM, Dudas MJ, Arocena JM. 1996. Heterogeneous distribution of radionuclides, barium and strontium in phosphogypsum by-product. Sci Total Environ 180:201-209.

*Sahai N, Carroll SA, Roberts S, et al. 2000. X-ray absorption spectroscopy of strontium(II) coordination: II. Sorption and precipitation at kaolinite, amorphous silica, and goethite surfaces. J Colloid Interface Sci 222:198-212.

*Sairanen S, Karkkainen M, Tahtela R, et al. 2000. Bone mass and markers of bone and calcium metabolism in postmenopausal women treated with 1,25-dihydroxyviuamin D (calcitrol) for four years. Calcif Tissue Int 67:122-127.

*Sala E, Olsen JH. 1993. Thyroid cancer in the age group 0-19: Time trends and temporal changes in radioactive fallout. Eur J Cancer 29A(10):1443-1445.

*Samachson J. 1966. The gastrointestinal clearance of strontium-85 and calcium-45 in man. Radiat Res 27:64-74.

Samachson J, Schmitz A. 1969. The effects of Zn^{2+} on the uptake of Ca^{2+}, Sr^{2+} and Ba^{2+} by bone powder and inorganic bone. Biochim Biophys Acta 192:238-242.

Samachson J, Dennis J, Fowler R. 1968. Uptake of calcium, strontium, and barium by the surfaces of bone powder and bone mineral. J Dent Res 47(1):121-126.

Sanchez AL, Singleton DL. 1996. A radioanalytical scheme for determining transuranic nuclides and ^{90}Sr in environmental samples. J Radioanal Nucl Chem 209(1):41-50.

Santoliquido PM, Southwick HW, Olwin JH. 1976. Trace metal levels in cancer of the breast. Surg Gynecol Obstet 142:65-70.

Sariego Muniz C, Marchante-Gayón JM, García Alonso JI, et al. 1999. Multi-elemental trace analysis of human serum by double-focusing ICP-MS. J Anal Atom Spectrom 14:193-198.

*Sato N, Kato T, Suzuki N. 1977. Multi-elemental determination in tobacco leaver by photon activation analysis. J Radioanal Chem 36:221-238.

*Sawyer RT, Strausbauh PH, Volkman A. 1982. Resident macrophage proliferation in mice depleted of blood monocytes by strontium-89. Lab Invest 46(2):165-170.

*Scarpitta S, Odin-McCabe J, Gaschott R, et al. 1999. Comparison of four ^{90}Sr groundwater analytical methods. Health Phys 76(6):644-656.

Scasnar V. 1984. Determination of strontium-90 in urine by extraction without ashing. Anal Chem 56:605-608.

Schardein JL. 1993. Metals. In: Chemically induced birth defects. New York: Marcel Dekker, Inc., 722-750.

Schell WR, Sugai S. 1980. Radionuclides at the U.S. radioactive waste disposal site near the Farallon Islands. Health Phys 39:475-496.

*Schmahl W, Kollmer WE. 1981. Radiation-induced meningeal and pituitary tumors in the rat after prenatal application of strontium-90. J Cancer Res Clin Oncol 100:13-18.

*Schmahl W, Kollmer WE, Berg D, et al. 1979. Postnatal effects on Wistar rat pituitary morphology and function after application of strontium-90 on day 18 of pregnancy. Biological Implications of Radionuclides Released from Nuclear Industries. Proceeding of an International Symposium on Biological Implications 1:329-337.

*Schoenberg HP. 1963. Extent of strontium substitution for calcium in hydroxyapatite. Biochim Biophys Acta 75:96-103.

Schoeters GER, de Saint-Georges L, Van Den Heuvel R, et al. 1988. Mineralization of adult mouse bone marrow *in vitro*. Cell Tissue Kinet 21:363-374.

Schroeder HA. 1971. Metals in the air. Environment 13(8):18-32.

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

*Schrooten I, Cabrera W, Goodman WG, et al. 1998. Strontium causes osteomalacia in chronic renal failure rats. Kidney Int 54:448-456.

*Schrooten I, Elseviers MM, Lamberts LV, et al. 1999. Increased serum strontium levels in dialysis patients: An epidemiological survey. Kidney Int 56:1886-1892.

Schubert J, Brodsky A, Tyler S. 1967. The log-normal function as a stochastic model of the distribution of strontium-90 and other fission products in humans. Health Phys 13:1187-1204.

*Sciuto R, Festa A, Pasqualoni R, et al. 2001. Metastic bone pain palliation with 89-Sr and 186-Re-HEDP in breast cancer patients. Breast Cancer Res Treat 66:101-109.

9. REFERENCES

*Scott BR. 1980. A model for early death caused by radiation pneumonitis and pulmonary fibrosis after inhaling insoluble radioactive particles. Bull Math Biol 42:447-459.

Scott BR. 1982. Method of analysis of monotone dose-response probabilities after long-term exposure to a toxicant. Health Phys 42(3):305-315.

Scuderi P, Rosse C. 1981a. The dependence of tumor neutralization on bone-marrow-derived cells. Int J Cancer 28:85-90.

*Scuderi P, Rosse C. 1981b. The role of bone marrow cells in the growth inhibition of trasplanted methylcholanthrene-induced sarcoma (MCA). XIII(1):747-751.

Seaman WE, Blackman MA, Greenspan JS, et al. 1980. Effect of ^{89}Sr on immunity and autoimmunity in NZB/NZW F_1 mice. J Immunol 124(2):812-818.

Season EH, Eyring EJ, Samuels LD. 1972. Uptake of ^{87m}Sr in the knee region of children as a parameter of bone turnover. Clin Orthop Relat Res 87:281-286.

Seifert MF, Marks SC. 1985. The regulation of hemopoiesis in the spleen. Experientia 41:192-199.

Seltzer SM, Romanyukha AA, Nagy V. 2001. Monte Carlo calculation of the dose distribution in teeth due to internal exposure from 90Sr application to EPR tooth dosimetry. Radiat Prot Dosim 93(3):245-260.

Semb H. 1966. Plasma clearance of Sr^{85} by bone: An attempt to study the rate of blood flow through normal and immobilized bone in dogs. Acta Soc Med Ups 71(5):227-236.

Semb H. 1968. Effect of immobilization on bone blood flow estimated by initial uptake of radioactive strontium. Surg Gynecol Obstet 127(2):275-281.

Sherman EJ, Pfister DG, Ruchlin HS, et al. 2001. The collection of indirect and nonmedical direct costs (COIN) form. Cancer 91(4):841-853.

*Setchell BP, Waites GMH. 1975. The blood-testis barrier. In: Creep RO, Astwood EB, Geiger SR, eds. Handbook of physiology: Endocrinology V. Washington, DC: American Physiological Society.

*Shagina NB, Kozheurov VP, Degteva MO, et al. 2000. Study of ^{90}Sr body-burden variability for the population of the Urals region. Prague, Czech Republic: Fifth International Symposium and Exhibition of Environmental Contamination in Central and Eastern Europe, 12-14 September.

*Shaw RF, Smith AP. 1970. Strontium-90 and infant mortality in Canada. Nature 228:667-669.

Shibata S, Yamashita Y. 2001. An ultrastuctural study of osteoclasts and chondroclasts in poorly calcified mandible induced by high doses of strontium diet to fetal mice. Ann Anatomie Pathol 183(4):357-361.

Shibata Y, Bautista AP, Pennington SN, et al. 1987. Eicosanoid production by peritoneal and splenic macrophages in mice depleted of bone marrow by ^{89}Sr. Am J Physiol 127:75-82.

*Shibata Y, Dempsey WL, Morahan PS, et al. 1985. Selectively eliminated blood monocytes and splenic suppressor macrophages in mice depleted of bone marrow by strontium-89. J Leukoc Biol 38:659-669.

Shimmins J, Smith DA. 1966. Estimation of bone mineral transfer rate by the measurement of long-term retention of SR^{85}. Metabolism 15(5):436-443.

Shimmins J, Smith DA. 1972. Discrimination between calcium and strontium in bone uptake and loss. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 389-396.

Shine KI, Douglas AM, Ricchiuti NV. 1978. Calcium, strontium, and barium movements during ischemia and reperfusion in rabbit ventricle. Circ Res 43(5):712-720.

Shishkina EA, Lyubashevskii NM, Tolstykh EI, et al. 2001. A mathematical model for calculation of ^{90}Sr absorbed dose in dental tissues: elaboration and comparison to EPR measurement. Appl Radiat Isot 55(3):363-374.

*Shorr E, Carter AC. 1952. The usefulness of strontium as an adjuvant to calcium in the remineralization of the skeleton in man. Bull Hosp Joint Dis 13(1):59-66.

Shutov VN, Bruk GY, Balonov MI, et al. 1993. Cesium and strontium radionuclide migration in the agricultural ecosystem and estimation of internal doses to the population. In: Merwin SE, Balonov MI, eds. The Chernobyl papers: Doses to the Soviet population and early health effects studies. Richland, WA: Research Enterprises, Inc, Vol. I, 167-219.

Shvedov VL, Panteleev LI, Goloschapov PV. 1972. An evaluation of the danger of impairment to the human body from a constant intake of ^{90}Sr. In: International Conference on Strontium Metabolism, ed. Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 173-180.

*Sigma-Aldrich. 2000. Strontium fluoride - material safety data sheet. Product number 01155. http://www.sigma-aldrich.com/sacatalog.nsf/productlookup/Riedel-de+Haen01155?OpenDocument.

Sikov MR. 1989. Tumour development following internal exposures to radionuclides during the perinatal period. In: Napalkov NP, Rice JM, Tomatis L, et al., eds. Perinatal and multigeneration carcinogenisis. Lyon, France. International Agency for Research on Cancer, 403-419.

Sikov MR, Meznarich HK, Thrall KD, et al. 1993. Use of data from experimental animals for dosimetry of radionuclides in the human embryo/fetus. Teratology 47(5):436.

*Sikov MR, Meznarich HK, Traub RJ. 1991. Comparison of placental transfer and localization of caesium strontium and iodine in experimental animals and women. Int J Radiat Biol 60(3):553-555.

*Silberstein T, Hallak M, Gonen R, et al. 2001. Toxic trace elements (TE) can be found in the maternal and fetal compartments. Am J Obstet Gynecol 184(1):S177.

Silva AJ, Fleshman DG, Shore B. 1970. The effects of sodium alginate on the absorption and retention of several divalent cations. Health Phys 19:245-251.

Simmonds JR, Failla P. 1966. Strontium retention in mice treated with thyroid hormone. Health Phys 12:1249-1257.

Simmonds JR, Linsley GS. 1982. Parameters for modelling the interception and retention of deposits from atmosphere by grain and leafy vegetables. Health Phys 43(5):679-691.

Simpson LL. 1973. The interaction between divalent cations and botulinum toxin type A in the paralysis of the rat phrenic nerve-hemidiaphragm preparation. Neuropharmacology 12(2):165-176.

Sims NA, White CP, Sunn KL, et al. 1997. Human and murine osteocalcin gene expression: Conserved tissue restricted expression and divergent responses to 1,25-dihydroxyvitamin D_3 in vivo. Mol Endocrinol 11:1695-1797.

*Sips AJAM, Barto R, Netelenbos JC, et al. 1997. Preclinical screening of the applicability of strontium as a marker for intestinal calcium absorption. Am J Physiol 272(PE):422-428.

*Sips AJAM, Netelenbos JC, Barto R, et al. 1994. One-hour test for estimating intestinal absorption of calcium by using stable strontium as a marker. Clin Chem 40(2):257-259.

*Sips AJAM, van der Vijgh WJF, Barto R, et al. 1996. Intestinal absorption of strontium chloride in healthy volunteers: Pharmacokinetics and reproducibility. Br J Clin Pharmacol 41:543-549.

*Sips AJAM, van der Vijgh WJF, Netelenbos JC. 1995. Intestinal strontium absorption: From bioavailability to validation of a simple test representative for intestinal calcium absorption. Clin Chem 41(10):1446-1450.

*Skoryna SC. 1981a. Effects of oral supplementation with stable strontium. Can Med Assoc J 125:703-712.

*Skoryna SC. 1981b. Handbook of stable strontium. New York, NY: Plenum Press.

*Skoryna SC. 1984. Metabolic aspects of the pharmacologic use of trace elements in human subjects with specific reference to stable strontium. Trace Subst Env Health 18:3-20.

Skoryna SC, Hong KC, Tanaka Y, et al. 1972. Inhibition of radiostrontium absorption by chemically and enzymatically degraded products of alginates. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 297-308.

*Skoryna SC, Pivon RJ, Hakim TS, et al. 1986. Hemodynamic effects of stable strontium in dogs. Trace Subst Environ Health 20:17-28.

Small TD, Warren LA, Roden EE, et al. 1999. Sorption of strontium by bacteria, Fe(III) oxide, and bacteria - Fe(III) oxide compounds. Environ Sci Technol 33:4465-4470.

Smith DA, Aitken JM, Anderson J, et al. 1972. The skeletal uptake of ^{85}Sr in relation to age and bone loss in women. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 413-436.

Smith DA, Speirs CF, Shimmins J. 1967. The long-term skeletal retention and recirculation of ^{85}Sr in man. Calcif Tissue Res 1:144-152.

9. REFERENCES

*Snipes MB, Boecker BB, Hahn FF, et al. 1974a. Toxicity of inhaled ^{90}Sr fused clay particles in beagle dogs, V. In: Annual reports of the Inhalation Toxicology Research Institute. Albuquerque, NM: Inhalation Toxicology Research Institute, 126-129.

*Snipes MB, Boecker BB, Hahn FF, et al. 1976. Toxicity of inhaled ^{90}Sr fused aluminosilicate particles in beagle dogs, VII. In: Annual reports of the Inhalation Toxicology Research Institute. Albuquerque, NM: Inhalation Toxicology Research Institute, 195-199.

*Snipes MB, Hahn FF, Muggenburg BA, et al. 1977. Toxicity of inhaled ^{90}Sr fused aluminosilicate particles in beagle dogs, VIII. In: Annual reports of the Inhalation Toxicology Research Institute. Albuquerque, NM: Inhalation Toxicology Research Institute, 195-199.

*Snipes MB, Hahn FF, Muggenburg BA, et al. 1978. Toxicity of ^{90}Sr inhaled in a relatively insoluble form by beagle dogs. IX. In: McClellan RO, ed. Annual report of the inhalation toxicology research institute. Albuquerque, NM: Lovelace Biomedical and Environmental Research Institute, 108-112.

*Snipes MB, Hahn FF, Muggenburg BA, et al. 1979. Toxicity of ^{90}Sr inhaled in a relatively insoluble form by beagle dogs, X. In: Annual reports of the Inhalation Toxicology Research Institute. Albuquerque, NM: Inhalation Toxicology Research Institute, 101-106.

*Snipes MB, Runkle GE, Hulbert AJ. 1974b. Absorbed dose distribution patterns in the beagle thorax after inhalation of ^{90}Sr-^{90}Y fused clay particles, II. In: Annual reports of the Inhalation Toxicology Research Institute. Albuquerque, NM: Inhalation Toxicology Research Institute, 65-68.

*Snyder WS, Cook MJ, Ford MR. 1964. Estimates of $(MPC)_w$ for occupational exposure to Sr^{90}, Sr^{89} and Sr^{85}. Health Phys 10:171-182.

*Sokolik GA, Ivanova TG, Leinova SL, et al. 2001. Migration ability of radionuclides in soil-vegetation cover of Belarus after Chernobyl accident. Environ Int 26:183-187.

Somlyo AV, Somlyo AP. 1971. Strontium accumulation by sarcoplasmic reticulum and mitochondria in vascular smooth muscle. Science 174:955-958.

*Song CW, Drescher JJ, Tabachnick J. 1968. Effect of anti-inflammatory compounds on beta-irradiation-induced increase in vascular permeability. Radiat Res 34:616-625.

Spalding BP, Spalding IR. 2001. Chemical equilibria of strontium adsorption and transport in soil response to dynamic conditions. Environ Sci Technol 35:365-373.

Spencer CI, Berlin JR. 1997. Calcium-induced release of strontium ions from the sarcoplasmic reticulum of rat cardiac ventricular myocytes. J Phys 504(3):565-578.

Spencer H, Kramer L, Hardy EP. 1977. Effect of phosphorus on the ^{90}Sr balance in man. Health Phys 33:417-423.

*Spencer H, Kramer L, Norris C, et al. 1972a. Certain aspects of radiostrontium metabolism in man. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 335-346.

Spencer H, Kramer L, Samachson J, et al. 1973a. Strontium-90 calcium interrelationships in man. Health Phys 24:525-533.

*Spencer H, Lewin I, Belcher MJ, et al. 1969a. Inhibition of radiostrontium absorption by aluminum phosphate gel in man and its comparative effect on radiocalcium absorption. Int J Appl Radiat Isot 20:507-516.

*Spencer H, Lewin I, Samachson J, et al. 1969b. Effect of aluminum phosphate gel on radiostrontium absorption in man. Radiat Res 38:307-320.

*Spencer H, Lewin I, Samachson J. 1967a. Effect of magnesium on radiostrontium excretion in man. Int J Appl Radiat Isot 18:407-415.

Spencer H, Lewin I, Samachson J. 1967b. Inhibition of radiostrontium absorption in man. Int J Appl Radiat Isot 18:779-782.

*Spencer H, Li M, Samachson J, et al. 1960. Metabolism of strontoum^{85} and calcium^{45} in man. Metabolism 9:916.

Spencer H, Menczel J, Samachson J. 1967c. Effect of mercuhydrin alone and in conjunction with ammonium chloride on radiostrontium excretion in man. Proc Soc Exp Biol Med 124(4):1110-1116.

*Spencer H, Samachson J, Hardy EP, et al. 1967d. Effect of low and high calcium intake on Sr^{90} metabolism in adult man. Int J Appl Radiat Isot 18:605-614.

Spencer H, Samachson J, Hardy EP, et al. 1967e. Effect of stable calcium on strontium-90 absorption in man. J Nucl Med 5(5):398-399.

Spencer H, Samachson J, Hardy EP, et al. 1968. Some aspects of the effects of age and of calcium intake on strontium-90 metabolism in man. Health Phys 15:499-504.

Spencer H, Samachson J, Hardy EP, et al. 1972b. Effect of orally and intravenously administered stable strontium on ^{90}Sr metabolism in man. Radiat Res 51:190-203.

Spencer H, Warren JM, Kramer L, et al. 1973b. Passage of calcium and strontium across the intestine in man. Clin Orthop Relat Res 91:225-234.

Spiers FW. 1966. Dose to bone from strontium-90: Implications for the setting of the maximum permissible body burden. Radiat Res 28:624-642.

Spiers FW. 1974. Radionuclides and bone - from 226Ra to ^{90}Sr. Br J Radiol 47:833-844.

Spiers FW, Whitwell JR. 1972. Theoretical comparisons of dosage from ^{90}Sr and ^{226}Ra in human and beagle bone. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 1-16.

Spreng P. 1967. Effect of parathyroid hormone and vitamin A on the retention of radiostrontium in the rat. Nature 214:513-514.

*Srivastava PK, Srivastava VK, Nisra UK. 1984a. Translocation of intratracheally administered ^{89}Sr enriched fly ash into extrapulmonary organs in rats. J Environ Sci Health Part A 19(8):925-941.

9. REFERENCES

*Srivastava VK, Chauhan SS, Srivastava PK, et al. 1990. Placental transfer of metals of coal fly ash into various fetal organs of rat. Arch Toxicol 64:153-156.

*Srivastava VK, Sengupta S, Kumar R, et al. 1984b. Distribution of metals of inhaled fly ash in various organs of rats at various periods after exposure. J Environ Sci Health Part A 19(6):663-677.

*Stanic M, Gruden N. 1974. Calcium and strontium transfer through the intestinal wall in 6- and 26-week old rats. Arh Hig Rada Toksikol 25(4):423-426.

Stara JF, Nelson NS, Della Rosa RJ, et al. 1971. Comparative metabolism of radionuclides in mammals: A review. Health Phys 20:113-137.

*Stather JW. 1972. Distribution studies on ^{32}P, ^{45}Ca, ^{85}Sr and ^{133}Ba in the mouse. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 111-123.

Stather JW, Harrison JD, Kendall GM. 1992. Radiation doses to the embryo and fetus following intakes of radionuclides by the mother. Radiat Prot Dosim 41(2/4):111-118.

Steffens W, Führ F, Mittelstaedt W. 1980a. Evaluation of small scale laboratory and pot experiments to determine the realistic transfer factors for the radionuclides ^{90}Sr, ^{137}Cs, ^{60}Co and ^{54}Mn. In: Radiation protection: A systemic approach to safety: Proceedings of the 5th congress of the International Radiation Protection Society, Jerusalem, March 1980. New York, NY: Pergamon Press, Vol. 2, 1135-1138.

Steffens W, Mittelstaedt W, Führ F. 1980b. The transfer of Sr-90, Cs-137, Co-60 and Mn-54 from soils to plants results from Lysimeter experiments. In: Radiation protection: A systemic approach to safety: Proceedings of the 5th congress of the International Radiation Protection Society, Jerusalem, March 1980. New York, NY: Pergamon Press, Vol. 2, 1139-1142.

*Steinbach I. 1968. Wirksamkeit von weiblichen Geschlechtshormonen und P-armer und Ca-reicher Diät auf die ^{90}Sr-Dekorporation. Z Naturforsch B 23:820-824.

Stevenson AFG. 1975. The influence of age and sex on the activity ratio of yttrium-90 to strontium-90 in the rat skeleton after incorporation of strontium-90. Health Phys 29:285-290.

Stevenson AFG. 1977. Endocrine influences on the activity ration of ^{90}Y to ^{90}Sr in the rat skeleton after incorporation of ^{90}Sr. Acta Radiol Ther Phys Biol 16(2):137-144.

Stevenson AFG, Daculsi R, Mönig H. 1982. Haematological studies on ^{90}Sr-^{90}Y-toxicity: II. Femoral CFU-s kinetics and mitogen response of spleen cells. Radiat Environ Biophys 20:275-287.

Stössel R-P, Prange A. 1985. Determination of trace elements in rainwater by total-reflection x-ray fluorescence. Anal Chem 57:2880-2885.

*Storey E. 1961. Strontium "rickets": Bone, calcium and strontium changes. Austral Ann Med 10:213-222.

*Storey E. 1962. Intermittent bone changes and multiple cartilage defects in chronic strontium rickets in rats. J Bone Jt Surg Am 44B(1):194-208.

Storey E. 1968. Calcium and strontium changes in bone associated with continuous administration of stable strontium to rats. Arch Biochem Biophys 103:575-581.

*Storm DL. 1994. Chemical monitoring of California's public drinking water sources: Public exposures and health impacts. In: Wang RGM, ed. Water contamination and health: Integration of exposure assessment, toxicology, and risk assessment. New York, NY: Marcel Dekker, Inc., 67-124.

Strain WH, Pories WJ, Flynn A. 1972. Accumulation of radiostrontium in hair. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 247-254.

Strong AB, Porter CR, Kahn B. 1972. Stable strontium: Calcium ratios in U.S. bone and total diet samples. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory / U.S. Atomic Energy Commission, 513-520.

Stulc J, Stulcova B, Svihovec J. 1990. Transport of calcium across the dually perfused placenta of the rat. J Physiol 420:295-311.

Sugihira N, Kusama T. 1992. Biokinetics of radionuclides in pregnant mice and compartment models by the system analysis methods. Radiat Prot Dosim 41(2/4):153-156.

Sugihira N, Suzuki KT. 1991. Discrimination between strontium and calcium in suckling rats. Biol Trace Elem Res 29:1-10.

*Sugihira N, Aoki Y, Suzuki KT. 1992. ATP-dependent strontium uptake by basolateral membrane vesicles from rat renal cortes in the absence of presence of calcium. Biol Trace Elem Res 34:45-54.

Sugihira N, Kobayashi E, Suzuki KT. 1990. Age-related change in strontium to calcium ratios in rat tissues. Biol Trace Elem Res 25:79-88.

Sumerling TJ, Dodd NJ, Green N. 1984. The transfer of strontium-90 and caesium-137 to milk in a dairy herd grazing near a major nuclear installation. Sci Total Environ 34:57-72.

Sundelin P, Nilsson A. 1968. Cytoplasmic ultraviolet extinction of strontium-90-induced fibroblastic osteosarcomas correlated to histologic appearance and ultrastructure. Acta Radiol 7:161-170.

Sures B, Steiner W, Rydlo M, et al. 1999. Concentrations of 17 elements on the zebra mussel (*Dreissena polymorphia*), in different tissues of perch (*Perca fluviatilis*), and in perch intestinal parasites (*Acanthocephalus lucii*) from the subalpine Lake Mondsee, Austria. Environ Toxicol Chem 18(11):2574-2579.

*Sutherland BM, Bennett PV, Sidorkina O et al. 2000a. Clustered DNA damages induced in isolated DNA and in human cells by low doses of ionizing radiation. Proc Natl Acad Sci 97:103-108.

*Sutherland BM, Bennett PV, Sidorkina O, et al. 2000b. Clustered damages and total lesions induced in DNA by ionizing radiation: Oxidized bases and strand breaks. Biochemistry 39:8026-8031.

Sutton A. 1967. Reduction of strontium absorption in man by the addition of alginate to the diet. Nature 216:1005-1007.

*Sutton A, Harrison GE, Carr TEF. 1971a. Reduction in the absorption of dietary strontium in children by an alginate derivative. Int J Radiat Biol 19(1):79-80.

*Sutton A, Shepherd H, Harrison GE, et al. 1971b. Excretion and retention of stable strontium in children. Nature 230:396-397.

*Svensson O, Hjerpe A, Reinholt FP, et al. 1985. The effect of strontium and manganese on freshly isolated chondrocytes. Acta Pathol Microbiol Immunol Scand Sect A 93:115-120.

*Svensson O, Reinholt FP, Engfeldt B. 1987. The parathyroid gland in metal rickets: A stereological study. Acta Pathol Microbiol Immunol Scand Sect A 95:309-314.

*Sweet CW, Vermette SJ, Landsberger S. 1993. Sources of toxic trace elements in urban air in Illinois. Environ Sci Technol 27(12):2502-2510.

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

Szymendera J, Madajewicz S. 1968. Comparative ultrafiltrability of calcium and strontium in human plasma. Nature 217:968-969.

Takagi K, Takayanagi I. 1968. Electrophysical experiments on the action of some partial agonists and their application to receptor theory. Nature 218:275-276.

Takahashi S, Takahashi I, Sato H, et al. 2001. Age-related changes in the concentrations of major and trace elements in the brain of rats and mice. Biol Trace Elem Res 80(2):145-158.

Talbot V, Chang W-J. 1987. Rapid multielement analysis of oyster and cockle tissue using x-ray fluorescence spectrometry, with application to reconnaissance marine pollution investigations. Sci Total Environ 66:213-223.

*Tan E-L, Williams MW, Schenley RL, et al. 1984. The toxicity of sixteen metallic compounds in Chinese hamster ovary cells. Toxicol Appl Pharmacol 74:330-336.

*Tanaka G-I, Kawamura H, Nomura E. 1981. Reference Japanese man--II: Distribution of strontium in the skeleton and in the mass of mineralized bone. Health Phys 40:601-614.

Tanaka Y, Inoue S, Skoryna SC. 1970. Studies on inhibition of intestinal absorption of radioactive strontium: IX. Relationship between biological activity and electron microscopic appearance of alginic acid components. Can Med Assoc J 103(5):484-486.

Tanaka Y, Skoryna SC, Waldron-Edward D. 1968a. Studies on the inhibition of intestinal absorption of radioactive strontium: VI. Alginate degradation as potent *in vivo* sequestering agents of radioactive strontium. Can Med Assoc J 98:1179-1182.

Tanaka Y, Waldron-Edward D, Skoryna SC. 1968b. Studies on the inhibition of intestinal absorption of radioactive strontium: VII. Relationship of biological activity to chemical composition of alginates obtained from North American seaweeds. Can Med Assoc J 99:169-175.

Taniyama K, Yoshida N, Takahashi N, et al. 1977. Actions of Ba and Sr ions on isolated rat ileum. Jpn J Pharmacol 27:327-329.

Tanner TM, Young JA, Cooper JA. 1974. Multielement analysis of St. Louis aerosols by nondestructive techniques. Chemosphere 3(5):211-220.

Taylor DM. 1958. Comparative aspects of the transfer of strontium and calcium from mother to offspring in rats. Br J Radiol 31:715.

*Taylor DM. 1968. The effect of L-thyroxine on the absorption of calcium and strontium. Experientia 24(8):837-838.

*Taylor DM, Bligh PH. 1992. The transfer of ^{45}Ca, ^{85}Sr and ^{140}Ba from mother to newborn in rats. Radiat Prot Dosim 41(2/4):143-145.

*Taylor GN, Christensen WR, Jee WSS, et al. 1966. Intercomparison of pathological fractures in beagles injected with ^{226}Ra, ^{228}Ra, ^{239}Pu or ^{90}Sr. Health Phys 12:361-367.

ten Bolscher M, de Valk-de Roo G, Barto R, et al. 1999. Oestrogen has no short-term effect on intestinal strontium absorption in healthy postmenopausal women. Clin Endocrinol 50:387-392.

*Teree TM, Cohn SH. 1966. The determination of strontium in human serum using neutron activation analysis. J Nucl Med 7:848-858.

*Teree TM, Gusmano EA, Cohn SH. 1965. Decrement in radiostrontium retention following stable strontium prefeeding in the growing rat. J Nutr 87:399-406.

Testa C. 1970. Column reversed-phase partition chromatography for the isolation of some radionuclides from biological materials. Anal Chim Acta 50:447-455.

Thomas RG, Thomas RL, Wright SR. 1968. Retention of cesium-137 and strontium-90 administered in lethal doses to rats. Am Ind Hyg Assoc J 29:593-600.

Thomasset M. 1982. Strontium metabolism and toxicity of strontium. In: Galle P, Masse R, eds. Radionuclide Metabolism and Toxicity: Proceedings of the Symposium organized in 1982 by the Société Francaise de Biophysique et de Médecine Nucléaire and IRU-Environnement del'Université Paris-Val de Marne. Paris; Masson, 98-121.

Thorne MC, Vennart J. 1976. The toxicity of ^{90}Sr, ^{226}Ra and ^{239}Pu. Nature 263:555-558.

Thurman GB, Mays CW, Taylor GN, et al. 1971. Growth dynamics of beagle osteosarcomas. Growth 35:119-125.

Thurman GB, Mays CW, Taylor GN, et al. 1973. Skeletal location of radiation-induced and naturally occurring osteosarcomas in man and dog. Cancer Res 33:1604-1607.

Timmermans R, Van Hees M, Vandecasteele CH, et al. 1992. Transfer of radionuclides from maternal food to the fetus and nursing infants of minipigs. Radiat Prot Dosim 41(2/4):127-130.

Tinker A, Williams AJ. 1992. Divalent cation conduction in the ryanodine receptor channel of sheep cardiac muscle sarcoplasmic reticulum. J Gen Physiol 100:479-493.

*Tipton IH, Cook MJ. 1963. Trace elements in human tissue: Part II: Adult subjects from the United States. Health Phys 9:103-145.

*Tipton TH. 1981. Gross and elemental content of reference man. In: Snyder WS, Cook MJ, Nassett ES, et al. eds. New York, NY: Pergamon Press. International Commission on Radiological Protection. 273-334.

Toda M. 1972. Modification by Ca++ removal, Mg++ and Sr++ of the membrane effect and the inotropic effect of norepinephrine in rabbit left atria. J Pharmacol Exp Ther 180(3):698-709.

*Togna G, Gallozzi S, Caprino L. 1989. Influence of strontium chloride on blood platelet function. Arch Toxicol Suppl 13:366-369.

*Tokareva EE, Koxheurov VP, Tolstykh EI, et al. 2000. Analysis of *in vivo* measurements of ^{90}Sr in human teeth and body. Prague, Czech Republic: Fifth International Symposium and Exhibition of Environmental Contamination in Central and Eastern Europe, 12-14 September.

Toledano A, Barca MA, Moradillo I, et al. 1988. Mitochondrial accumulation of Sr^{2+} supported by pyruvate in the cerebellar cortex of the rat. Cellular variations during aging. Acta Histochem Cytochem 21(4):365-381.

*Tolstykh EI, Degteva MO, Kozheurov VP, et al. 1998. Strontium transfer from maternal skeleton to the fetus estimated on the basis of the Techa river data. Radiat Prot Dosim 79(1-4):307-310.

*Tolstykh EI, Degteva MO, Vorobiova MI, et al. 2001. Fetal dose assessment for the offspring of the Techa riverside residents. Radiat Environ Biophys 40(4):279-286.

*Tolstykh EI, Kozheurov VP, Vyushkova OV, et al. 1997. Analysis of strontium metabolism in humans on the basis of the Techa river data. Radiat Environ Biophys 36:25-29.

*Tong ECK, Zaret MM, Rubenfeld S. 1969. Cellular changes in the conjunctiva after strontium 90 treatment for pterygium. Am J Roentgenol Radium Ther Nucl Med 106(4):848-853.

*Toran L. 1994. Radionuclide contamination in groundwater: Is there a problem? In: Groundwater contamination and control. Environmental science pollution control series 11. New York, NY: M. Dekker, 437-455.

Toran L, Bryant S, Saunders J, et al. 1998. A two-tiered approach to reactive transport: Application to Sr mobility under variable pH. Ground Water 36(3):404-408.

*Torres JM, Tent J, Llaurado M, et al. 2002. A rapid method for ^{90}Sr determination in the presence of 137 Cs in environmental samples. J Environ Radioact 59:113-125.

*Toshioka T, Ishida M, Oami S, et al. 1974. Effects of cations on the bactericidal systems of normal rabbit serum: II. Effects of calcium and strontium ions. Nihon Univ J Med 16:5-23.

*Tothill P, Smith MA, Cohn SH. 1983. Whole-body and part-body turnover of ^{85}Sr in Paget's disease. Phys Med Biol 28(2):149-159.

Travnikova IG, Shutov VN, Bruk GY, et al. 2002. Assessment of current exposure levels in different population groups of the Kola Peninsula. J Environ Radioact 60:235-248.

Triffitt JT. 1968. Binding of calcium and strontium by alginates. Nature 217:457-458.

Triffitt JT, Sutton A. 1969. Strontium and calcium contents of bone density fractions. Calcif Tissue Res 4:174-179.

Triffitt JT, Jones RO, Patrick G. 1972. Uptake of ^{45}calcium and ^{85}strontium by bone in tissue culture. Calcif Tissue Res 8:211-216.

*Tsalev DL. 1984. Atomic absorption spectrometry in occupational and environmental health practice. Boca Raton, FL: CRC Press, Inc. Volume II: Determination of individual elements

Tsutsumi S, Amagai T, Kawaguchi M, et al. 1980. Effects of strontium chloride ($SrCl_2$) on ^{3}H-thymidine uptake into rat lymphocytes. Bull Tokyo Dent Coll 21(4):253-259.

Turoczy NJ, Laurenson LJB, Allinson G, et al. 2000. Observations on metal concentrations in three species of shark (*Deania Calcea, Centroscymnus crepidater*, and *Centroscymnus owstoni*) from Southeastern Australian waters. J Agric Food Chem 48:4357-4364.

Twardock AR, Austin MK. 1970. Calcium transfer in perfused guinea pig placenta. Am J Physiol 219(2):540-545.

Twardock AR, Downey HF, Kirk ES, et al. 1969. Comparative transfer of calcium and strontium and of potassium and cesium in the guinea pig placenta. AEC Symp Ser 17:97-104.

*Twardock AR, Kuo EY-H, Austin MK, et al. 1971. Protein binding of calcium and strontium in guinea pig maternal and fetal blood plasma. Am J Obstet Gynecol 110(7):1008-1014.

*Uchiyama M, Tanaka G, Yabumoto E. 1973. ^{85}Sr retention in Japanese after a single administration. J Radiat Res 14:169-179.

*U.S. Congress. 1990. Clean Air Act. Title III. Section 112. Hazardous air pollutants. One Hundred and First Congress of the United States. Public Law 101-549. 42 USC 7412. November 15, 1990.

*USNRC. 1991. Occupational dose limits. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 20, Subpart C.

*USNRC. 1993a. Radioactive materials released from nuclear power plants: Annual report 1993. Washington, DC: U.S. Nuclear Regulatory Commission. NUREG/CR-2907. BNL-NUREG-51581.

*USNRC. 1993b. Standards for protection against radiation. Annual limits on intake (ALIs) and derived air concentrations (DACs) of radionuclides for occupational exposure; effluent concentrations; concentrations for release to sewerage. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 20, Appendix B.

*USNRC. 1995. Standards for protection against radiation. Quantities of licensed material requiring labeling. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 20, Appendix C.

*USNRC. 1996. Technical specifications on effluents from nuclear power reactors. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 50.36a. 61 FR 39299. http://www.nrc.gov/NRC/CFR/PART050/part050-0036a.html. July 29, 1996

*USNRC. 1997. Radiation dose limits for individual members of the public. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 20, Subpart D.

*USNRC. 1998a. Physical protection for spent nuclear fuel and high-level radioactive waste; final rule. U.S. Nuclear Regulatory Commission. Federal Register. 63 FR 26955. May 15, 1998.

*USNRC. 1998b. Subpart O-Enforcement. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 20 Sub O.

*USNRC. 2000a. Schedule C-Quantities of radioactive materials requiring consideration of the need for an emergency plan for responding to a release. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 30.72.

*USNRC. 2000b. Use of sources for brachytherapy. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 35.400.

*USNRC. 2001a. Byproduct material. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 30.71, Sch. B. http://www.nrc.gov/NRC/CFR/PART030/part030-0071.html. March 13, 2001

*USNRC. 2001b. Byproduct material. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 33.100, Sch. A. http://www.nrc.gov/NRC/CFR/PART033/part033-0100.html. March 13, 2001

*USNRC. 2001c. General license for strontium 90 in ice detection devices. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 31.10. http://www.nrc.gov/NRC/CFR/PART031/part031-0010.html. March 13, 2001

*USNRC. 2001d. Quantities of licensed material requiring labeling. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 30, App. B. http://www.nrc.gov/NRC/CFR/PART030/part030-appb.html. March 13, 2001

*USNRC. 2001e. Quantities of licensed material requiring labeling. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 20, App. C. http://www.nrc.gov/NRC/CFR/TABLES/ISOTOPES/PART020-APPC/index.htm. March 13, 2001

*USNRC. 2001f. Quantities of radioactive materials requiring consideration of the need for an emergency plan for responding to a release. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 30.72, Sch. C. http://www.nrc.gov/NRC/CFR/PART030/part030-0072.html.

*USNRC. 2001g. Occupational values, effluent concentrations, and releases to sewers. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 20, App. B. http://www.nrc.gov/NRC/CFR/TABLES/ISOTOPES/PART020-APPB/Strontium-80.html.

*USNRC. 2001h. Quality assurance; prohibition of transfer. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 32.62. http://www.nrc.gov/NRC/CFR/PART032/part032-0062.html.

9. REFERENCES

*USNRC. 2001i. Table A-1.-A_1 and A_2 values for radionuclides. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 71. http://www.nrc.gov/NRC/CFR/TABLES/ISOTOPES/PART071/index.html.

*USNRC. 2001j. Use of sources for brachytherapy. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 35.400. http://www.nrc.gov/NRC/CFR/PART035/part035-0400.html.

*USNRC. 2001k. Use of unsealed byproduct material for uptake, dilution, and excretion studies. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 35.100. http://www.,nrc.gov/NRC/CFR/PART035/part035-0100.html.

*USNRC. 2001l. Waste classification. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 61.55. http://www.nrc.gov/NRC/CFR/PART061/part061-0055.html.

*USNRC. 2001m. Dose to an embryo/fetus. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 20.1208. http://www.nrc.gov/NRC/CFR/PART020/part020-1208.html. May 11, 2001.

*USNRC. 2001n. Occupational dose limits for adults. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 20.1201. http://www.nrc.gov/NRC/CFR/PART020/part020-1201.html. May 11, 2001.

*USNRC. 2001o. Occupational dose limits for minors. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 20.1207. http://www.nrc.gov/NRC/CFR/PART020/part020-1207.html. May 11, 2001.

*USNRC. 2001p. Physical protection for spent nuclear fuel and high-level radioactive waste. U.S. Nuclear Regulatory Commission. Federal Register. 63 FR 26955. http://frwebgate5.access.gpo.gov/. May 11, 2001.

*USNRC. 2001q. Standards for the protection against radiation. U.S. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 20.1301. http://www.nrc.gov/NRC/CFR/PART020/part020-1301.html. May 10, 2001.

*USDA. 1997. Animal and plant health inspection service, department of agriculture. Hawaiian fruits and vegetables. U.S. Department of Agriculture. Code of Federal Regulations. 7 CFR 318.

*USGS. 1963. Occurrence and distribution of strontium in natural water: Chemistry of strontium in natural water: Geological survey water-supply paper 1496-D. Washington, DC: U.S. Atomic Energy Commission. U.S. Geological Survey.

*USGS. 1980. Elements in fruits and vegetables from areas of commercial production in the conterminous United States: Geological survey professional paper 1178: A biogeochemical study of selected food plants based on field sampling of plant material and soil. Washington, DC: U.S. Department of the Interior. U.S. Geological Survey.

*USGS. 1998. Strontium. Minerals Yearbook (Volume I. Metals and Minerals). U.S. Geological Survey, VVV1-VVV4.

*USGS. 1999. Strontium. Mineral Commodity Summaries. U.S. Geological Survey. 166-167.

9. REFERENCES

*USGS. 2000a. Srontium. U.S. Geological Survey. 160-161. http//:www.usgs.gov/minerals/pubs/commodity/copper/index.html.

*USGS. 2000b. Strontium. U.S. Geological Survey. 74.1-74.7. http//:www.usgs.gov/minerals/pubs/commodity/copper/index.html.

*USGS. 2002. Strontium. U.S. Geological Survey. 74.1-74.5. http//:www.usgs.gov/minerals/pubs/commodity/copper/index.html.

Uvelius B, Sigurdsson SB, Johansson B. 1974. Strontium and barium as substitutes for calcium on electrical and mechanical activity in rat portal vein. Blood Vessels 11:245-259.

Vaca F, Manjon G, Garcia-Leon M. 2001. The presence of some artificial and natural radionulcides in a eucalyptus forest in the south of Spain. J Environ Radioact 56:309-325.

Vainio H, Mela L, Chance B. 1970. Energy dependent bivalent cation translocation in rat liver mitochondria. Eur J Biochem 12:387-391.

Vajda N, Ghods-Esphahani A, Cooper E, et al. 1992. Determination of radiostrontium in soil samples using a crown ether. J Radioanal Nucl Chem 162(2):307-323.

vam Puymbroeck S, van der Borght O. 1971. Enhancement of strontium absorption in the nitrous oxide-acetylene flame by potassium and sodium and the determination of strontium in biological material. Anal Chim Acta 57:441-446.

Van Barneveld AA, Van Puymbroeck S, Vanderborght O. 1977. The action of sodium alginate in the food on a ^{85}Sr body-burden in mice. Health Phys 33:533-537.

Vandecasteele C, Vanhoe H, Dams R, et al. 1990. Determination of strontium in human serum by inductively coupled plasma mass spectrometry and neutron activation analysis: A comparison. Talanta 37(8):819-823.

Vanderborght O, Keslev D, Van Puymbroeck S, et al. 1972. Combined influence of diet, alginate, parathyroid hormone and vitamin D on ^{85}Sr and ^{47}Ca mobilization from bone. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 397-402.

Vanderborght OLJ, Van Puymbroeck S, Babakova I. 1978. Effect of combined alginate treatments on the distribution and excretion of an old radiostrontium contamination. Health Phys 35:255-258.

*Varga LP, Sztanyik LB, Ronai E, et al. 1994. Mobilization of radioactive strontium from mouse and rat using dicarboxylic acid derivatives of cryptand (2.2). Int J Radiat Biol 66(4):399-405.

Vasington FD. 1966. Accumulation of Ca^{2+} and Sr^{2+} by rat-liver mitochondria: Preferential loss of the adenosine triphosphate-dependent mechanism for Sr^{2+} accumulation. Biochim Biophys Acta 113:414-416.

*Vaughan J, Williamson M. 1969. ^{90}Sr in the rabbit: The relative risks of osteosarcoma and squamous cell carcinoma. In: Mays CW, Jee WSS, Lloyd RD, et al. eds. Delayed effects of bone seeking radionuclides. Salt Lake City, UT: University of Utah Press, 337-355.

*Venier P, Montaldi A, Gava C, et al. 1985. Effects of nitrilotracetic acid on the induction of gene mutations and sister-chromatid exchanges by insoluble chromium compounds. Mutat Res 156:219-228.

Verdonck F, Carmeliet E. 1971. Isometric contractions in cardiac purkyne fibres: Characteristics in Na free Sr tyrode. Cardiovasc Res (Suppl. 1):76-83.

Vereecke J, Carmeliet E. 1971. Sr action potentials in cardiac purkyne fibres: II. Dependence of the Sr conductance on the external Sr concentration and Sr-Ca antagonism. Pflugers Arch 322:73-82.

Versieck J, Vanballenberghe L, Wittoek A, et al. 1993. The determination of strontiumin human blood serum and packed blood cells by radiochemical neutron activation analysis. J Radioanal Nucl Chem 168(1):243-248.

*Vezzoli G, Baragetti I, Zerbi S, et al. 1998. Strontium absorption and excretion in normoclaciuric subjects: Relation to calcium metabolism. Clin Chem 44(3):586-590.

Vezzoli G, Caumo A, Baragetti I, et al. 1999. Study of calcium metabolism in idiopathic hypercalciuria by strontium oral load test. Clin Chem 45(2):257-261.

*Vezzoli G, Soldati L, Provervio MC, et al. 2002. Polymorphism of vitamin D receptor gene start codon in patients with calcium kidney stones. 15(2):158-164.

*Viccellio P, ed. 1998. Emergency toxicology. 2nd ed. Philadelphia, PA: Lippincott-Raven, 991-996.

*Vieira I, Sonnier M, Cresteil T. 1996. Developmental expression of *CYP2E1* in the human liver: Hypermethylation control of gene expression during the neonatal period. Eur J Biochem 238:476-483.

Viglione PN, Pereyra K, Reyes-Toso CF, et al. 1996. Extracellular acidification related to the stimulation of catecholamines release by strontium in the bovine adrenal medulla. Arch Physiol Biochem 104(7):833-837.

Voight G. 1993. Chemical methods to reduce the radioactive contamination of animals and their products in agricultural ecosystems. Sci Total Environ 137:205-225.

*Volf V. 1964. Effect of sulphates on the intestinal absorption of Sr-85 in rats. Experientia 20(11):626-627.

Volf V. 1965. Effect of phosphates, carbonates, and magnesium oxide upon the intestinal absorption of Sr-85 in rats. Experientia 21(10):571-572.

Volf V, Roth Z. 1966a. Retention of strontium 85 in rats: II. Effect of various barium sulphate preparations as influenced by soluble sulphates, carrier strontium and by the physiologic state of animals. Acta Radiol 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 sulphates and role of the time factor. Acta Radiol Ther Phys Biol 4:481-493.

Von Zallinger C, Tempel K. 1998. Transplacental transfer of radionuclides. A review. Vet Med (Prague) A45:581-590.

Waite BA, Blauvelt SC. 1988. Oil and gas waste fluids of Pennsylvania. Northeast Environ Sci 7(2):105-110.

Wakabayashi S, Goshima K. 1981. Kinetic studies on sodium-dependent calcium uptake by myocardial cells and neuroblastoma cells in culture. Biochim Biophys Acta 642:158-172.

Waldron-Edward D. 1968. Studies on the inhibition of intestinal absorption of radioactive strontium: VIII. The effect of alginate-containing diets on water metabolism. Can Med Assoc J 99:986-992.

Waldron-Edward D, Paul TM, Skoryna SC. 1965a. Suppression of intestinal absorption of radioactive strontium by naturally occurring non-absorbable polyeletrolytes. Nature 205(4976):1117-1118.

Waldron-Edward D, Paul TM, Skoryna SC. 1966. Effects of counter ion and pH on intestinal absorption of calcium and strontium. Proc Soc Exp Biol Med 123(2):532-538.

Waldron-Edward D, Thyvalikakath PM, Skoryna SC. 1965b. Suppression of intestinal absorption of radioactive strontium by naturally occurring non-absorbable polyelectrolytes. Nature 205:1117-1118.

Walinder G, Feinstein RE, Gimeno EJ. 1986. Effect of high ^{131}I doses on the bone uptake and retention of ^{90}Sr and ^{90}Y. Acta Radiol Oncol 25:255-260.

*Wang Y, Qin J, Wu S, et al. 1990. Study on the relation of Se, Mn, Fe, Sr, Pb, Zn, Cu, and Ca to liver cancer mortality from analysis of scalp hair. Sci Total Environ 91:191-198.

*Warren JM. 1972a. Strontium-90 in diet - 1971. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 483-488.

Warren JM. 1972b. Strontium-90 in human bone 1959-70. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 521-580.

Warren JM, Spencer H. 1971. Intestinal excretion of ^{85}Sr and ^{47}Ca during feeding and fasting in rats. Radiat Res 48:578-588.

Warren JM, Spencer H. 1972a. Analysis of stable strontium in biological materials by atomic absorption spectrophotometry. Clin Chim Acta 38:435-439.

Warren JM, Spencer H. 1972b. Passage of ^{85}Sr and ^{47}Ca into the intestinal tract of rats. In:. Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 347-356.

Warren JM, Spencer H. 1972c. Stable strontium balances in man. In:. Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 325-334.

Warren JM, Spencer H. 1973. Passage of ^{85}Sr and ^{47}Ca into the gastrointestinal tract in rats during feeding and fasting. Radiat Res 56:110-121.

*Warren JM, Spencer H. 1976. Metabolic balances of strontium in man. Clin Orthop Relat Res 117:307-320.

Warren JM, Spencer H. 1978. Comparative excretions of strontium isotopes in man. Health Phys 34:67-70.

Washizu Y. 1968. Strontium and barium ions and guinea-pig ureter. Comp Biochem Physiol 25:367-371.

Wasserman RH, Romney EM, Skougstad MW, et al. 1977. Strontium. In: Geochemistry and the environment. Washington, DC: National Academy of Sciences, Vol. II: The relation of other selected trace elements to health and disease, 73-87.

*Watanabe N, Yokoyama K, Kinuya S, et al. 1998. Radio toxicity after strontium-89 therapy for bone metastases using the micronucleus assay. J Nucl Med 39:2077-2079.

Weber DA, Greenberg EJ, Dimich A, et al. 1969. Kinetics of radionuclides used for bone studies. J Nucl Med 10(1):8-17.

*Webling DD'A, Holdsworth ES. 1966. Bile and the absorption of strontium and iron. Biochem J 100:661-663.

*Wedin B. 1972. Cold - A possibility to increase the excretion of radiostrontium. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 369-378.

*Wedin B, Nilsson A, Ronnback C. 1972. Influence of cold on radiostrontium excretion. Nature (London) New Biol 236:212-213.

Weiss M. 2000. Acute myelogenous. Cancer 89(1):226-227.

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

Wenger P, Cosandey M. 1976. Retention and excretion of radium-226 and strontium-90 in two doubly contaminated persons. Health Phys 31:225-229.

*Wenger P, Soucas K. 1975. Retention and excretion curves of persons containing ^{90}Sr and ^{226}Ra after a chronic contamination. Health Phys 28:145-152.

*Wesberry JMJ, Wesberry JMS. 1993. Optimal use of beta irradiation in the treatment of pterygia. South Med J 86(6):633-637.

*West JR, Smith HW, Chasis H. 1948. Glomerular filtration rate, effective renal blood flow, and maximal tubular excretory capacity in infancy. J Pediatr 32:10-18.

*White RG, Raabe OG, Culbertson MR, et al. 1993. Bone sarcoma characteristics and distribution in beagle fed strontium-90. Radiat Res 136:178-189.

Widdowson EM. 1992. Absorption, excretion and storage of trace elements: Studies over 50 years. Food Chem 43:203-207.

*Widdowson EM, Dickerson JWT. 1964. Chemical composition of the body. In: Comar CL, Bronner F, eds. Mineral metabolism: An advanced treatise. Volume II: The elements Part A. New York: Academic Press.

Wigström H, Swann JW. 1980. Strontium supports synaptic transmission and long lasting potentiation in the hippocampus. Brain Res 194:181-191.

*Willard DH, Snyder MD. 1966. Strontium inhalation studies. In: Thompson RC, Swezea EG, eds. Pacific Northwest Laboratory annual report for 1965 in the biological sciences. Richland, WA: Pacific Northwest Laboratory, BNWL-280, 53-55.

*Williams MW, Hoeschele JD, Turner JE, et al. 1982. Chemical softness and acute metal toxicity in mice and *Drosophilia*. Toxicol Appl Pharmacol 63:461-469.

*Wiltrout RH, Gruys ME, Urias PE. 1989. Inhibition of organ-associated NK activity by ^{89}Sr. In: Natural killer cells and host defense. International Natural Killer Cell Workshop. Basel, NY: Karger, 55-58.

Wing KR. 1975. Turnover of ^{65}Zn and ^{85}Sr in growing rats: A comparative investigation. Acta Radiol Ther Phys Biol 14(1):1-24.

*Witkamp M. 1966. Biological concentrations of ^{137}Cs and ^{90}Sr in arctic food chains. Nuclear Safety 8(1):58-62.

*Witz S, Wood JA, Wadley MW. 1986. Toxic metal and hydrocarbon concentrations in automobile interiors during freeway transit. In: ACS Division of Environmental Chemistry 192nd National Meeting. 26:302-305.

*Wolf RL, Cauley JA, Baker CE, et al. 2000. Factors with calcium absorption effiency in pre- and perimenopausal woman[1-3]. Am J Clin Nutr 72:466-471.

Woodard HQ, Dwyer AJ. 1972. Whole-body retention of ^{85}Sr in three children aged 10 to 11 years. In: Second international conference on strontium metabolism, Glasgow and Strontian, 16-19 August, 1972. TID 4500 59th ed. Health and Safety Laboratory/U.S. Atomic Energy Commission, 91-110.

Woodard HQ, Harley JH. 1965. Strontium-90 in the long bones of patients with sarcoma. Health Phys 11:991-998.

*Woodson GC. 1998. An interesting case of osteomalacia due to antacid use associated with stainable bone aluminum in a patient with normal renal function. Bone 22:695-698.

Wrenn ME, Taylor GN, Stevens W, et al. 1983. DOE life-span radiation effects studies in experimental animals at University of Utah division of radio biology. In: Thompson RC, Mahaffey JA, eds. Life-span radiation effects studies in animals: What can they tell us? Proceedings of the twenty-second Hanford life science symposium held at Richland, Washington, September 27-29, 1983. Hanford Life Sciences Symposium 22nd. Springfield, VA: United States Department of Energy, 32-52.

*Wykoff MH. 1971. Distribution of strontium-85 in conceptuses of the pregnant rat. Radiat Res 48:394-401.

9. REFERENCES

*Xu GB, Yu CP. 1986. Effects of age on deposition of inhaled particles in the human lung. Aerosol Sci Technol 5:349-357.

*Yang H-S, Hwang D-W, Lee H-P, et al. 2002. Distribution of ^{90}Sr in coastal seawater, sediments and organisms off two atomic power stations in Korea. J Environ Radioact 59:105-112.

Yasuda H, Uchida S, Muramatsu Y, et al. 1995. Sorption of manganese, cobalt, zinc, strontium, and cesium onto agricultural soils: Statistical analysis on effects of soil properties. Water Air Soil Pollut 83:85-96.

Yifeng G, Zhaojian H, Meiyu Q, et al. 1991. Suppression of radioactive strontium absorption by sodium alginate in animals and human subjects. Biomed Environ Sci 4:273-282.

Yongxian W, Jinfa Q, Simin W, et al. 1990. Study on the relation of Se, Mn, Fe, Sr, Pb, Zn, Cu, and Ca to liver cancer mortality from analysis of scalp hair. Sci Total Environ 91:191-198.

*Ysart G, Miller P, Crews H, et al. 1999. Dietary exposure estimates of 30 elements from the UK total diet study. Food Addit Contam 16(9):391-403.

Yu KN. 1993. Monitoring ^{90}Sr contamination in terms of ^{131}I contamination in imported food. Health Phys 65(3):318-321.

*Yu X, Inesi G. 1995. Variable stoichiometric efficiency of Ca^{2+} and Sr^{2+} transport by the sarcoplasmic reticulum ATPase. J Biol Chem 270(9):4361-4367.

Yudintseva YV, Mamontova LA. 1979. Behavior of Sr^{90} in soils upon application of phosphates, lime, and peat. Sov Soil Sci 11(6):705-711.

*Zander-Principati GE, Kuzma JF. 1964. Reduction of strontium-90 bone cancer by zirconium citrate. Int J Radiat Biol 8(5):427-437.

*Zapol'Skaya NA, Borisova VV, Zhorno LY, et al. 1974. Comparison of the biological effect of strontium-90, cesium-137, iodine-131 and external irradiation. In: Third International Congress of the International Radiation Protection Association. Springfield, VA: U.S. Atomic Energy Commission, 147-152.

Zhai H, Hannon W, Hahn GS, et al. 2000. Strontium nitrate suppresses chemically-induced sensory irritation in humans. Contact Dermatitis 42:98-100.

*Ziegler EE, Edwards BB, Jensen RL, et al. 1978. Absorption and retention of lead by infants. Pediatr Res 12:29-34.

Zittermann A, Sabatschus O, Jantzen S, et al. 2000. Exercise-trained young men have higher calcium absorption rates and plasma calcitrol levels compared with age-matched sedentary controls. Calcif Tissue Int 67:215-219.

10. GLOSSARY

Some terms in this glossary are generic and may not be used in this profile.

Absorbed Dose, Chemical—The amount of a substance that is either absorbed into the body or placed in contact with the skin. For oral or inhalation routes, this is normally the product of the intake quantity and the uptake fraction divided by the body weight and, if appropriate, the time, expressed as mg/kg for a single intake or mg/kg/day for multiple intakes. For dermal exposure, this is the amount of material applied to the skin, and is normally divided by the body mass and expressed as mg/kg.

Absorbed Dose, Radiation—The mean energy imparted to the irradiated medium, per unit mass, by ionizing radiation. Units: rad (rad), gray (Gy).

Absorbed Fraction—A term used in internal dosimetry. It is that fraction of the photon energy (emitted within a specified volume of material) which is absorbed by the volume. The absorbed fraction depends on the source distribution, the photon energy, and the size, shape and composition of the volume.

Absorption—The process by which a chemical penetrates the exchange boundaries of an organism after contact, or the process by which radiation imparts some or all of its energy to any material through which it passes.

Absorption Coefficient—Fractional absorption of the energy of an unscattered beam of x- or gamma-radiation per unit thickness (linear absorption coefficient), per unit mass (mass absorption coefficient), or per atom (atomic absorption coefficient) of absorber, due to transfer of energy to the absorber. The total absorption coefficient is the sum of individual energy absorption processes (see Compton Effect, Photoelectric Effect, and Pair Production).

Absorption Coefficient, Linear—A factor expressing the fraction of a beam of x- or gamma radiation absorbed in a unit thickness of material. In the expression $I=I_oe^{-\mu x}$, I_o is the initial intensity, I the intensity of the beam after passage through a thickness of the material x, and μ is the linear absorption coefficient.

Absorption Coefficient, Mass—The linear absorption coefficient per cm divided by the density of the absorber in grams per cubic centimeter. It is frequently expressed as μ/ρ, where μ is the linear absorption coefficient and ρ the absorber density.

Absorption Ratio, Differential—Ratio of concentration of a nuclide in a given organ or tissue to the concentration that would be obtained if the same administered quantity of this nuclide were uniformly distributed throughout the body.

Activation—The process of making a material radioactive by bombardment with neutrons or protons.

Activity—The number of radioactive nuclear transformations occurring in a material per unit time (see Curie, Becquerel). The term for activity per unit mass is specific activity.

Activity Median Aerodynamic Diameter (AMAD)—The diameter of a unit-density sphere with the same terminal settling velocity in air as that of the aerosol particle whose activity is the median for the entire size distribution of the aerosol.

Acute Exposure, Chemical—Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

Acute Exposure, Radiation—The absorption of a relatively large amount of radiation (or intake of a radioactive material) over a short period of time.

Acute Radiation Syndrome—The symptoms which taken together characterize a person suffering from the effects of intense radiation. The effects occur within hours or days.

***Ad libitum*—**Available in excess and freely accessible.

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

Adsorption Ratio (K_d)—See Distribution Coefficient

Alpha Particle—A positively charged particle ejected spontaneously from the nuclei of some radioactive elements. It is identical to a helium nucleus, i.e., 2 neutrons and two protons, with a mass number of 4 and an electrostatic charge of +2.

Alpha Track—The track of ionized atoms (pattern of ionization) left in a medium by an alpha particle that has traveled through the medium.

Annihilation (Positron-Electron)—An interaction between a positive and a negative electron in which they both disappear; their rest mass, being converted into electromagnetic radiation (called annihilation radiation) with two 0.51 MeV gamma photons emitted at an angle of 180° to each other.

Annual Limit on Intake (ALI)—The derived limit for the amount of radioactive material taken into the body of an adult worker by inhalation or ingestion in a year. It is the smaller value of intake of a given radionuclide in a year by the reference man that would result in a committed effective dose equivalent of 5 rem or a committed dose equivalent of 50 rem to any organ or tissue.

Atom—The smallest particle of an element that cannot be divided or broken up by chemical means. It consists of a central core called the *nucleus*, which contains *protons* and *neutrons* and an outer shell of *electrons*.

Atomic Mass (u)—The mass of a neutral atom of a nuclide, usually expressed in terms of "atomic mass units." The "atomic mass unit" is one-twelfth the mass of one neutral atom of carbon-12; equivalent to 1.6604×10^{-24} g.

Atomic Mass Number—See Mass Number.

Atomic Number—The number of protons in the nucleus of an atom. The "effective atomic number" is calculated from the composition and atomic numbers of a compound or mixture. An element of this atomic number would interact with photons in the same way as the compound or mixture. (Symbol: Z).

Atomic Weight—The weighted mean of the masses of the neutral isotopes of an element expressed in atomic mass units.

Attenuation—A process by which a beam from a source of radiation is reduced in intensity by absorption and scattering when passing through some material.

Attenuation Coefficient—The fractional reduction in the intensity of a beam of radiation as it passes through an absorbing medium. It may be expressed as reduction per unit distance, per unit mass thickness, or per atom, and is called the linear, mass, or atomic attenuation coefficient, respectively.

Auger Effect—The emission of an electron from the extranuclear portion of an excited atom when the atom undergoes a transition to a less excited state.

Background Radiation—The amount of radiation to which a member of the general population is exposed from natural sources, such as terrestrial radiation from naturally occurring radionuclides in the soil, cosmic radiation originating from outer space, and naturally occurring radionuclides deposited in the human body.

Becquerel (Bq)—International System of Units unit of activity and equals that quantity of radioactive material in which one transformation (disintegration) occurs per second (see Units).

Terabecquerel (TBq)—One trillion becquerel.
Gigabecquerel (GBq)—One billion becquerel.
Megabecquerel (MBq)—One million becquerel.
Kilobecquerel (kBq))—One thousand becquerel.
Millibecquerel (mBq)—One-thousandth of a becquerel.
Microbecquerel (µBq)—One-millionth of a becquerel.

Beta Particle—An electron that is emitted from the nucleus of an atom during one type of radioactive transformation. A beta particle has a mass and charge equal in magnitude to that of the electron. The charge may be either +1 or -1. Beta particles with +1 charges are called positrons (symbolized β^+), and beta particles with -1 charges are called negatrons (symbolized β^-).

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.

Biologic Effectiveness of Radiation—See Relative Biological Effectiveness.

Biological Half-time—The time required for a biological system, such as that of a human, to eliminate by natural process half of the amount of a substance (such as a chemical substance, either stable or radioactive) that has entered it.

Biomagnification—The progressive increase in the concentration of a bioaccumulated chemical in organisms as that chemical is passed from the bottom to the top of the food web.

Biomarkers—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.

Body Burden, Chemical—The total amount of a chemical found in an animal or human body.

Body Burden, Radioactivity—The amount of radioactive material found in an animal or human body.

Bone Seeker—Any compound or ion which migrates in the body and preferentially deposits into bone.

Branching—The occurrence of two or more modes by which a radionuclide can undergo radioactive decay. For example, ^{214}Bi can undergo alpha or beta minus decay, ^{64}Cu can undergo beta minus, beta plus, or electron capture decay. An individual atom of a nuclide exhibiting branching disintegrates by one mode only. The fraction disintegrating by a particular mode is the "branching fraction" for that mode. The "branching ratio" is the ratio of two specified branching fractions (also called multiple disintegration).

Bremsstrahlung—X rays that are produced when a charged particle accelerates (speeds up, slows down, or changes direction) in the strong field of a nucleus.

Buildup Factor—The ratio of the radiation intensity, including both primary and scattered radiation, to the intensity of the primary (unscattered) radiation.

Cancer Effect Level (CEL)—The lowest dose of chemical or radiation 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.

Capture, Electron—A mode of radioactive decay involving the capture of an orbital electron by its nucleus. Capture from a particular electron shell, e.g., K or L shells, is designated as "K-electron capture" or "L-electron capture."

Capture, K-Electron—Electron capture from the K shell by the nucleus of the atom. Also loosely used to designate any orbital electron capture process.

Carcinogen—A chemical or radiation that is capable of inducing cancer.

Carcinoma—Malignant neoplasm composed of epithelial cells, regardless of their derivation.

Case-Control Study—A type of epidemiological study which examines the relationship between a particular outcome (disease or condition) and a variety of potential causative agents (such as toxic chemicals). In a case-controlled study, a group of people with a specified and well-defined outcome is identified and compared to a similar group of people without outcome.

Case Report—Describes a single individual with a particular disease or exposure. These may suggest some potential topics for scientific research but are not actual research studies.

Cataract—A clouding of the crystalline lens of the eye which obstructs the passage of light.

Ceiling Value—A concentration of a substance that should not be exceeded, even temporarily.

Charged Particle—A nuclear particle, atom, or molecule carrying a positive or negative charge.

Chronic Exposure—A long-term, continuous exposure to a chemical or radioactive material. For example, exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Cohort Study—A type of epidemiological study of a specific group or groups of people who have had a common insult (e.g., exposure to an agent suspected of causing disease or a common disease) and are followed forward from exposure to outcome. At least one exposed group is compared to one unexposed group.

Collective Dose—The sum of the individual doses received in a given period of time by a specified population from exposure to a specified source of radiation. Collective dose is expressed in units such as man-rem and person-sievert.

Compton Effect—An attenuation process observed for x- or gamma radiation in which an incident photon interacts with an orbital electron of an atom to produce a recoil electron and a scattered photon whose energy is less than the incident photon.

Containment—The confinement of a chemical or radioactive substance in such a way that it is prevented from being dispersed from its container or into the environment, or is released only at a specified rate.

Contamination—Deposition of a stable or radioactive substance in any place where it is not desired.

Cosmic Rays—High-energy particulate and electromagnetic radiations that originate outside the earth's atmosphere and interact with the atmosphere to produce a shower of secondary cosmic rays.

Count (Radiation Measurements)—The external indication of a radiation-measuring device designed to enumerate ionizing events. It refers to a single detected event. The term “count rate” refers to the total number registered in a given period of time. The term is sometimes erroneously used to designate a disintegration, ionizing event, or voltage pulse.

Counter, Gas-flow Proportional (GPC)—An instrument for detecting beta particle radiation. Beta particles are detected by ionization of the counter gas which results in an electrical impulse at an anode wire.

Counter, Geiger-Mueller (GM counter)—Highly sensitive, gas-filled radiation-measuring device that detects (counts) individual photons or particulate radiation.

Counter, Scintillation—The combination of a crystal or phosphor, photomultiplier tube, and associated circuits for counting light emissions produced in the phosphors by ionizing radiation. Scintillation counters generally are more sensitive than GM counters for gamma radiation.

Counting, Cerenkov—Relatively energetic β-particles pass through a transparent medium of high refractive index and a highly-directional, bluish-white light ("Cerenkov" light) is emitted. This light is detected using liquid scintillation counting equipment.

Cross-sectional Study—A type of epidemiological study of a group or groups which examines the relationship between exposure and outcome to a chemical or to chemicals at one point in time.

Curie (Ci)—A unit of radioactivity. One curie equals that quantity of radioactive material in which there are 3.7×10^{10} nuclear transformations per second. The activity of 1 gram of radium is approximately 1 Ci.

Attocurie (aCi)—One-thousandth of a femtocurie (3.7×10^{-8} disintegrations per second).
Femtocurie (fCi)—One-billionth of a microcurie (3.7×10^{-5} disintegrations per second).
Megacurie (MCi)—One million curies (3.7×10^{16} disintegrations per second).
Microcurie (µCi)—One-millionth of a curie (3.7×10^{4} disintegrations per second).
Millicurie (mCi)—One-thousandth of a curie (3.7×10^{7} disintegrations per second).
Nanocurie (nCi)—One-billionth of a curie (3.7×10^{1} disintegrations per second).
Picocurie (pCi)—One-millionth of a microcurie (3.7×10^{-2} disintegrations per second).

Daughter Products—See Progeny and Decay Product

Decay Chain or Decay Series—A sequence of radioactive decays (transformations) beginning with one nucleus. The initial nucleus, the parent, decays into a daughter or progeny nucleus that differs from the first by whatever particles were emitted during the decay. If further decays take place, the subsequent nuclei are also usually called daughters or progeny. Sometimes, to distinguish the sequence, the daughter of the first daughter is called the granddaughter, etc.

Decay Constant (λ)—The fraction of the number of atoms of a radioactive nuclide which decay in unit time (see Disintegration Constant).

Decay Product, Daughter Product, Progeny—A new nuclide formed as a result of radioactive decay. A nuclide resulting from the radioactive transformation of a radionuclide, formed either directly or as the result of successive transformations in a radioactive series. A decay product (daughter product or progeny) may be either radioactive or stable.

Decay, Radioactive—Transformation of the nucleus of an unstable nuclide by spontaneous emission of radiation, such as charged particles and/or photons (see Disintegration).

Delta Ray—An electron removed from an atom of a medium that is irradiated, or through which radiation passes, during the process of ionization (also called secondary electron). Delta rays cause a track of ionizations along their path.

Derived Air Concentration (DAC)—The concentration of radioactive material in air that, if breathed by the reference man for a working year of 2000 hours under conditions of light work (at a rate of 1.2 liters of air per hour), would result in an intake of one ALI (see Annual Limit on Intake).
Deterministic Effect—A health effect, the severity of which varies with the dose and for which a threshold is believed to exist (also called a non-stochastic effect).

Developmental Toxicity—The occurrence of adverse effects on the developing organism that may result from exposure to a chemical or radiation 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.

Disintegration Constant—Synonymous with decay constant. The fraction of the number of atoms of a radioactive material that decays per unit time (see Decay Constant.)

Disintegration, Nuclear—A spontaneous nuclear transformation (radioactivity) characterized by the emission of energy and mass from the nucleus. When large numbers of nuclei are involved, the process is characterized by a definite half-life (see Transformation, Nuclear).

Distribution Coefficient (K_d)—Describes the distribution of a chemical between the solid and aqueous phase at thermodynamic equilibrium, is given as follows:

$$K_d = \frac{[C]_s}{[C]_w}, \text{ Units = (L solution)/(kg solid),}$$

where $[C]_s$ is the concentration of the chemical associated with the solid phase in units of (mg)/(kg solid), and $[C]_w$ is the concentration of the chemical in the aqueous phase in units of (mg)/(L solution). As the magnitude of K_d decreases, the potential mobility of the chemical to groundwater systems increases and vice versa.

Dose—A general term denoting the quantity of a substance, radiation, or energy absorbed. For special purposes it must be appropriately qualified. If unqualified, it refers to radiation absorbed dose.

Absorbed Dose—The energy imparted to matter by ionizing radiation per unit mass of irradiated material at the place of interest. The unit of absorbed dose is the rad. One rad equals 100 ergs per gram. In SI units, the absorbed dose is the gray which is 1 J/kg (see Rad).

Cumulative Dose (Radiation)—The total dose resulting from repeated or continuous exposures to radiation.

Dose Assessment—An estimate of the radiation dose to an individual or a population group usually by means of predictive modeling techniques, sometimes supplemented by the results of measurement.

Dose Equivalent (DE)—A quantity used in radiation safety practice to account for the relative biological effectiveness of the several types of radiation. It expresses all radiations on a common scale for calculating the effective absorbed dose. The NRC defines it as the product of the absorbed dose, the quality factor, and all other modifying factors at the location of interest. ICRP has changed its definition to be the product of the absorbed dose and the radiation weighting factor. (The unit of dose equivalent is the rem. In SI units, the dose equivalent is the sievert, which equals 100 rem.)

Dose, Fractionation—A method of administering therapeutic radiation in which relatively small doses are given daily or at longer intervals.

Dose, Protraction—A method of administering therapeutic radiation by delivering it continuously over a relatively long period at a low dose rate.

Dose, Radiation—The amount of energy imparted to matter by ionizing radiation per unit mass of the matter, usually expressed as the unit rad, or in SI units, the gray. 100 rad = 1 gray (Gy) (see Absorbed Dose).

Committed Dose Equivalent ($H_{T,50}$)—The dose equivalent to organs or tissues of reference (T) that will be received from an intake of radioactive material by an individual during the 50 years following the intake.

Committed Effective Dose Equivalent ($H_{E,50}$)—The sum of the products of the weighting factors applicable to each of the body organs or tissues that are irradiated and the committed dose equivalent to those organs or tissues.

Effective Dose —A dose value that attempts to normalize the detriment to the body (for cancer mortality and morbidity, hereditary effects, and years of life lost) from a non-uniform exposure to that of a uniform whole body exposure. Effective dose is calculated as the sum of products of the equivalent dose and the tissue weighting factor (w_T) for each tissue exposed. ($E = \sum D_{T,R}\, w_R\, w_{T)}$).

Effective Dose Equivalent (H_E)—This dose type is limited to internal exposures and is the sum of the products of the dose equivalent to the organ or tissue (H_T) and the weighting factors (w_T) applicable to each of the body organs or tissues that are irradiated. ($H_E = \sum w_T\, H_T$).

Equivalent Dose—A dose quantity that places the biological effect of all radiation types on a common scale for calculating tissue damage. Alpha particles, for example, are considered to cause 20 times more damage than gamma rays. Equivalent dose is calculated as the sum of products of the average absorbed dose (in gray) in an organ or tissue ($_{DT,R}$) from each type of radiation and the radiation weighting factor (w_R) for that radiation ($\sum D_{T,R}\ w_R$).

External Dose—That portion of the dose equivalent received from radiation sources outside the body.

Internal Dose—That portion of the dose equivalent received from radioactive material taken into the body.

Limit—A permissible upper bound on the radiation dose.

Maximum Permissible Dose (MPD)—The greatest dose equivalent that a person or specified part thereof shall be allowed to receive in a given period of time.

Median Lethal Dose (MLD)—Dose of radiation required to kill, within a specified period (usually 30 days), 50% of the individuals in a large group of animals or organisms. Also called the LD_{50}, or $LD_{50/30}$ if for 30 days.

Threshold Dose—The minimum absorbed dose that will produce a detectable degree of any given effect.

Tissue Dose—Absorbed dose received by tissue in the region of interest, expressed in rad (see Dose, Gray, and Rad).

Dose Rate—The amount of radiation dose delivered per unit time. Generically, the rate at which radiation dose is delivered to any material or tissue.

Dose-Response Relationship—The quantitative relationship between the amount of exposure to a toxicant and the incidence of the adverse effects.

Dosimetry—Quantification of radiation doses to cells, tissues, organs, individuals or populations resulting from radiation exposures.

Early Effects (of radiation exposure)—Effects that appear within 60 days of an acute exposure.

Electron—A stable elementary particle having an electric charge equal to $\pm 1.60210 \times 10^{-19}$ C (Coulombs) and a rest mass equal to 9.1091×10^{-31} kg. A positron is a positively charged "electron" (see Positron).

Electron Volt—A unit of energy equivalent to the energy gained by an electron in passing through a potential difference of one volt. Larger multiple units of the electron volt are frequently used: keV for thousand or kilo electron volts; MeV for million or mega electron volts (eV). $1\ eV = 1.6 \times 10^{-12}$ erg.

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.

Energy—Capacity for doing work. Gravitationally, "potential energy" is the energy inherent in a mass because of its spatial relation to other masses. Chemically or radiologically, “potential energy” is the energy released when a chemical reaction or radiological transformation goes to completion. "Kinetic energy" is the energy possessed by a mass because of its motion (SI unit: joules):

> **Binding Energy (Electron)—**The amount of energy that must be expended to remove an electron from an atom.
>
> **Binding Energy (Nuclear)—**The energy represented by the difference in mass between the sum of the component parts and the actual mass of the nucleus. It represents the amount of energy that must be expended to break a nucleus into its component neutrons and protons.
>
> **Excitation Energy—**The energy required to change a system from its ground state to an excited state. Each different excited state has a different excitation energy.
>
> **Ionizing Energy—**The energy required to knock an electron out of an atom. The average energy lost by electrons or beta particles in producing an ion pair in air or in soft tissue is about 34 eV.
>
> **Radiant Energy—**The energy of electromagnetic radiation, such as radio waves, visible light, x and gamma rays.

Enrichment, Isotopic—An isotopic separation process by which the relative abundances of the isotopes of a given element are altered, thus producing a form of the element that has been enriched in one or more isotopes and depleted in others. In uranium enrichment, the percentage of uranium-235 in natural uranium can be increased from 0.7% to >90% in a gaseous diffusion process based on the different thermal velocities of the constituents of natural uranium (^{234}U, ^{235}U, ^{238}U) in the molecular form UF_6.

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.

Epidemiology—Refers to the investigation of factors that determine the frequency and distribution of disease or other health-related conditions within a defined human population during a specified period.

Equilibrium, Radioactive—In a radioactive series, the state which prevails when the ratios between the activities of two or more successive members of the series remains constant.

> **Secular Equilibrium—**If a parent element has a very much longer half-life than the daughters (so there is not appreciable change in its amount in the time interval required for later products to attain equilibrium) then, after equilibrium is reached, equal numbers of atoms of all members of the series disintegrate in unit time. This condition is never exactly attained, but is essentially established in such a case as ^{226}Ra and its transformation series to stable ^{206}Pb. The half-life of ^{226}Ra is about 1,600 years; of ^{222}Rn, approximately 3.82 days, and of each of the subsequent members, a few minutes. After about a month, essentially the equilibrium amount of radon is present; then (and for a long time) all members of the series disintegrate the same number of atoms per unit time. At this time, the activity of the daughter is equal to the activity of the parent.

Transient Equilibrium—If the half-life of the parent is short enough so the quantity present decreases appreciably during the period under consideration, but is still longer than that of successive members of the series, a stage of equilibrium will be reached after which all members of the series decrease in activity exponentially with the period of the parent. At this time, the ratio of the parent activity to the daughter activity is constant.

Equilibrium, Electron—The condition in a radiation field where the energy of the electrons entering a volume equals the energy of the electrons leaving that volume.

Excitation—The addition of energy to a system, thereby transferring it from its ground state to an excited state. Excitation of a nucleus, an atom, or a molecule can result from absorption of photons or from inelastic collisions with other particles. The excited state of an atom is an unstable or metastable state and will return to ground state by radiation of the excess energy.

Exposure (Chemical)—Contact of an organism with a chemical or physical agent. Exposure is quantified as the amount of the agent available at the exchange boundaries of the organism (e.g., skin, lungs, gut) and available for absorption.

Exposure (Radiation)—Subjection to ionizing radiation or to a radioactive material. For example, exposure in air is a measure of the ionization produced in air by x or gamma radiation; the sum of the electric charges on all ions of one sign produced in air when all electrons liberated by photons in a volume of air are completely stopped in air (dQ), divided by the mass of the air in the volume (dm). The unit of exposure in air is the roentgen, or coulomb per kilogram (SI units). One roentgen is equal to 2.58×10^{-4} coulomb per kilogram (C/kg).

Fission, Nuclear—A nuclear transformation characterized by the splitting of a nucleus into at least two other nuclei with emission of several neutrons, accompanied by the release of a relatively large amount of energy.

Gamma Ray, Penetrating—Short wavelength electromagnetic radiation of nuclear origin.

Genetic Effect of Radiation—Inheritable change, chiefly mutations, produced by the absorption of ionizing radiation by germ cells. Genetic effects have not been observed in any human population exposed at any dose level.

Genotoxicity—A specific adverse effect on the genome of living cells that, upon the duplication of affected cells, can be expressed as a mutagenic, clastogenic or carcinogenic event because of specific alteration of the molecular structure of the genome.

Gray (Gy)—SI unit of absorbed dose, 1 J/kg. One gray equals 100 rad (see Units).

Half-life, Effective—See Half-Time, Effective.

Half-life, Radioactive—Time required for a radioactive substance to lose 50% of its activity by decay. Each radio-nuclide has a unique physical half-life. Known also as physical half-time and symbolized as T_r or T_{rad}.

Half-time, Biological—Time required for an organ, tissue, or the whole body to eliminate one-half of any absorbed substance by regular processes of elimination. This is the same for both stable and radioactive isotopes of a particular element, and is sometimes referred to as half-time, symbolized as t_{biol} or T_b.

Half-time, Effective—Time required for a radioactive element in an organ, tissue, or the whole body to be diminished 50% as a result of the combined action of radioactive decay and biological elimination, symbolized as T_e or T_{eff}.

$$\text{Effective half-time} = \frac{\text{Biological half-time} \times \text{Radioactive half-life}}{\text{Biological half-time} + \text{Radioactive half-life}}$$

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

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

Immunological Effects—Functional changes in the immune response.

***In Vitro*—**Isolated from the living organism and artificially maintained, as in a test tube. Literally, "in glass."

***In Vivo*—**Occurring within the living organism. Literally, "in life."

Intensity—Amount of energy per unit time passing through a unit area perpendicular to the line of propagation at the point in question.

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

Internal Conversion—Process in which a gamma ray knocks an electron out of the same atom from which the gamma ray was emitted. The ratio of the number of internal conversion electrons to the number of gamma quanta emitted in the de-excitation of the nucleus is called the "conversion ratio."

Ion—Atomic particle, atom or chemical radical bearing a net electrical charge, either negative or positive.

Ion Pair—Two particles of opposite charge, usually referring to the electron and positive atomic or molecular residue resulting after the interaction of ionizing radiation with the orbital electrons of atoms.

Ionization—The process by which a neutral atom or molecule acquires a positive or negative charge.

> **Primary Ionization—**(1) In collision theory: the ionization produced by the primary particles as contrasted to the "total ionization" which includes the "secondary ionization" produced by delta rays. (2) In counter tubes: the total ionization produced by incident radiation without gas amplification.
>
> **Specific Ionization—**Number of ion pairs per unit length of path of ionizing radiation in a medium; e.g., per centimeter of air or per micrometer of tissue.
>
> **Total Ionization—**The total electric charge of one sign on the ions produced by radiation in the process of losing its kinetic energy. For a given gas, the total ionization is closely proportional to the initial ionization and is nearly independent of the nature of the ionizing radiation. It is frequently used as a measure of absorption of radiation energy.

Ionization Density—Number of ion pairs per unit volume.

Ionization Path (Track)—The trail of ion pairs produced by an ionizing particle in its passage through matter.

Ionizing Radiation—Any radiation capable of knocking electrons out of atoms and producing ions. Examples: alpha, beta, gamma and x rays, and neutrons.

Isobars—Nuclides having the same mass number but different atomic numbers.

Isomers—Nuclides having the same number of neutrons and protons but capable of existing, for a measurable time, in different quantum states with different energies and radioactive properties. Commonly the isomer of higher energy decays to one with lower energy by the process of isomeric transition.

Isotopes—Nuclides having the same number of protons in their nuclei, and hence the same atomic number, but differing in the number of neutrons, and therefore in the mass number. Identical chemical properties exist in isotopes of a particular element. The term should not be used as a synonym for nuclide because isotopes refer specifically to different nuclei of the same element.

Stable Isotope—A nonradioactive isotope of an element.

Joule—The S.I. unit for work and energy. It is equal to the work done by raising a mass of one newton through a distance of one meter (J = Nm), which corresponds to about 0.7 ft-pound.

Kerma (k)—A measure of the kinetic energy transferred from gamma rays or neutrons to a unit mass of absorbing medium in the initial collision between the radiation and the absorber atoms. The SI unit is J/kg. The special name of this unit is the rad (traditional system of units) or Gray (SI).

Labeled Compound—A compound containing one or more radioactive atoms intentionally added to its structure. By observations of radioactivity or isotopic composition, this compound or its fragments may be followed through physical, chemical, or biological processes.

Late Effects (of radiation exposure)—Effects which appear 60 days or more following an acute exposure.

$LD_{50/30}$—The dose of a chemical or radiation expected to cause 50% mortality in those exposed within 30 days. For radiation, this is about 350 rad (3.5 gray) received by humans over a short period of time.

Lethal Concentration$_{(Lo)}$ (LC_{Lo})—The lowest concentration of a chemical in air that 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 in 50% of a defined experimental animal population within a specified time, usually 30 days.

Lethal Dose$_{(Lo)}$ (LD_{Lo})—The lowest dose of a chemical introduced by a route other than inhalation that is expected to have caused death in humans or animals within a specified time, usually 30 days.

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.

Linear Energy Transfer (LET)—A measure of the energy that a charged particle transfers to a material per unit path length.

> **Average LET—**The energy of a charged particle divided by the length of the path over which it deposits all its energy in a material. This is averaged over a number of particles.
>
> **High-LET—**Energy transfer characteristic of heavy charged particles such as protons and alpha particles where the distance between ionizing events is small on the scale of a cellular nucleus.
>
> **Low-LET—**Energy transfer characteristic of light charged particles such as electrons produced by x and gamma rays where the distance between ionizing events is large on the scale of a cellular nucleus.

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.

Lung Clearance Class (fast, F; medium, M; slow, S)—A classification scheme for inhaled material according to its rate of clearance from the pulmonary region of the lungs to the blood and the gastrointestinal tract.

Lymphoreticular Effects—Represent morphological effects involving lymphatic tissues such as the lymph nodes, spleen, and thymus.

Malformations—Permanent structural changes that may adversely affect survival, development, or function.

Mass Numbers (A)—The number of nucleons (protons and neutrons) in the nucleus of an atom.

Minimal Risk Level—An estimate of daily human exposure to a substance that is likely to be without an appreciable risk of adverse noncancerous effects over a specified duration of exposure.

Morbidity—State of being diseased; morbidity rate is the incidence or prevalence of disease in a specific population.

Mutagen—A substance that causes changes (mutations) in the genetic material in a cell. Mutations can lead to birth defects, miscarriages, or cancer.

Necropsy—The gross examination of the organs and tissues of a dead body to determine the cause of death or pathological conditions.

Neurotoxicity—The occurrence of adverse effects on the nervous system following exposure to a substance.

Neutrino (ν)—A neutral particle of infinitesimally small rest mass emitted during beta plus or beta minus decay. This particle accounts for conservation of energy in beta plus and beta minus decays. It plays no role in damage from radiation.

No-Observed-Adverse-Effect Level (NOAEL)—The dose of a substance 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.

Nuclear Reactor—A power plant that heats the medium (typically water) by using the energy released from the nuclear fission of uranium or plutonium isotopes instead of burning coal, oil, or natural gas. All of these sources of energy simply heat water and use the steam which is produced to turn turbines that make electricity or propel a ship.

Nucleon—Common name for a constituent particle of the nucleus. Applied to a proton or neutron.

Nuclide—A species of atom characterized by the constitution of its nucleus. The nuclear constitution is specified by the number of protons (Z), number of neutrons (N), and energy content; or, alternatively, by the atomic number (Z), mass number A(N+Z), and atomic mass. To be regarded as a distinct nuclide, the atom must be capable of existing for a measurable time. Thus, nuclear isomers are separate nuclides, whereas promptly decaying excited nuclear states and unstable intermediates in nuclear reactions are not so considered.

Octanol-Water Partition Coefficient (K_{ow})—The equilibrium ratio of the concentrations of a chemical in n-octanol and water, in dilute solution.

Odds Ratio (OR)—A means of measuring the association between an exposure (such as toxic substances and a disease or condition) which represents the best estimate of relative risk (risk as a ratio of the incidence among subjects exposed to a particular risk factor divided by the incidence among subjects who were not exposed to the risk factor). An odds ratio of greater than 1 is considered to indicate greater risk of disease in the exposed group compared to the unexposed.

Pair Production—An absorption process for x- and gamma radiation in which the incident photon is absorbed in the vicinity of the nucleus of the absorbing atom, with subsequent production of an electron and positron pair (see annihilation). This reaction can only occur for incident photon energies exceeding 1.02 MeV.

Parent—Any radionuclide nuclide which, upon disintegration, yields a new nuclide (termed the progeny or daughter), either directly or as a later member of a radioactive series.

Permissible Exposure Limit (PEL)—A maximum allowable atmospheric level of a substance in workplace air averaged over an 8-hour shift.

Pharmacokinetic Model—A set of equations that can be used to describe the time course of a parent chemical or metabolite in an animal system. There are two types of pharmacokinetic models: data-based and physiologically-based. A data-based model divides the animal system into a series of compartments which, in general, do not represent real, identifiable anatomic regions of the body whereas the physiologically-based model compartments represent real anatomic regions of the body.

Pharmacokinetics—The dynamic behavior of a material in the body, used to predict the fate (disposition) of an exogenous substance in an organism. Utilizing computational techniques, it provides the means of studying the absorption, distribution, metabolism and excretion of chemicals by the body.

Physiologically Based Pharmacodynamic (PBPD) Model—A type of physiologically-based dose-response model which quantitatively describes the relationship between target tissue dose and toxic end points. These models advance the importance of physiologically based models in that they clearly describe the biological effect (response) produced by the system following exposure to an exogenous substance.

Physiologically Based Pharmacokinetic (PBPK) Model—A model comprising a series of compartments representing organs or tissue groups with realistic weights and blood flows. These models require a variety of physiological information: tissue volumes, blood flow rates to tissues, cardiac output, alveolar ventilation rates and, possibly membrane permeabilities. The models also utilize biochemical information such as air/blood partition coefficients, and metabolic parameters. PBPK models are also called biologically based tissue dosimetry models.

Photoelectric Effect—An attenuation process observed for x and gamma radiation in which an incident photon interacts with a tightly bound inner orbital electron of an atom delivering all of its energy to knock the electron out of the atom. The incident photon disappears in the process.

Photon—A quantum of electromagnetic energy (E) whose value is the product of its frequency (ν) in hertz and Planck's constant (h). The equation is: $E = h\nu$.

Population dose—See Collective dose.

Positron—A positively charged electron.

Potential, Ionization—The energy expressed as electron volts (eV) necessary to separate one electron from an atom, resulting in the formation of an ion pair.

Power, Stopping—A measure of the ability of a material to absorb energy from an ionizing particle passing through it; the greater the stopping power, the greater the energy absorbing ability (see Linear Energy Transfer).

Progeny—The decay product or daughter products resulting after a radioactive decay or a series of radioactive decays. The progeny can also be radioactive, and the chain continues until a stable nuclide is formed.

Proton—Elementary nuclear particle with a positive electric charge equal numerically to the charge of the electron and a rest mass of 1.007 mass units.

Quality—A term describing the distribution of the energy deposited by a particle along its track; radiations that produce different densities of ionization per unit intensity are said to have different "qualities."

Quality Factor (Q)—The linear-energy-transfer-dependent factor by which absorbed doses are multiplied to obtain (for radiation protection purposes) a quantity that expresses - on a common scale for all ionizing radiation - the approximate biological effectiveness of the absorbed dose.

Type of radiation	Quality Factor
X, gamma, or beta	1
Alpha particles	20
Neutrons of unknown energy	10
High energy protons	10

Rad—The traditional unit of absorbed dose equal to 100 ergs per gram, or 0.01 joule per kilogram (0.01 Gy) in any medium (see Absorbed Dose).

Radiation—The emission and propagation of energy through space or through a material medium in the form of waves (e.g., the emission and propagation of electromagnetic waves, or of sound and elastic waves). The term radiation or radiant energy, when unqualified, usually refers to electromagnetic radiation. Such radiation commonly is classified according to frequency, as microwaves, infrared, visible (light), ultraviolet, and x and gamma rays (see Photon.) and, by extension, corpuscular emission, such as alpha and beta radiation, neutrons, or rays of mixed or unknown type, as cosmic radiation.

Radiation, Annihilation—Photons produced when an electron and a positron unite and cease to exist. The annihilation of a positron-electron pair results in the production of two photons, each of 0.51 MeV energy.

Radiation, Background—See Background Radiation.

Radiation, Characteristic (Discrete)—Radiation originating from an excited atom after removal of an electron from an atom. The wavelength of the emitted radiation is specific, depending only on the element and particular energy levels involved.

Radiation, External—Radiation from a source outside the body.

Radiation, Internal—Radiation from a source within the body (as a result of deposition of radionuclides in body tissues).

Radiation, Ionizing—Any electromagnetic or particulate radiation capable of producing ions, directly or indirectly, in its passage through matter (see Radiation).

Radiation, Monoenergetic—Radiation of a given type in which all particles or photons originate with and have the same energy.

Radiation, Scattered—Radiation which during its passage through a substance, has been deviated in direction. It may also have been modified by a decrease in energy.

Radiation, Secondary—A particle or ray that is produced when the primary radiation interacts with a material, and which has sufficient energy to produce its own ionization, such as bremsstrahlung or electrons knocked from atomic orbitals with enough energy to then produce ionization (see Delta Rays).

Radiation Weighting Factor (also called Quality Factor)—In radiation protection, a factor (1 for x-rays, gamma rays, beta particles; 20 for alpha particles) weighting the absorbed dose of radiation of a specific type and energy for its effect on tissue.

Radioactive Material—Material containing radioactive atoms.

Radioactivity—Spontaneous nuclear transformations that result in the formation of new elements. These transformations are accomplished by emission of alpha or beta particles from the nucleus or by the capture of an orbital electron. Each of these reactions may or may not be accompanied by a gamma photon.

> **Radioactivity, Artificial—**Man-made radioactivity produced by particle bombardment or nuclear fission, as opposed to naturally occurring radioactivity.
>
> **Radioactivity, Induced—**Radioactivity produced in a substance after bombardment with neutrons or other particles. The resulting activity is "natural radioactivity" if formed by nuclear reactions occurring in nature and "artificial radioactivity" if the reactions are caused by man.
>
> **Radioactivity, Natural—**The property of radioactivity exhibited by more than 50 naturally occurring radionuclides.

Radioisotope—An unstable or radioactive isotope of an element that decays or disintegrates spontaneously, emitting radiation.

Radionuclide—Any radioactive isotope of any element. Approximately 5,000 natural and artificial radioisotopes have been identified.

Radiosensitivity—Relative susceptibility of cells, tissues, organs, organisms, or any living substance to the injurious action of radiation. Radiosensitivity and its antonym, radioresistance, are used comparatively, rather than absolutely.

Reference Dose (RfD)—An estimate 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 non-threshold effects such as cancer.

Relative Biological Effectiveness (RBE)—The RBE is a factor used to compare the biological effectiveness of absorbed radiation doses (i.e., rad) due to different types of ionizing radiation. More specifically, it is the experimentally determined ratio of an absorbed dose of a radiation in question to the absorbed dose of a reference radiation (typically ^{60}Co gamma rays or 200 kVp x rays) required to produce an identical biological effect in a particular experimental organism or tissue (see Quality Factor).

Rem—The traditional unit of dose equivalent that is used in the regulatory, administrative, and engineering design aspects of radiation safety practice. The dose equivalent in rem is numerically equal to the absorbed dose in rad multiplied by the quality factor (1 rem is equal to 0.01 sievert).

Reportable Quantity (RQ)—The quantity of a hazardous substance that is considered reportable under CERCLA. Reportable quantities are (1) 1 pound 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.

Roentgen (R)—A unit of exposure (in air) to ionizing radiation. It is the amount of x or gamma rays required to produce ions carrying 1 electrostatic unit of electrical charge in 1 cubic centimeter of dry air under standard conditions. Named after William Roentgen, a German scientist who discovered x rays in 1895.

Retrospective Study—A type of cohort study based on a group of persons known to have been exposed at some time in the past. Data are collected from routinely recorded events, up to the time the study is undertaken. Retrospective studies are limited to causal factors that can be ascertained from existing records and/or examining survivors of the cohort.

Self-Absorption—Absorption of radiation (emitted by radioactive atoms) by the material in which the atoms are located; in particular, the absorption of radiation within a sample being assayed.

Short-Term Exposure Limit (STEL)—The maximum concentration to which workers can be exposed for up to 15 minutes continually. No more than four excursions are allowed per day, and there must be at least 60 minutes between exposure periods. The daily TLV-TWA may not be exceeded.

SI Units—The International System of Units as defined by the General Conference of Weights and Measures in 1960. These units are generally based on the meter/kilogram/second units, with special quantities for radiation including the becquerel, gray, and sievert.

Sickness, Acute Radiation (Syndrome)—The complex symptoms and signs characterizing the condition resulting from excessive exposure of the whole body (or large part) to ionizing radiation. The earliest of these symptoms are nausea, fatigue, vomiting, and diarrhea, and may be followed by loss of hair (epilation), hemorrhage, inflammation of the mouth and throat, and general loss of energy. In severe cases, where the radiation dose is relatively high (over several hundred rad or several gray), death may occur within two to four weeks. Those who survive six weeks after exposure of a single high dose of radiation may generally be expected to recover.

Sievert (Sv)—The SI unit of any of the quantities expressed as dose equivalent. The dose equivalent in sieverts is equal to the absorbed dose, in gray, multiplied by the quality factor (1 sievert equals 100 rem). The sievert is also the SI unit for effective dose equivalent, which is the sum of the products of the dose equivalent to each organ or tissue and its corresponding tissue weighting factor.

Specific-Activity—Radioactivity per unit mass of a radionuclide, expressed, for example, as Ci/gram or Bq/kilogram.

Specific Energy—The actual energy per unit mass deposited per unit volume in a small target, such as the cell or cell nucleus, as the result of one or more energy-depositing events. This is a stochastic quantity as opposed to the average value over a large number of instance (i.e., the absorbed dose).

Standardized Mortality Ratio (SMR)—A ratio of the observed number of deaths and the expected number of deaths in a specific standard population.

Stochastic Effect—A health effect that occurs randomly and for which the probability of the effect occurring, rather than its severity, is assumed to be a linear function of dose without a threshold (also called a nondeterministic effect).

Stopping Power—The average rate of energy loss of a charged particle per unit thickness of a material or per unit mass of material traversed.

Surface-seeking Radionuclide—A bone-seeking internal emitter that deposits and remains on the bone surface for a long period of time, although it may eventually diffuse into the bone mineral. This contrasts with a volume seeker, which deposits more uniformly throughout the bone volume.

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.

Target Theory (Hit Theory)—A theory explaining some biological effects of radiation on the basis that ionization, occurring in a discrete volume (the target) within the cell, directly causes a lesion which subsequently results in a physiological response to the damage at that location. One, two, or more "hits" (ionizing events within the target) may be necessary to elicit the response.

Teratogen—A chemical that causes birth defects.

Threshold Limit Value (TLV)—The maximum concentration of a substance to which most workers can be exposed without adverse effect. TLV is a term used exclusively by the ACGIH. Other terms used to express similar concepts are the MAC (Maximum Allowable Concentration) and PEL (Permissible Exposure Limits).

Time-Weighted Average (TWA)—An allowable exposure concentration averaged over a normal 8-hour workday or 40-hour workweek.

Tissue Weighting Factor (W_t)—Organ- or tissue-specific factor by which the equivalent dose is multiplied to give the portion of the effective dose for that organ or tissue. Recommended values of tissue weighting factors are:

Tissue/Organ	Tissue Weighting Factor
Gonads	0.70
Bone marrow (red)	0.12
Colon	0.12
Lung	0.12
Stomach	0.12
Bladder	0.05
Breast	0.05
Liver	0.05
Esophagus	0.05
Thyroid	0.05
Skin	0.01
Bone surface	0.01
Remainder (adrenals, brain, upper large intestine, small intestine, pancreas, spleen, thymus, and uterus)	0.05

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.

Toxicokinetic—The absorption, distribution and elimination of toxic compounds in the living organism.

Toxicosis—A diseased condition resulting from poisoning.

Transformation, Nuclear—The process of radioactive decay by which a nuclide is transformed into a different nuclide by absorbing or emitting particulate or electromagnetic radiation.

Transition, Isomeric—The process by which a nuclide decays to an isomeric nuclide (i.e., one of the same mass number and atomic number) of lower quantum energy. Isomeric transitions (often abbreviated I.T.) proceed by gamma ray and internal conversion electron emission.

Tritium—The hydrogen isotope with one proton and two neutrons in the nucleus (Symbol: ^{3}H). It is radioactive and has a physical half-life of 12.3 years.

Unattached Fraction—That fraction of the radon daughters, usually ^{218}Po and ^{214}Po, which has not yet attached to a dust particle or to water vapor. As a free atom, it has a high probability of being exhaled and not retained within the lung. It is the attached fraction which is primarily retained.

Uncertainty Factor (UF)—A factor used in operationally deriving the RfD from experimental data. 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.

Units, Prefixes—Many units of measure are expressed as submultiples or multiples of the primary unit (e.g., 10^{-3} curie is 1 mCi and 10^{3} becquerel is 1 kBq).

Factor	Prefix	Symbol	Factor	Prefix	Symbol
10^{-18}	atto	A	10^{3}	kilo	k
10^{-15}	femto	F	10^{6}	mega	M
10^{-12}	pico	p	10^{9}	giga	G
10^{-9}	nano	N	10^{12}	tera	T
10^{-6}	micro	M	10^{15}	peta	P
10^{-3}	milli	M	10^{18}	exa	E
10^{-2}	centi	C			

Units, Radiological—

Units	Equivalents
Becquerel* (Bq)	1 disintegration per second = 2.7×10^{-11} Ci
Curie (Ci)	3.7×10^{10} disintegrations per second = 3.7×10^{10} Bq
Gray* (Gy)	1 J/kg = 100 rad
Rad (rad)	100 erg/g = 0.01 Gy
Rem (rem)	0.01 sievert
Sievert* (Sv)	100 rem

*International Units, designated (SI)

Working Level (WL)—Any combination of short-lived radon daughters in 1 liter of air that will result in the ultimate emission of 1.3×10^{5} MeV of potential alpha energy.

Working Level Month (WLM)—A unit of exposure to radon daughters corresponding to the product of the radon daughter concentration in Working Level (WL) and the exposure time in nominal months (1 nominal month = 170 hours). Inhalation of air with a concentration of 1 WL of radon daughters for 170 working hours results in an exposure of 1 WLM.

X rays—Penetrating electromagnetic radiations whose wave lengths are very much shorter than those of visible light. They are usually produced by bombarding a metallic target with fast electrons in a high vacuum. X rays (called characteristic x rays) are also produced when an orbital electron falls from a high energy level to a low energy level.

Zero-Threshold Linear Hypothesis (or No-Threshold Linear Hypothesis)—The assumption that a dose-response curve derived from data in the high dose and high dose-rate ranges may be extrapolated through the low dose and low dose range to zero, implying that, theoretically, any amount of radiation will cause some damage.

APPENDIX A. ATSDR MINIMAL RISK LEVELS AND WORKSHEETS

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) [42 U.S.C. 9601 et seq.], as amended by the Superfund Amendments and Reauthorization Act (SARA) [Pub. L. 99–499], requires that the Agency for Toxic Substances and Disease Registry (ATSDR) develop jointly with the U.S. Environmental Protection Agency (EPA), in order of priority, a list of hazardous substances most commonly found at facilities on the CERCLA National Priorities List (NPL); prepare toxicological profiles for each substance included on the priority list of hazardous substances; and assure the initiation of a research program to fill identified data needs associated with the substances.

The toxicological profiles include an examination, summary, and interpretation of available toxicological information and epidemiologic evaluations of a hazardous substance. During the development of toxicological profiles, Minimal Risk Levels (MRLs) are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration for a given route of exposure. An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. MRLs are based on noncancer health effects only and are not based on a consideration of cancer effects. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors to identify contaminants and potential health effects that may be of concern at hazardous waste sites. It is important to note that MRLs are not intended to define clean-up or action levels.

MRLs are derived for hazardous substances using the no-observed-adverse-effect level/uncertainty factor approach. They are below levels that might cause adverse health effects in the people most sensitive to such chemical-induced effects. MRLs are derived for acute (1–14 days), intermediate (15–364 days), and chronic (365 days and longer) durations and for the oral and inhalation routes of exposure. Currently, MRLs for the dermal route of exposure are not derived because ATSDR has not yet identified a method suitable for this route of exposure. MRLs are generally based on the most sensitive chemical-induced end point considered to be of relevance to humans. Serious health effects (such as irreparable damage to the liver or kidneys, or birth defects) are not used as a basis for establishing MRLs. Exposure to a level above the MRL does not mean that adverse health effects will occur.

MRLs are intended only to serve as a screening tool to help public health professionals decide where to look more closely. They may also be viewed as a mechanism to identify those hazardous waste sites that

are not expected to cause adverse health effects. Most MRLs contain a degree of uncertainty because of the lack of precise toxicological information on the people who might be most sensitive (e.g., infants, elderly, nutritionally or immunologically compromised) to the effects of hazardous substances. ATSDR uses a conservative (i.e., protective) approach to address this uncertainty consistent with the public health principle of prevention. Although human data are preferred, MRLs often must be based on animal studies because relevant human studies are lacking. In the absence of evidence to the contrary, ATSDR assumes that humans are more sensitive to the effects of hazardous substance than animals and that certain persons may be particularly sensitive. Thus, the resulting MRL may be as much as 100-fold below levels that have been shown to be nontoxic in laboratory animals.

Proposed MRLs undergo a rigorous review process: Health Effects/MRL Workgroup reviews within the Division of Toxicology, expert panel peer reviews, and agency-wide MRL Workgroup reviews, with participation from other federal agencies and comments from the public. They are subject to change as new information becomes available concomitant with updating the toxicological profiles. Thus, MRLs in the most recent toxicological profiles supersede previously published levels. For additional information regarding MRLs, please contact the Division of Toxicology, Agency for Toxic Substances and Disease Registry, 1600 Clifton Road NE, Mailstop F-32, Atlanta, Georgia 30333.

APPENDIX A

MINIMAL RISK LEVEL (MRL) WORKSHEET

Chemical name(s): Strontium
CAS number(s): 7440-24-6
Date: March 2004
Profile status: Third draft, post-public
Route: [ ] Inhalation [X] Oral
Duration: [ ] Acute [X] Intermediate [ ] Chronic
Key to figure: 16
Species: Rat

MRL: 2.0 [X] mg/kg/day [ ] ppm [ ] mg/m^3

Reference: Storey E. 1961. Strontium 'rickets': Bone calcium and strontium changes. Austral Ann Med 10:213-222.

Experimental design: Groups of five young (40–60 g) and three adult (200–250 g) female rats were fed a diet containing 1.6% calcium, 0.9% phosphorus, and 0, 0.19, 0.38, 0.75, 1.0 (young only), 1.5, or 3% strontium as strontium carbonate for 20 days. Initial and final body weights were recorded. Terminal levels of calcium and strontium were measured in serum and in five selected ashed bones for each dose level. Both tibia from each animal were processed histologically, and the proximal epiphyseal cartilages were measured.

Effects noted in study and corresponding doses: The strontium intakes were calculated to be 0, 140, 550, 1,080, 1,460, 2,220, or 4,975 mg strontium/kg/day in young rats, and 0, 170, 350, 690, 1,370, or 2,750 mg strontium/kg/day in adult rats. The serum calcium levels were not significantly changed in either young or adult animals, but at the high doses, the serum calcium/strontium ratio was about 1 in young rats and 1.4 in adults. In young rats, increased strontium ingestion resulted in abnormal thickening of the epiphyseal cartilage plate, approximately doubled at the highest dose. No histological effect was noted at the lowest dose (140 mg strontium/kg/day), but alterations in the appearance of the cartilage plate (irregular, thicker, with areas of uncalcified bone matrix in the distal ends of the metaphyseal trabeculae and proximal end of the diaphysis) were observed at 550 mg strontium/kg/day. Irregularities in the organization of the cells of hypertrophic zone, in the pattern of calcification, and in the deposition of osteoid were more conspicuous with increasing dose. In tibias, the dry weight, ash weight, ash percentage, and calcium in ash were significantly reduced with increased strontium intake. Adult rats were less affected by strontium ingestion than young animals. In adult rats, the no-effect level was 690 mg strontium/kg/day. In adults, changes in tibia histology (thicker epiphyseal cartilage, increased width of metaphyseal osteoid seams) were noted at or above 1,370 mg strontium/kg/day. At 2,750 mg strontium/kg/day, osteoid tissue was deposited near vascular canals and the areas of bone resorption were reduced. In adult rat tibias, the dry weight, ash weight, ash percentage, and calcium in ash were only significantly affected at the highest dose. This study demonstrates the difference in sensitivity to strontium between young and old animals. The LOAEL for the young rats (550 mg/strontium/kg/day) is a NOAEL for the adults (<690 mg strontium/kg/day).

Dose and end point used for MRL derivation:
This study identifies a NOAEL of 140 mg/kg/day for skeletal toxicity in young rats.

[X] NOAEL [] LOAEL:

Uncertainty factors used in MRL derivation:

[ ] 1 [ ] 3 [] 10 (for use of a LOAEL)
[ ] 1 [] 3 [X] 10 (for extrapolation from animals to humans)
[ ] 1 [X] 3 [] 10 (for human variability)

Modifying factor used in MRL derivation: 3

MRL = NOAEL / (UF)(MF) = 140 mg/kg/day / (30)(3) = 2 mg/kg/day

Was a conversion factor used from ppm in food or water to a mg/body weight dose?
Food intake was based upon an allometric equation using the average body weight in kg (EPA 1988):
$F = 0.056 \times bw^{0.6611}$.

If an inhalation study in animals, list conversion factors used in determining human equivalent dose: NA

Was a conversion used from intermittent to continuous exposure? If so, explain: NA

Other additional studies or pertinent information that lend support to this MRL: If an MRL were to be derived from the adult rat NOAEL of 690 mg/kg/day, then an uncertainty factor of 100 would be applied (10 for interspecies extrapolation and 10 for human variability), giving a value of 690/100=6.9 mg/kg/day. Because the young rats represent a sensitive population, just as juveniles would be the most sensitive human group, the selection of the NOAEL implicitly factors in human variability to some degree. Therefore, a smaller uncertainty factor is chosen for intraspecies extrapolation (3 for human variability). However, since the study duration was only 20 days, there is uncertainty whether the NOAEL would be valid for intermediate exposures extending up to 1 year. In addition, the focus of the study was skeletal effects, and no other organ system was examined. To adjust for these potential sources of uncertainty, a modifying factor of 3 is applied to the NOAEL. The MRL is derived using the young rat NOAEL of 140 mg/kg/day and a total uncertainty factor of 30 (10 for interspecies extrapolation and 3 for human variability), and a modifying factor of 3 (for short study duration and limited end point evaluation), giving a value of 140/(30x)=1.6 mg/kg/day; rounding off to whole numbers, the intermediate oral MRL is 2.0 mg/kg/day.

Abnormal bone mineralization (rickets) resulting from ingestion of excess strontium has been observed in many rodent studies. Several studies identified a similar NOAEL (110–168 mg strontium/kg/day) in weanling rats (Grynpas et al. 1996; Kroes et al. 1977; Morohashi et al. 1994). Similar LOAELs (500–565 mg strontium/kg/day) for abnormal bone mineralization in weanling rats have been reported (Johnson et al. 1968; Morohashi et al. 1994; Neufeld and Boskey 1994). Slight skeletal effects were noted in mice at 350 mg/kg/day (Marie and Hott 1986). The relevance of the rodent studies to humans is suggested by a Turkish epidemiological study indicating that excess oral exposure to strontium may contribute to the development of rickets in children (Ögzür et al. 1996).

The skeletal effects of excess strontium are known to be related to its chemical similarity to calcium. Excess strontium adversely affects bone development in several ways. In chickens and rats, excess strontium suppresses the activation of vitamin D3 in the kidney, which severely reduces the expression of calbindin D mRNA and the translation of calbindin D protein in the duodenum (Armbrecht et al. 1979, 1998; Omdahl and DeLuca 1972). As a result, duodenal absorption of calcium is reduced. Strontium also binds directly to hydroxyapatite crystals, which may interfere with the normal crystalline structure of bone in rats (Storey 1961). In addition, excess strontium may prevent the normal maturation of chondrocytes in the epiphyseal plates of long bones of rats (Matsumoto 1976). Excess strontium apparently interferes with the mineralization of complexed acidic phospholipids that is thought to help

initiate the formation of hydroxyapatite crystals in developing bone (Neufeld and Boskey 1994). As a result, affected bone contains an excess of complexed acidic phospholipid and a significantly lower ash weight, reducing its strength.

APPENDIX B. USER'S GUIDE

Chapter 1

Public Health Statement

This chapter of the profile is a health effects summary written in non-technical language. Its intended audience is the general public, especially people living in the vicinity of a hazardous waste site or chemical 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 chemical.

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

Relevance to Public Health

This chapter provides a health effects summary based on evaluations of existing toxicologic, epidemiologic, 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 chapter covers end points in the same order that they appear within the Discussion of Health Effects by Route of Exposure section, by route (inhalation, oral, and dermal) and within route by effect. Human data are presented first, then animal data. Both are organized by duration (acute, intermediate, chronic). *In vitro* data and data from parenteral routes (intramuscular, intravenous, subcutaneous, etc.) are also considered in this chapter.

The carcinogenic potential of the profiled substance is qualitatively evaluated, when appropriate, using existing toxicokinetic, genotoxic, and carcinogenic data. ATSDR does not currently assess cancer potency or perform cancer risk assessments. Minimal Risk Levels (MRLs) for noncancer end points (if derived) and the end points from which they were derived are indicated and discussed.

Limitations to existing scientific literature that prevent a satisfactory evaluation of the relevance to public health are identified in the Chapter 3 Data Needs section.

Interpretation of Minimal Risk Levels

Where sufficient toxicologic information is available, ATSDR has derived MRLs for inhalation and oral routes of entry at each duration of exposure (acute, intermediate, and chronic). These MRLs are not meant to support regulatory action, but to acquaint health professionals with exposure levels at which adverse health effects are not expected to occur in humans.

MRLs should help physicians and public health officials determine the safety of a community living near a chemical emission, given the concentration of a contaminant in air or the estimated daily dose in water. MRLs are based largely on toxicological studies in animals and on reports of human occupational exposure.

MRL users should be familiar with the toxicologic information on which the number is based. Chapter 2, "Relevance to Public Health," contains basic information known about the substance. Other sections such as Chapter 3 Section 3.10, "Interactions with Other Substances," and Section 3.11, "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 that the Environmental Protection Agency (EPA) provides (Barnes and Dourson 1988) to determine reference doses (RfDs) for lifetime exposure.

To derive an MRL, ATSDR generally selects the most sensitive 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 systemic, neurological, and developmental effects. If this information and reliable quantitative data on the chosen end point are available, ATSDR derives an MRL using the most sensitive species (when information from multiple species is available) with the highest no-observed-adverse-effect level (NOAEL) that does not exceed any adverse effect levels. When a NOAEL is not available, a lowest-observed-adverse-effect level (LOAEL) can be used to derive an MRL, and an uncertainty factor (UF) of 10 must be employed. Additional uncertainty factors of 10 must be used both 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 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 levels of significant exposure (LSE) Tables.

Chapter 3

Health Effects

Tables and Figures for Levels of Significant Exposure (LSE)

Tables and figures are used to summarize health effects and illustrate graphically levels of exposure associated with those effects. These levels cover health effects observed at increasing dose concentrations and durations, differences in response by species, 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. Use the LSE tables and figures 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. All entries in these tables and figures represent studies that provide reliable, quantitative estimates of NOAELs, LOAELs, or Cancer Effect Levels (CELs).

The legends presented below demonstrate the application of these tables and figures. Representative examples of LSE Table 3-1 and Figure 3-1 are shown. The numbers in the left column of the legends correspond to the numbers in the example table and figure.

LEGEND

See Sample LSE Table 3-1 (page B-6)

(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. Typically when sufficient data exists, 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 3-1, 3-2, and 3-3, respectively). LSE figures are limited to the inhalation (LSE Figure 3-1) and oral (LSE Figure 3-2) routes. Not all substances will have data on each route of exposure and will not, therefore, have all five of the tables and figures.

(2) Exposure Period. Three exposure periods—acute (less than 15 days), intermediate (15–364 days), and chronic (365 days or more)—are presented within each relevant route of exposure. In this example, an inhalation study of intermediate exposure duration is reported. For quick reference to health effects occurring from a known length of exposure, locate the applicable exposure period within the LSE table and figure.

(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 (see key number 18).

(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 derive a NOAEL and a Less Serious LOAEL (also see the two "18r" data points in sample Figure 3-1).

(5) Species. The test species, whether animal or human, are identified in this column. Chapter 2, "Relevance to Public Health," covers the relevance of animal data to human toxicity and Section 3.4, "Toxicokinetics," contains any available information on comparative toxicokinetics. Although NOAELs and LOAELs are species specific, the levels are extrapolated to equivalent human doses to derive an MRL.

(6) Exposure Frequency/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 “Chemical x” via inhalation for 6 hours/day, 5 days/week, for 13 weeks. For a more complete review of the dosing regimen refer to the appropriate sections of the text or the original reference paper (i.e., Nitschke et al. 1981).

(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.

(8) NOAEL. A 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 MRL of 0.005 ppm (see footnote "b").

(9) LOAEL. A LOAEL is the lowest dose 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 increasing dose. A brief description of the specific end point used to quantify the adverse effect accompanies the LOAEL. The respiratory effect reported in key number 18 (hyperplasia) is a Less Serious LOAEL of 10 ppm. MRLs are not derived from Serious LOAELs.

(10) Reference. The complete reference citation is given in Chapter 9 of the profile.

(11) CEL. A CEL is the lowest exposure level associated with the onset of carcinogenesis in experimental or epidemiologic studies. CELs are always considered serious effects. The LSE tables and figures do not contain NOAELs for cancer, but the text may report doses not causing measurable cancer increases.

(12) Footnotes. Explanations of abbreviations or reference notes for data in the LSE tables are found in the footnotes. Footnote "b" indicates that the NOAEL of 3 ppm in key number 18 was used to derive an MRL of 0.005 ppm.

LEGEND

See Sample Figure 3-1 (page B-7)

LSE figures graphically illustrate the data presented in the corresponding LSE tables. Figures help the reader quickly compare health effects according to exposure concentrations for particular exposure periods.

(13) Exposure Period. The same exposure periods appear as in the LSE table. In this example, health effects observed within the acute and intermediate exposure periods are illustrated.

(14) Health Effect. These are the categories of health effects for which reliable quantitative data exists. The same health effects appear in the LSE table.

(15) Levels of Exposure. Concentrations or doses for each health effect in the LSE tables are graphically displayed in the LSE figures. Exposure concentration or dose is measured 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, the open circle designated 18r identifies a NOAEL critical end point in the rat upon which an intermediate inhalation exposure MRL is based. 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 CELs were derived. The diamond symbol refers to a CEL for the test species-mouse. 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 the 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

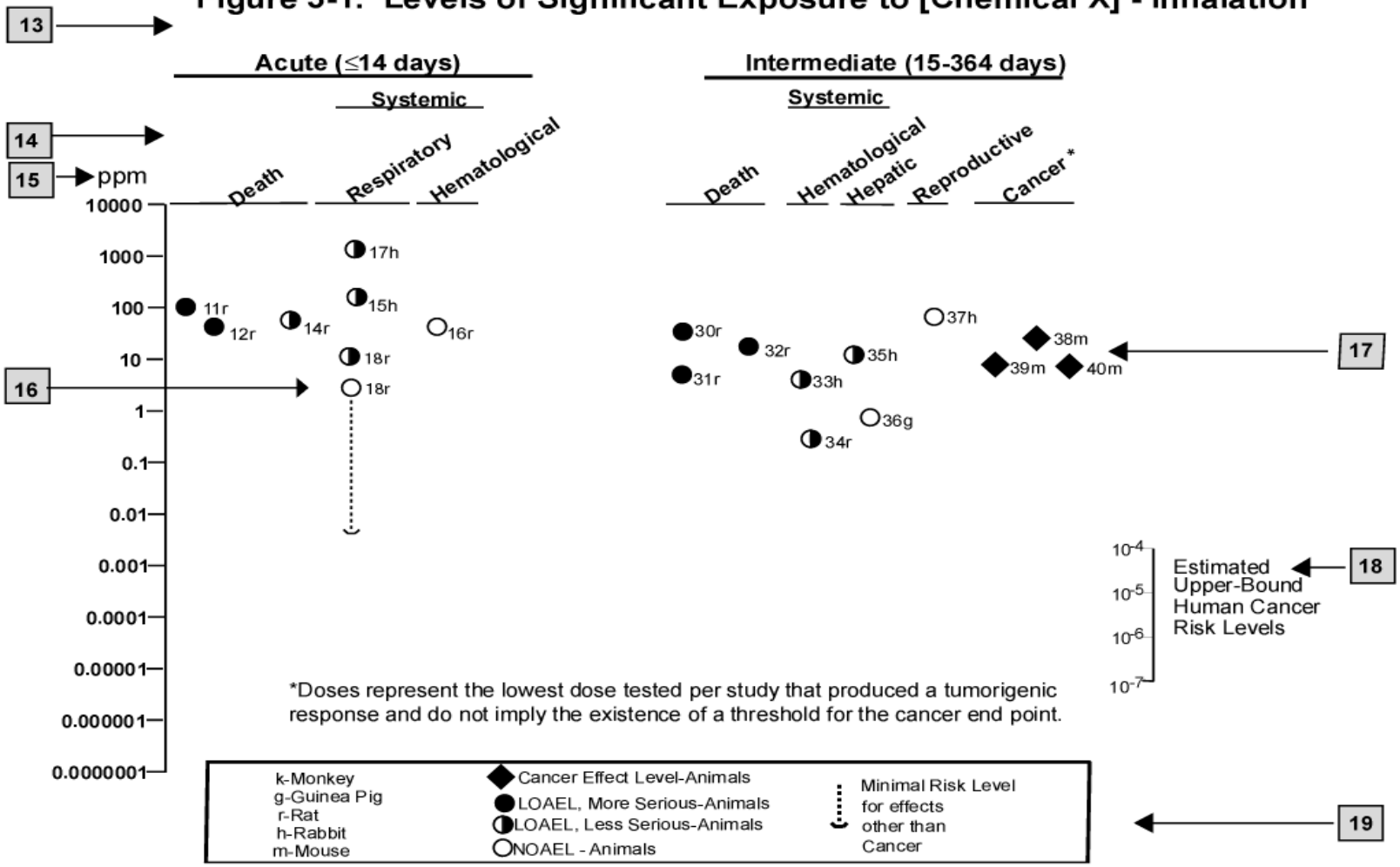
1 → **TABLE 3-1. Levels of Significant Exposure to [Chemical x] – Inhalation**

Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect) Less serious (ppm)	Serious (ppm)	Reference
2 → INTERMEDIATE EXPOSURE							
	5	6	7	8	9		10
3 → Systemic	↓	↓	↓	↓	↓		↓
18	Rat	13 wk 5 d/wk 6 hr/d	Resp	3[b]	10 (hyperplasia)		Nitschke et al. 1981
4 → CHRONIC EXPOSURE							
Cancer						11	
						↓	
38	Rat	18 mo 5 d/wk 7 hr/d				20 (CEL, multiple organs)	Wong et al. 1982
39	Rat	89-104 wk 5 d/wk 6 hr/d				10 (CEL, lung tumors, nasal tumors)	NTP 1982
40	Mouse	79-103 wk 5 d/wk 6 hr/d				10 (CEL, lung tumors, hemangiosarcomas)	NTP 1982

12 → a The number corresponds to entries in Figure 3-1.
b Used to derive an intermediate inhalation Minimal Risk Level (MRL) of 5x10-3 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).

SAMPLE

Figure 3-1. Levels of Significant Exposure to [Chemical X] - Inhalation



APPENDIX C. ACRONYMS, ABBREVIATIONS, AND SYMBOLS

Some terms are generic and may not be used in this profile.

ACGIH	American Conference of Governmental Industrial Hygienists
ACOEM	American College of Occupational and Environmental Medicine
ADI	acceptable daily intake
ADME	absorption, distribution, metabolism, and excretion
AED	atomic emission detection
AFID	alkali flame ionization detector
AFOSH	Air Force Office of Safety and Health
ALI	annual limit on intake
ALT	alanine aminotransferase
AML	acute myeloid leukemia
AOAC	Association of Official Analytical Chemists
AOEC	Association of Occupational and Environmental Clinics
AP	alkaline phosphatase
APHA	American Public Health Association
AST	aspartate aminotransferase
atm	atmosphere
ATSDR	Agency for Toxic Substances and Disease Registry
AWQC	Ambient Water Quality Criteria
BAT	best available technology
BCF	bioconcentration factor
BEI	Biological Exposure Index
BMD	benchmark dose
BMR	benchmark response
BSC	Board of Scientific Counselors
C	centigrade
CAA	Clean Air Act
CAG	Cancer Assessment Group of the U.S. Environmental Protection Agency
CAS	Chemical Abstract Services
CDC	Centers for Disease Control and Prevention
CEL	cancer effect level
CELDS	Computer-Environmental Legislative Data System
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
Ci	curie
CI	confidence interval
CL	ceiling limit value
CLP	Contract Laboratory Program
cm	centimeter
CML	chronic myeloid leukemia
CPSC	Consumer Products Safety Commission
CWA	Clean Water Act
DAC	derived air concentration
DHEW	Department of Health, Education, and Welfare
DHHS	Department of Health and Human Services
DNA	deoxyribonucleic acid
DOD	Department of Defense

DOE	Department of Energy
DOL	Department of Labor
DOT	Department of Transportation
DOT/UN/ NA/IMCO	Department of Transportation/United Nations/ North America/International Maritime Dangerous Goods Code
DWEL	drinking water exposure level
ECD	electron capture detection
ECG/EKG	electrocardiogram
EEG	electroencephalogram
EEGL	Emergency Exposure Guidance Level
EPA	Environmental Protection Agency
F	Fahrenheit
F_1	first-filial generation
FAO	Food and Agricultural Organization of the United Nations
FDA	Food and Drug Administration
FEMA	Federal Emergency Management Agency
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FPD	flame photometric detection
fpm	feet per minute
FR	Federal Register
FSH	follicle stimulating hormone
g	gram
GC	gas chromatography
gd	gestational day
GLC	gas liquid chromatography
GPC	gel permeation chromatography
HPLC	high-performance liquid chromatography
HRGC	high resolution gas chromatography
HSDB	Hazardous Substance Data Bank
IARC	International Agency for Research on Cancer
IDLH	immediately dangerous to life and health
ILO	International Labor Organization
IRIS	Integrated Risk Information System
Kd	adsorption ratio
kg	kilogram
kkg	metric ton
K_{oc}	organic carbon partition coefficient
K_{ow}	octanol-water partition coefficient
L	liter
LC	liquid chromatography
LC_{50}	lethal concentration, 50% kill
LC_{Lo}	lethal concentration, low
LD_{50}	lethal dose, 50% kill
LD_{Lo}	lethal dose, low
LDH	lactic dehydrogenase
LH	luteinizing hormone
LOAEL	lowest-observed-adverse-effect level
LSE	Levels of Significant Exposure
LT_{50}	lethal time, 50% kill
m	meter
MA	*trans,trans*-muconic acid

MAL	maximum allowable level
mCi	millicurie
MCL	maximum contaminant level
MCLG	maximum contaminant level goal
MF	modifying factor
MFO	mixed function oxidase
mg	milligram
mL	milliliter
mm	millimeter
mmHg	millimeters of mercury
mmol	millimole
mppcf	millions of particles per cubic foot
MRL	Minimal Risk Level
MS	mass spectrometry
NAAQS	National Ambient Air Quality Standard
NAS	National Academy of Science
NATICH	National Air Toxics Information Clearinghouse
NATO	North Atlantic Treaty Organization
NCE	normochromatic erythrocytes
NCEH	National Center for Environmental Health
NCI	National Cancer Institute
ND	not detected
NFPA	National Fire Protection Association
ng	nanogram
NHANES	National Health and Nutrition Examination Survey
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute for Occupational Safety and Health
NIOSHTIC	NIOSH's Computerized Information Retrieval System
NLM	National Library of Medicine
nm	nanometer
nmol	nanomole
NOAEL	no-observed-adverse-effect level
NOES	National Occupational Exposure Survey
NOHS	National Occupational Hazard Survey
NPD	nitrogen phosphorus detection
NPDES	National Pollutant Discharge Elimination System
NPL	National Priorities List
NR	not reported
NRC	National Research Council
NS	not specified
NSPS	New Source Performance Standards
NTIS	National Technical Information Service
NTP	National Toxicology Program
ODW	Office of Drinking Water, EPA
OERR	Office of Emergency and Remedial Response, EPA
OHM/TADS	Oil and Hazardous Materials/Technical Assistance Data System
OPP	Office of Pesticide Programs, EPA
OPPT	Office of Pollution Prevention and Toxics, EPA
OPPTS	Office of Prevention, Pesticides and Toxic Substances, EPA
OR	odds ratio
OSHA	Occupational Safety and Health Administration

OSW	Office of Solid Waste, EPA
OTS	Office of Toxic Substances
OW	Office of Water
OWRS	Office of Water Regulations and Standards, EPA
PAH	polycyclic aromatic hydrocarbon
PBPD	physiologically based pharmacodynamic
PBPK	physiologically based pharmacokinetic
PCE	polychromatic erythrocytes
PEL	permissible exposure limit
pg	picogram
PHS	Public Health Service
PID	photo ionization detector
pmol	picomole
PMR	proportionate mortality ratio
ppb	parts per billion
ppm	parts per million
ppt	parts per trillion
PSNS	pretreatment standards for new sources
RBC	red blood cell
REL	recommended exposure level/limit
RfC	reference concentration
RfD	reference dose
RNA	ribonucleic acid
RQ	reportable quantity
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
SCE	sister chromatid exchange
SGOT	serum glutamic oxaloacetic transaminase
SGPT	serum glutamic pyruvic transaminase
SIC	standard industrial classification
SIM	selected ion monitoring
SMCL	secondary maximum contaminant level
SMR	standardized mortality ratio
SNARL	suggested no adverse response level
SPEGL	Short-Term Public Emergency Guidance Level
STEL	short term exposure limit
STORET	Storage and Retrieval
TD_{50}	toxic dose, 50% specific toxic effect
TLV	threshold limit value
TOC	total organic carbon
TPQ	threshold planning quantity
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
TWA	time-weighted average
UF	uncertainty factor
U.S.	United States
USDA	United States Department of Agriculture
USGS	United States Geological Survey
USNRC	United States Nuclear Regulatory Commission
VOC	volatile organic compound

WBC	white blood cell
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
γ	gamma
δ	delta
μm	micrometer
μg	microgram
q_1^*	cancer slope factor
–	negative
+	positive
(+)	weakly positive result
(–)	weakly negative result

APPENDIX D. OVERVIEW OF BASIC RADIATION PHYSICS, CHEMISTRY, AND BIOLOGY

Understanding the basic concepts in radiation physics, chemistry, and biology is important to the evaluation and interpretation of radiation-induced adverse health effects and to the derivation of radiation protection principles. This appendix presents a brief overview of the areas of radiation physics, chemistry, and biology and is based to a large extent on the reviews of Mettler and Moseley (1985), Hobbs and McClellan (1986), Eichholz (1982), Hendee (1973), Cember (1996), and Early et al. (1979).

D.1 RADIONUCLIDES AND RADIOACTIVITY

The substances we call elements are composed of atoms. Atoms in turn are made up of neutrons, protons and electrons: neutrons and protons in the nucleus and electrons in a cloud of orbits around the nucleus. Nuclide is the general term referring to any nucleus along with its orbital electrons. The nuclide is characterized by the composition of its nucleus and hence by the number of protons and neutrons in the nucleus. All atoms of an element have the same number of protons (this is given by the atomic number) but may have different numbers of neutrons (this is reflected by the atomic mass numbers or atomic weight of the element). Atoms with different atomic mass but the same atomic numbers are referred to as isotopes of an element.

The numerical combination of protons and neutrons in most nuclides is such that the nucleus is quantum mechanically stable and the atom is said to be stable, i.e., not radioactive; however, if there are too few or too many neutrons, the nucleus is unstable and the atom is said to be radioactive. Unstable nuclides undergo radioactive transformation, a process in which a neutron or proton converts into the other and a beta particle is emitted, or else an alpha particle is emitted. Each type of decay is typically accompanied by the emission of gamma rays. These unstable atoms are called radionuclides; their emissions are called ionizing radiation; and the whole property is called radioactivity. Transformation or decay results in the formation of new nuclides some of which may themselves be radionuclides, while others are stable nuclides. This series of transformations is called the decay chain of the radionuclide. The first radionuclide in the chain is called the parent; the subsequent products of the transformation are called progeny, daughters, or decay products.

In general there are two classifications of radioactivity and radionuclides: natural and artificial (man-made). Naturally-occurring radioactive materials (NORMs) exist in nature and no additional energy is necessary to place them in an unstable state. Natural radioactivity is the property of some naturally occurring, usually heavy elements, that are heavier than lead. Radionuclides, such as radium and uranium, primarily emit alpha particles. Some lighter elements such as carbon-14 and tritium (hydrogen-3) primarily emit beta particles as they transform to a more stable atom. Natural radioactive atoms heavier than lead cannot attain a stable nucleus heavier than lead. Everyone is exposed to background radiation from naturally-occurring radionuclides throughout life. This background radiation is the major source of radiation exposure to man and arises from several sources. The natural background exposures are frequently used as a standard of comparison for exposures to various artificial sources of ionizing radiation.

Artificial radioactive atoms are produced either as a by-product of fission of uranium or plutonium atoms in a nuclear reactor or by bombarding stable atoms with particles, such as neutrons or protons, directed at the stable atoms with high velocity. These artificially produced radioactive elements usually decay by emission of particles, such as positive or negative beta particles and one or more high energy photons (gamma rays). Unstable (radioactive) atoms of any element can be produced.

Both naturally occurring and artificial radioisotopes find application in medicine, industrial products, and consumer products. Some specific radioisotopes, called fall-out, are still found in the environment as a result of nuclear weapons use or testing.

D.2 RADIOACTIVE DECAY

D.2.1 Principles of Radioactive Decay

The stability of an atom is the result of the balance of the forces of the various components of the nucleus. An atom that is unstable (radionuclide) will release energy (decay) in various ways and transform to stable atoms or to other radioactive species called daughters, often with the release of ionizing radiation. If there are either too many or too few neutrons for a given number of protons, the resulting nucleus may undergo transformation. For some elements, a chain of daughter decay products may be produced until stable atoms are formed. Radionuclides can be characterized by the type and energy of the radiation emitted, the rate of decay, and the mode of decay. The mode of decay indicates how a parent compound undergoes transformation. Radiations considered here are primarily of nuclear origin, i.e., they arise from nuclear excitation, usually caused by the capture of charged or uncharged nucleons by a nucleus, or by the radioactive decay or transformation of an unstable nuclide. The type of radiation may be categorized as charged or uncharged particles, protons, and fission products) or electromagnetic radiation (gamma rays and x rays). Table D-1 summarizes the basic characteristics of the more common types of radiation encountered.

D.2.2 Half-Life and Activity

For any given radionuclide, the rate of decay is a first-order process that is constant, regardless of the radioactive atoms present and is characteristic for each radionuclide. The process of decay is a series of random events; temperature, pressure, or chemical combinations do not effect the rate of decay. While it may not be possible to predict exactly which atom is going to undergo transformation at any given time, it is possible to predict, on average, the fraction of the radioactive atoms that will transform during any interval of time.

The *activity* is a measure of the quantity of radioactive material. For these radioactive materials it is customary to describe the activity as the number of disintegrations (transformations) per unit time. The unit of activity is the curie (Ci), which was originally related to the activity of one gram of radium, but is now defined as that quantity of radioactive material in which there are:

1 curie (Ci) = 3.7×10^{10} disintegrations (transformations)/second (dps) or 2.22×10^{12} disintegrations (transformations)/minute (dpm).

The SI unit of activity is the becquerel (Bq); 1 Bq = that quantity of radioactive material in which there is 1 transformation/second. Since activity is proportional to the number of atoms of the radioactive material, the quantity of any radioactive material is usually expressed in curies, regardless of its purity or concentration. The transformation of radioactive nuclei is a random process, and the number of transformations is directly proportional to the number of radioactive atoms present. For any pure radioactive substance, the rate of decay is usually described by its radiological half-life, T_R, i.e., the time it takes for a specified source material to decay to half its initial activity. The specific activity is the activity of a radionuclide per mass of that radionuclide. If properly qualified, it can refer to activity per unit mass of related materials, such as the element itself or a chemical compound labeled with the radionuclide. The higher the specific activity of a radioisotope, the faster it is decaying.

The activity of a radionuclide at time t may be calculated by:

$$A = A_o e^{-0.693t/Trad}$$

where A is the activity in dps or curies or becquerels, A_o is the activity at time zero, t is the time at which measured, and T_{rad} is the radiological half-life of the radionuclide (T_{rad} and t must be in the same units of time). The time when the activity of a sample of radioactivity becomes one-half its original value is the radioactive half-life and is expressed in any suitable unit of time.

Table D-1. Characteristics of Nuclear Radiations

Radiation	Rest mass[a]	Charge	Typical energy range	Path length[b]		Comments
				Air	Solid	
Alpha (α)	4.00 amu	+2	4–10 MeV	5–10 cm	25–80 μm	Identical to ionized He nucleus
Negatron (β^-)	$5.48x10^{-4}$ amu; 0.51 MeV	–1	0–4 MeV	0–10 m	0–1 cm	Identical to electron
Positron (β^+)	$5.48x10^{-4}$ amu; 0.51 MeV	+1	0-4 MeV	0–10 m	0–1 cm	Identical to electron except for sign of charge
Neutron	1.0086 amu; 939.55 MeV	0	0–15 MeV	b	b	Free half-life: 16 min
X ray (e.m. photon)	–	0	5 keV–100 keV	b	b	Photon from transition of an electron between atomic orbits
Gamma (ɣ) (e.m. photon)	–	0	10 keV–3 MeV	b	b	Photon from nuclear transformation

[a] The rest mass (in amu) has an energy equivalent in MeV that is obtained using the equation $E=mc^2$, where 1 amu = 932 MeV.
[b] Path lengths are not applicable to x- and gamma rays since their intensities decrease exponentially; path lengths in solid tissue are variable, depending on particle energy, electron density of material, and other factors.

amu = atomic mass unit; e.m. = electromagnetic; MeV = Megaelectron Volts

The specific activity is a measure of activity, and is defined as the activity of a radionuclide per mass of that radionuclide. This activity is usually expressed in curies per gram and may be calculated by

$$\text{curies/gram} = 1.3x10^8 / (T_{rad})\ (\text{atomic weight}) \quad \text{or}$$

$$[3.577 \times 10^5 \times \text{mass(g)}] / [T_{rad} \times \text{atomic weight}]$$

where T_{rad} is the radiological half-life in days.

In the case of radioactive materials contained in living organisms, an additional consideration is made for the reduction in observed activity due to regular processes of elimination of the respective chemical or biochemical substance from the organism. This introduces a rate constant called the biological half-life (T_{biol}) which is the time required for biological processes to eliminate one-half of the activity. This time is virtually the same for both stable and radioactive isotopes of any given element.

Under such conditions the time required for a radioactive element to be halved as a result of the combined action of radioactive decay and biological elimination is the effective clearance half-time:

$$T_{eff} = (T_{biol} \times T_{rad}) / (T_{biol} + T_{rad}).$$

Table D-2 presents representative effective half-lives of particular interest.

Table D-2. Half-Lives of Some Radionuclides in Adult Body Organs

		Half-life[a]		
Radionuclide	Critical organ	Physical	Biological	Effective
Uranium 238	Kidney	4,460,000,000 y	4 d	4 d
Hydrogen 3[b] (Tritium)	Whole body	12.3 y	10 d	10 d
Iodine 131	Thyroid	8 d	80 d	7.3 d
Strontium 90	Bone	28 y	50 y	18 y
Plutonium 239	Bone surface	24,400 y	50 y	50 y
	Lung	24,400 y	500 d	474 d
Cobalt 60	Whole body	5.3 y	99.5 d	95 d
Iron 55	Spleen	2.7 y	600 d	388 d
Iron 59	Spleen	45.1 d	600 d	42 d
Manganese 54	Liver	303 d	25 d	23 d
Cesium 137	Whole body	30 y	70 d	70 d

[a]d = days, y = years
[b]Mixed in body water as tritiated water

D.2.3 Interaction of Radiation with Matter

Both ionizing and nonionizing radiation will interact with materials; that is, radiation will lose kinetic energy to any solid, liquid or gas through which it passes by a variety of mechanisms. The transfer of energy to a medium by either electromagnetic or particulate radiation may be sufficient to cause formation of ions. This process is called ionization. Compared to other types of radiation that may be absorbed, such as ultraviolet radiation, ionizing radiation deposits a relatively large amount of energy into a small volume.

The method by which incident radiation interacts with the medium to cause ionization may be direct or indirect. Electromagnetic radiations (x rays and gamma photons) are indirectly ionizing; that is, they give up their energy in various interactions with cellular molecules, and the energy is then utilized to produce a fast-moving charged particle such as an electron. It is the electron that then may react with a target molecule. This particle is called a “primary ionizing particle. Charged particles, in contrast, strike the tissue or medium and directly react with target molecules, such as oxygen or water. These particulate radiations are directly ionizing radiations. Examples of directly ionizing particles include alpha and beta particles. Indirectly ionizing radiations are always more penetrating than directly ionizing particulate radiations.

Mass, charge, and velocity of a particle, as well as the electron density of the material with which it interacts, all affect the rate at which ionization occurs. The higher the charge of the particle and the lower the velocity, the greater the propensity to cause ionization. Heavy, highly charged particles, such as alpha

particles, lose energy rapidly with distance and, therefore, do not penetrate deeply. The result of these interaction processes is a gradual slowing down of any incident particle until it is brought to rest or "stopped" at the end of its range.

D.2.4 Characteristics of Emitted Radiation

D.2.4.1 Alpha Emission. In alpha emission, an alpha particle consisting of two protons and two neutrons is emitted with a resulting decrease in the atomic mass number by four and reduction of the atomic number of two, thereby changing the parent to a different element. The alpha particle is identical to a helium nucleus consisting of two neutrons and two protons. It results from the radioactive decay of some heavy elements such as uranium, plutonium, radium, thorium, and radon. The alpha particles emitted by a given radionuclide have the same energy and intensity combination. Most of the alpha particles that are likely to be found have energies in the range of about 4 to 8 MeV, depending on the isotope from which they came.

The alpha particle has an electrical charge of +2. Because of this double positive charge and their size, alpha particles have great ionizing power and, thus, lose their kinetic energy quickly. This results in very little penetrating power. In fact, an alpha particle cannot penetrate a sheet of paper. The range of an alpha particle (the distance the charged particle travels from the point of origin to its resting point) is about 4 cm in air, which decreases considerably to a few micrometers in tissue. These properties cause alpha emitters to be hazardous only if there is internal contamination (i.e., if the radionuclide is inside the body).

D.2.4.2 Beta Emission. A beta particle (β) is a high-velocity electron ejected from a disintegrating nucleus. The particle may be either a negatively charged electron, termed a negatron (β-) or a positively charged electron, termed a positron (β+). Although the precise definition of "beta emission" refers to both β- and β+, common usage of the term generally applies only to the negative particle, as distinguished from the positron emission, which refers to the β+ particle.

D.2.4.2.1 Beta Negative Emission. Beta particle (β-) emission is another process by which a radionuclide, with a neutron excess achieves stability. Beta particle emission decreases the number of neutrons by one and increases the number of protons by one, while the atomic mass number remains unchanged.[1] This transformation results in the formation of a different element. The energy spectrum of beta particle emission ranges from a certain maximum down to zero with the mean energy of the spectrum being about one-third of the maximum. The range of betas is much less in tissue than in air. Beta negative emitting radionuclides can cause injury to the skin and superficial body tissues, but mostly present an internal contamination hazard.

D.2.4.2.2 Positron Emission. In cases in which there are too many protons in the nucleus, positron emission may occur. In this case a proton may be thought of as being converted into a neutron, and a positron (β+) is emitted.1 This increases the number of neutrons by one, decreases the number of protons by one, and again leaves the atomic mass number unchanged. The gamma radiation resulting from the annihilation (see glossary) of the positron makes all positron emitting isotopes more of an external radiation hazard than pure β emitters of equal energy.

D.2.4.2.3 Gamma Emission. Radioactive decay by alpha, beta, or positron emission, or electron capture often leaves some of the energy resulting from these changes in the nucleus. As a result, the nucleus is raised to an excited level. None of these excited nuclei can remain in this high-energy state. Nuclei release this energy returning to ground state or to the lowest possible stable energy level. The

[1] Neutrinos also accompany negative beta particles and positron emissions

energy released is in the form of gamma radiation (high energy photons) and has an energy equal to the change in the energy state of the nucleus. Gamma and x rays behave similarly but differ in their origin; gamma emissions originate in the nucleus while x rays originate in the orbital electron structure or from rapidly changing the velocity of an electron (e.g., as occurs when shielding high energy beta particles or stopping the electron beam in an x ray tube).

D.3 ESTIMATION OF ENERGY DEPOSITION IN HUMAN TISSUES

Two forms of potential radiation exposures can result: internal and external. The term exposure denotes physical interaction of the radiation emitted from the radioactive material with cells and tissues of the human body. An exposure can be "acute" or "chronic" depending on how long an individual or organ is exposed to the radiation. Internal exposures occur when radionuclides, which have entered the body (e.g., through the inhalation, ingestion, or dermal pathways), undergo radioactive decay resulting in the deposition of energy to internal organs. External exposures occur when radiation enters the body directly from sources located outside the body, such as radiation emitters from radionuclides on ground surfaces, dissolved in water, or dispersed in the air. In general, external exposures are from material emitting gamma radiation, which readily penetrate the skin and internal organs. Beta and alpha radiation from external sources are far less penetrating and deposit their energy primarily on the skin's outer layer. Consequently, their contribution to the absorbed dose of the total body dose, compared to that deposited by gamma rays, may be negligible.

Characterizing the radiation dose to persons as a result of exposure to radiation is a complex issue. It is difficult to: (1) measure internally the amount of energy actually transferred to an organic material and to correlate any observed effects with this energy deposition; and (2) account for and predict secondary processes, such as collision effects or biologically triggered effects, that are an indirect consequence of the primary interaction event.

D.3.1 Dose/Exposure Units

D.3.1.1 Roentgen. The roentgen (R) is a unit of x or gamma-ray exposure and is a measured by the amount of ionization caused in air by gamma or x radiation. One roentgen produces 2.58×10^{-4} coulomb per kilogram of air. In the case of gamma radiation, over the commonly encountered range of photon energy, the energy deposition in tissue for a dose of 1 R is about 0.0096 joules (J) /kg of tissue.

D.3.1.2 Absorbed Dose and Absorbed Dose Rate. The absorbed dose is defined as the energy imparted by radiation to a unit mass of the tissue or organ. The unit of absorbed dose is the rad; 1 rad = 100 erg/gram = 0.01 J/kg in any medium. An exposure of 1 R results in a dose to soft tissue of approximately 0.01 J/kg. The SI unit is the gray which is equivalent to 100 rad or 1 J/kg. Internal and external exposures from radiation sources are not usually instantaneous but are distributed over extended periods of time. The resulting rate of change of the absorbed dose to a small volume of mass is referred to as the absorbed dose rate in units of rad/unit time.

D.3.1.3 Working Levels and Working Level Months. Working level (WL) is a measure of the atmospheric concentration of radon and its short-lived progeny. One WL is defined as any combination of short-lived radon daughters (through polonium-214), per liter of air, that will result in the emission of 1.3×10^5 MeV of alpha energy. An activity concentration of 100 pCi radon-222/L of air, in equilibrium with its daughters, corresponds approximately to a potential alpha-energy concentration of 1 WL. The WL unit can also be used for thoron daughters. In this case, 1.3×10^5 MeV of alpha energy (1 WL) is released by the thoron daughters in equilibrium with 7.5 pCi thoron/L. The potential alpha energy exposure of miners is commonly expressed in the unit Working Level Month (WLM). One WLM

corresponds to exposure to a concentration of 1 WL for the reference period of 170 hours, or more generally

WLM = concentration (WL) x exposure time (months) (one “month” = 170 working hours).

D.3.2 Dosimetry Models

Dosimetry models are used to estimate the dose from internally deposited to radioactive substances. The models for internal dosimetry consider the amount of radionuclides entering the body, the factors affecting their movement or transport through the body, distribution and retention of radionuclides in the body, and the energy deposited in organs and tissues from the radiation that is emitted during spontaneous decay processes. The dose pattern for radioactive materials in the body may be strongly influenced by the route of entry of the material. For industrial workers, inhalation of radioactive particles with pulmonary deposition and puncture wounds with subcutaneous deposition have been the most frequent. The general population has been exposed via ingestion and inhalation of low levels of naturally occurring radionuclides as well as radionuclides from nuclear weapons testing.

The models for external dosimetry consider only the photon doses (and neutron doses, where applicable) to organs of individuals who are immersed in air or are exposed to a contaminated object.

D.3.2.1 Ingestion. Ingestion of radioactive materials is most likely to occur from contaminated foodstuffs or water or eventual ingestion of inhaled compounds initially deposited in the lung. Ingestion of radioactive material may result in toxic effects as a result of either absorption of the radionuclide or irradiation of the gastrointestinal tract during passage through the tract, or a combination of both. The fraction of a radioactive material absorbed from the gastrointestinal tract is variable, depending on the specific element, the physical and chemical form of the material ingested, and the diet, as well as some other metabolic and physiological factors. The absorption of some elements is influenced by age, usually with higher absorption in the very young.

D.3.2.2 Inhalation. The inhalation route of exposure has long been recognized as being a major portal of entry for both nonradioactive and radioactive materials. The deposition of particles within the lung is largely dependent upon the size of the particles being inhaled. After the particle is deposited, the retention will depend upon the physical and chemical properties of the dust and the physiological status of the lung. The retention of the particle in the lung depends on the location of deposition, in addition to the physical and chemical properties of the particles. The converse of pulmonary retention is pulmonary clearance. There are three distinct mechanisms of clearance which operate simultaneously. Ciliary clearance acts only in the upper respiratory tract. The second and third mechanisms act mainly in the deep respiratory tract. These are phagocytosis and absorption. Phagocytosis is the engulfing of foreign bodies by alveolar macrophages and their subsequent removal either up the ciliary "escalator" or by entrance into the lymphatic system. Some inhaled soluble particles are absorbed into the blood and translocated to other organs and tissues.

D.3.3 Internal Emitters

An internal emitter is a radionuclide that is inside the body. The absorbed dose from internally deposited radionuclide depends on the energy absorbed per unit mass by the irradiated tissue. For a radionuclide distributed uniformly throughout an infinitely large medium, the concentration of absorbed energy must be equal to the concentration of energy emitted by the radionuclide. An infinitely large medium may be approximated by a tissue mass whose dimensions exceed the range of the particle. All alpha and most beta radiation will be absorbed in the organ (or tissue) of reference. Gamma-emitting radionuclide emissions are penetrating radiation, and a substantial fraction of gamma energy may be absorbed in

tissue. The dose to an organ or tissue is a function of the effective retention half-time, the energy released in the tissue, the amount of radioactivity initially introduced, and the mass of the organ or tissue.

D.4 BIOLOGICAL EFFECTS OF RADIATION

When biological material is exposed to ionizing radiation, a chain of cellular events occurs as the ionizing particle passes through the biological material. A number of theories have been proposed to describe the interaction of radiation with biologically important molecules in cells and to explain the resulting damage to biological systems from those interactions. Many factors may modify the response of a living organism to a given dose of radiation. Factors related to the exposure include the dose rate, the energy of the radiation, and the temporal pattern of the exposure. Biological considerations include factors such as species, age, sex, and the portion of the body exposed. Several excellent reviews of the biological effects of radiation have been published, and the reader is referred to these for a more in-depth discussion (Brodsky 1996; Hobbs and McClellan 1986; ICRP 1984; Mettler and Moseley 1985; Rubin and Casarett 1968).

D.4.1 Radiation Effects at the Cellular Level

According to Mettler and Moseley (1985), at acute doses up to 10 rad (100 mGy), single strand breaks in DNA may be produced. These single strand breaks may be repaired rapidly. With doses in the range of 50–500 rad (0.5–5 Gy), irreparable double-stranded DNA breaks are likely, resulting in cellular reproductive death after one or more divisions of the irradiated parent cell. At large doses of radiation, usually greater than 500 rad (5 Gy), direct cell death before division (interphase death) may occur from the direct interaction of free-radicals with essential cellular macromolecules. Morphological changes at the cellular level, the severity of which are dose-dependent, may also be observed.

The sensitivity of various cell types varies. According to the Bergonie-Tribondeau law, the sensitivity of cell lines is directly proportional to their mitotic rate and inversely proportional to the degree of differentiation (Mettler and Moseley 1985). Rubin and Casarett (1968) devised a classification system that categorized cells according to type, function, and mitotic activity. The categories range from the most sensitive type, "vegetative intermitotic cells", found in the stem cells of the bone marrow and the gastrointestinal tract, to the least sensitive cell type, "fixed postmitotic cells," found in striated muscles or long-lived neural tissues.

Cellular changes may result in cell death, which if extensive, may produce irreversible damage to an organ or tissue or may result in the death of the individual. If the cell recovers, altered metabolism and function may still occur, which may be repaired or may result in the manifestation of clinical symptoms. These changes may also be expressed at a later time as tumors or cellular mutations, which may result in abnormal tissue.

D.4.2 Radiation Effects at the Organ Level

In most organs and tissues the injury and the underlying mechanism for that injury are complex and may involve a combination of events. The extent and severity of this tissue injury are dependent upon the radiosensitivity of the various cell types in that organ system. Rubin and Casarett (1968) describe and schematically display the events following radiation in several organ system types. These include: a rapid renewal system, such as the gastrointestinal mucosa; a slow renewal system, such as the pulmonary epithelium; and a nonrenewal system, such as neural or muscle tissue. In the rapid renewal system, organ injury results from the direct destruction of highly radiosensitive cells, such as the stem cells in the bone marrow. Injury may also result from constriction of the microcirculation and from edema and inflammation of the basement membrane, designated as the histohematic barrier, which may progress to

fibrosis. In slow renewal and nonrenewal systems, the radiation may have little effect on the parenchymal cells, but ultimate parenchymal atrophy and death over several months result from fibrosis and occlusion of the microcirculation.

D.4.3 Low Level Radiation Effects

Cancer is the major latent harmful effect produced by ionizing radiation and the one that most people exposed to radiation are concerned about. The ability of alpha, beta, and gamma radiation to produce cancer in virtually every tissue and organ in laboratory animals has been well-demonstrated. The development of cancer is not an immediate effect. Radiation-induced leukemia has the shortest latent period at about 2 years, while other radiation induced cancers, such as osteosarcoma, have latent periods greater than 20 years. The mechanism by which cancer is induced in living cells is complex and is a topic of intense study. Exposure to ionizing radiation can produce cancer at any site within the body; however, some sites appear to be more common than others, such as the breast, lung, stomach, and thyroid.

DNA is the major target molecule during exposure to ionizing radiation. Other macromolecules, such as lipids and proteins, are also at risk of damage when exposed to ionizing radiation. The genotoxicity of ionizing radiation is an area of intense study, as damage to the DNA is ultimately responsible for many of the adverse toxicological effects ascribed to ionizing radiation, including cancer. Damage to genetic material is basic to developmental or teratogenic effects, as well. However, for effects other than cancer, there is little evidence of human effects at low levels of exposure.

D.5 UNITS IN RADIATION PROTECTION AND REGULATION

D.5.1 Dose Equivalent (or Equivalent Dose)

Dose equivalent (as measured in rem or sievert) is a special radiation protection quantity that is used for administrative and radiation safety purposes to express the absorbed dose in a manner which considers the difference in biological effectiveness of various kinds of ionizing radiation. ICRP (1990) changed this term to equivalent dose, but it has not yet been adopted by the USNRC or DOE.

The USNRC defines the dose equivalent, H, as the product of the absorbed dose, D, and the quality factor, Q, at the point of interest in biological tissue. This relationship is expressed as $H = D \times Q$. The dose equivalent concept is applicable only to doses that are not great enough to produce biomedical effects.

The quality factor or radiation weighting factor is a dimensionless quantity that depends in part on the stopping power for charged particles, and it accounts for the differences in biological effectiveness found among the types of radiation. Originally relative biological effectiveness (RBE) was used rather than Q to define the quantity, rem, which was of use in risk assessment. The generally accepted values for quality factors and radiation weighting factors for various radiation types are provided in Table D-3. The dose equivalent rate is the time rate of change of the dose equivalent to organs and tissues and is expressed as rem/unit time or sievert/unit time.

Table D-3. Quality Factors (Q) and Absorbed Dose Equivalencies

Type of radiation	Quality factor (Q)	Radiation weighting factor (w_r)*
X, gamma, or beta radiation	1	1
Alpha particles, multiple-charged particles, fission fragments and heavy particles of unknown charge	20	0.05
Neutrons (other than thermal >> 100 keV to 2 MeV), protons, alpha particles, charged particles of unknown energy	10	20
Neutrons of unknown energy	10	
High-energy protons	10	0.1
Thermal neutrons		5

*Absorbed dose in rad equal to 1 rem or the absorbed dose in gray equal to 1 sievert.

Source: USNRC. 2004. Standards for the protection against radiation, table 1004(b).1. 10 CFR 20.1004. U.S. Nuclear Regulatory Commission, Washington, D.C. NCRP 1993.

D.5.2 Relative Biological Effectiveness

RBE is used to denote the experimentally determined ratio of the absorbed dose from one radiation type to the absorbed dose of a reference radiation required to produce an identical biologic effect under the same conditions. Gamma rays from cobalt-60 and 200–250 kVp x-rays have been used as reference standards. The term RBE has been widely used in experimental radiobiology, and the term quality factor (or radiation weighting factor) used in calculations of dose equivalents for radiation safety purposes (ICRP 1977; NCRP 1971; UNSCEAR 1982). Any RBE value applies only to a specific biological end point, in a specific exposure, under specific conditions to a specific species. There are no generally applicable values of RBE since RBEs are specific to a given exposure scenario.

D.5.3 Effective Dose Equivalent (or Effective Dose)

The absorbed dose is usually defined as the mean energy imparted per unit mass to an organ or tissue. This represents a simplification of the actual problem. Normally when an individual ingests or inhales a radionuclide or is exposed to external radiation that enters the body (gamma), the dose is not uniform throughout the whole body. The simplifying assumption is that the detriment will be the same whether the body is uniformly or non-uniformly irradiated. In an attempt to compare detriment from absorbed dose of a limited portion of the body with the detriment from total body dose, the ICRP (1977) has derived a concept of effective dose equivalent. ICRP (1990) changed this term to effective dose, but it has not yet been adopted by the USNRC or DOE.

The effective dose equivalent, H_E, is

$$H_E = (\text{the sum of}) \; W_t \, H_t$$

where H_t is the dose equivalent (or equivalent dose) in the tissue t, W_t is the tissue weighting factor in that tissue, which represents the estimated proportion of the stochastic risk resulting from tissue, t, to the stochastic risk when the whole body is uniformly irradiated for occupational exposures under certain conditions (ICRP 1977). Tissue weighting factors for selected tissues are listed in Table D-4.

D.5.4 SI Units

The ICRU (1980), ICRP (1984), and NCRP (1985) now recommend that the rad, roentgen, curie, and rem be replaced by the SI units: gray (Gy), Coulomb per kilogram (C/kg), Becquerel (Bq), and sievert (Sv), respectively. The relationship between the customary units and the international system of units (SI) for radiological quantities is shown in Table D-5.

Table D-4. Tissue Weighting Factors for Calculating Effective Dose Equivalent and Effective Dose for Selected Tissues

	Tissue weighting factor	
Tissue	NCRP115/ ICRP60	USNRC/ICRP26
Bladder	0.05	–
Bone marrow	0.12	0.12
Bone surface	0.01	0.03
Breast	0.05	0.15
Colon	0.12	–
Esophagus	0.05	–
Gonads	0.20	0.25
Liver	0.05	–
Lung	0.12	0.12
Skin	0.01	–
Stomach	0.12	–
Thyroid	0.05	0.03
Remainder	0.05	0.30
Total	1.00	1.00

ICRP60 = International Commission on Radiological Protection, 1990 Recommendations of the ICRP
NCRP115 = National Council on Radiation Protection and Measurements. 1993. Risk Estimates for Radiation Protection, Report 115. Bethesda, Maryland
USNRC = Nuclear Regulatory Commission, Title 10, Code of Federal Regulations, Part 20

Table D-5. Comparison of Common and SI Units for Radiation Quantities

Quantity	Customary units	Definition	SI units	Definition
Activity (A)	curie (Ci)	3.7×10^{10} transformations s^{-1}	becquerel (Bq)	s^{-1}
Absorbed dose (D)	rad	10^{-2} Jkg^{-1}	gray (Gy)	Jkg^{-1}
Absorbed dose rate (Ď)	rad per second (rad s^{-1})	10^{-2} $Jkg^{-1}s^{-1}$	gray per second (Gy s^{-1})	Jkg^{-1} s^{-1}
Dose equivalent (H)	rem	10^{-2} Jkg^{-1}	sievert (Sv)	Jkg^{-1}
Dose equivalent rate ( )	rem per second (rem s^{-1})	10^{-2} $Jkg^{-1}s^{-1}$	sievert per second (Sv s^{-1})	Jkg^{-1} s^{-1}
Effective dose	rem	10^{-2} Jkg^{-1}	Sievert (Sv)	Jkg^{-1}
Equivalent dose (H)	rem	10^{-2} Jkg^{-1}	Sievert (Sv)	Jkg^{-1}
Linear energy transfer (LET)	kiloelectron volts per micrometer (keV μm^{-1})	1.602×10^{-10} Jm^{-1}	kiloelectron volts per micrometer (keV μm^{-1})	1.602×10^{-10} Jm^{-1}

Jkg^{-1} = Joules per kilogram; $Jkg^{-1}s^{-1}$ = Joules per kilogram per second; Jm^{-1} = Joules per meter; s^{-1} = per second

REFERENCES FOR APPENDIX D

ATSDR. 1990a. Toxicological profile for thorium. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. Atlanta, GA.

ATSDR. 1990b. Toxicological profile for radium. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. Atlanta, GA.

ATSDR. 1990c. Toxicological profile for radon. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. Atlanta, GA.

ATSDR. 1999. Toxicological profile for uranium. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. Atlanta, GA.

BEIR III. 1980. The effects on populations of exposure to low levels of ionizing radiation. Committee on the Biological Effects of Ionizing Radiations, National Research Council. Washington, DC: National Academy Press.

BEIR IV. 1988. Health risks of radon and other internally deposited alpha emitters. Committee on the Biological Effects of Ionizing Radiations, National Research Council. Washington, DC: National Academy Press.

BEIR V. 1988. Health effects of exposure to low levels of ionizing radiation. Committee on the Biological Effects of Ionizing Radiations, National Research Council. Washington, DC: National Academy Press.

Brodsky A. 1996. Review of radiation risks and uranium toxicity with application to decisions associated with decommissioning clean-up criteria. Hebron,Connecticut: RSA Publications.

Cember H. 1996. Introduction to health physics. New York., NY: McGraw Hill.

Early P, Razzak M, Sodee D. 1979. Nuclear medicine technology. 2nd ed. St. Louis: C.V. Mosby Company.

Eichholz G. 1982. Environmental aspects of nuclear power. Ann Arbor, MI: Ann Arbor Science.

Hendee W. 1973. Radioactive isotopes in biological research. New York, NY: John Wiley and Sons.

Hobbs C, McClellan R. 1986. Radiation and radioactive materials. In: Doull J, et al., eds. Casarett and Doull's Toxicology. 3rd ed. New York, NY: Macmillan Publishing Co., Inc., 497-530.

ICRP. 1977. International Commission on Radiological Protection. Recommendations of the International Commission on Radiological Protection. ICRP Publication 26. Vol 1. No. 3. Oxford: Pergamon Press.

ICRP. 1979. International Commission on Radiological Protection. Limits for intakes of radionuclides by workers. ICRP Publication 20. Vol. 3. No. 1-4. Oxford: Pergamon Press.

ICRP. 1979. Limits for Intakes of Radionuclides by Workers. Publication 30. International Commission on Radiological Protection. Pergamon Press.

ICRP. 1984. International Commission on Radiological Protection. A compilation of the major concepts and quantities in use by ICRP. ICRP Publication 42. Oxford: Pergamon Press.

ICRP. 1990. International Commission on Radiological Protection 1990 Recommendations of the ICRP

ICRU. 1980. International Commission on Radiation Units and Measurements. ICRU Report No. 33. Washington, DC.

James A. 1987. A reconsideration of cells at risk and other key factors in radon daughter dosimetry. In: Hopke P, ed. Radon and its decay products: Occurrence, properties and health effects. ACS Symposium Series 331. Washington, DC: American Chemical Society, 400-418.

James A, Roy M. 1987. Dosimetric lung models. In: Gerber G, et al., ed. Age-related factors in radionuclide metabolism and dosimetry. Boston: Martinus Nijhoff Publishers, 95-108.

Kondo S. 1993. Health effects of low-level radiation. Kinki University Press, Osaka, Japan (available from Medical Physics Publishing, Madison, Wisconsin).

Kato H, Schull W. 1982. Studies of the mortality of A-bomb survivors. Report 7 Part 8, Cancer mortality among atomic bomb survivors, 1950-78. Radiat Res 90;395-432.

Mettler F, Moseley R. 1985. Medical effects of ionizing radiation. New York: Grune and Stratton.

NCRP. 1971. Basic radiation protection criteria. National Council on Radiation Protection and Measurements. Report No. 39. Washington, DC.

NCRP. 1985. A handbook of radioactivity measurements procedures. 2nd ed. National Council on Radiation Protection and Measurements. Report No. 58. Bethesda, MD:

NCRP. 1993. Risk estimates for radiation protection. National Council on Radiation Protection and Measurements. Report 115. Bethesda, Maryland

Otake M, Schull W. 1984. Mental retardation in children exposed in utero to the atomic bombs: A reassessment. Technical Report RERF TR 1-83, Radiation Effects Research Foundation, Japan.

Rubin P, Casarett G. 1968. Clinical radiation pathology. Philadelphia: W.B. Sanders Company, 33.

UNSCEAR. 1977. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources and effects of ionizing radiation. New York: United Nations.

UNSCEAR. 1982. United Nations Scientific Committee on the Effects of Atomic Radiation. Ionizing radiation: Sources and biological effects. New York: United Nations.

UNSCEAR. 1986. United Nations Scientific Committee on the Effects of Atomic Radiation. Genetic and somatic effects of ionizing radiation. New York: United Nations.

UNSCEAR. 1988. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources, effects and risks of ionization radiation. New York: United Nations.

UNSCEAR. 1993. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources and effects of ionizing radiation. New York: United Nations.

USNRC. 1999. Standards for the protection against radiation, table 1004(b).1. 10 CFR 20.1004. U.S. Nuclear Regulatory Commission, Washington, D.C.

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