TOXICOLOGICAL PROFILE FOR RADIUM

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

In collaboration with:

U.S. Environmental Protection Agency

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FOREWORD

The Superfund Amendments and Reauthorization Act (SARA) of 1986 (Public Law 99-499) extended and amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law directed the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare toxicological profiles for hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List and which pose the most significant potential threat to human health, as determined by ATSDR and the Environmental Protection Agency (EPA). The lists of the 250 most significant hazardous substances were published in the <u>Federal Register</u> on April 17, 1987, on October 20, 1988, on October 26, 1989, and on October 17, 1990.

Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list. Each profile must include the following content:

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

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

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

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

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

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Foreword

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

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

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

Filliam C. Lox

William L. Roper, M.D., M.P.H. Administrator Agency for Toxic Substances and Disease Registry

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This Statement was prepared to give you information about radium and to emphasize the human health effects that may result from exposure to it. The Environmental Protection Agency (EPA) has identified 1,177 sites on its National Priorities List (NPL). Radium has been found above background levels at 18 of these sites. However, we do not know how many of the 1,177 NPL sites have been evaluated for radium. As EPA evaluates more sites, the number of sites at which radium is found above background levels may change. The information is important for you because radium may cause harmful health effects and because these sites are potential or actual sources of human exposure to radium.

When a radioactive chemical is released from a large area, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment as a radioactive chemical emission. This emission, which is also called a release, does not always lead to exposure. You can be exposed to a radioactive chemical when you come into contact with that chemical alone or with a substance that contains it. You may be exposed to it in the environment by breathing, eating, or drinking substances containing the radioactive chemical or from skin contact with it. Exposure can also occur by being near radioactive chemicals at concentrations that are found at hazardous waste sites or industrial accidents.

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

1.1 WHAT IS RADIUM?

Radium is a naturally-occurring silvery white radioactive metal that can exist in several forms called isotopes. It is formed when uranium and thorium (two other natural radioactive substances) decay (break down) in the environment. Radium has been found at very low levels in soil, water, rocks, coal, plants, and food. For example, a typical amount might be one picogram of radium per gram of soil or rock. This would be about one part of radium in one trillion (1,000,000,000,000) parts of soil or rock. These levels are not expected to change with time.

Some of the radiation from radium is constantly being released into the environment. It is this release of radiation that causes concern about the safety of radium and all other radioactive substances. Each isotope of radium releases radiation at its own rate, One isotope, radium-224 for example, releases half of its radiation in about three and a half days; whereas another isotope, radium-226, releases half of its radiation in about 1,600 years.

When radium decays it divides into two parts. One part is called radiation, and the second part is called a daughter. The daughter, like radium, is not stable; and it also divides into radiation and another daughter. The dividing continues until a stable, nonradioactive daughter is formed. During the decay process, alpha, beta, and gamma radiations are released. Alpha particles can travel only a short distance and cannot travel through your skin. Beta particles can penetrate through your skin, but they cannot go all the way through your body. Gamma radiation, however, can go all the way through your body. Thus, there are several types of decay products that result from radium decay.

More information about the properties and uses of radium is found in Chapters 3, 4, and 5.

1.2 HOW MIGHT I BE EXPOSED TO RADIUM?

Because radium is present, usually at very low levels, in the surrounding environment, you are always exposed to it and to the small amounts of radiation that it releases to its surroundings. You may be exposed to higher levels of radium if you live in an area where it is released into the air from the burning of coal or other fuels, or if your drinking water is taken from a source that is high in natural radium, such as a deep well, or from a source near a radioactive waste disposal site.

Levels of radium in public drinking water are usually less than one picocurie per liter of water (about one quart), although higher levels (more than 5 picocuries per liter) have been found. A picocurie (pCi) is a very small amount of radioactivity, and it is associated with about a trillionth of a gram (a picogram) of radium. (There are approximately 28 grams in an ounce.) No information is available about the amounts of radium that are generally present in food and air. You may also be exposed to higher levels of radium if you work in a uranium mine or in a plant that processes uranium ores.

You will find more information on how you can be exposed to radium in Chapter 5.

1.3 HOW CAN RADIUM ENTER AND LEAVE MY BODY?

Radium can enter the body when it is breathed in or swallowed. It is not known if it can be taken in through the skin. If you breathe radium into your lungs, some may remain there for months; but it will gradually enter the blood stream and be carried to all parts of the body, especially the bones. For months after exposure, very small amounts leave the body daily through the feces and urine.

If radium is swallowed in water or with food, most of it (about 80%) will promptly leave the body in the feces. The other 20% will enter the blood stream and be carried to all parts of the body, especially the bones. Some of this radium will then be excreted in the feces and urine on a daily basis.

You will find more information on this subject in Chapter 2.

1.4 HOW CAN RADIUM AFFECT MY HEALTH?

There is no clear evidence that long-term exposure to radium at the levels that are normally present in the environment (for example, 1 pCi of radium per gram of soil) is likely to result in harmful health effects. However, exposure to higher levels of radium over a long period of time may result in harmful effects including anemia, cataracts, fractured teeth, cancer (especially bone cancer), and death. Some of these effects may take years to develop and are mostly due to gamma radiation. Radium gives off gamma radiation, which can travel fairly long distances through air. Therefore, just being near radium at the high levels that may be found at some hazardous waste sites may be dangerous to your health.

More information on this subject is presented in Chapter 2.

1.5 WHAT LEVELS OF EXPOSURE HAVE RESULTED IN HARMFUL HEALTH EFFECTS?

Radium has been shown to cause adverse health effects such as anemia, cataracts, fractured teeth, cancer and death. As shown in Tables 1-1 through 1-4, the relationship between the amount of radium that you are exposed to and the amount of time necessary to produce these effects is not known. Although there is some uncertainty as to how much exposure to radium increases your chances of developing a harmful health effect, the greater the total amount of your exposure to radium, the more likely you are to develop one of these diseases. More information on this subject is presented in Chapter 2.

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1. PUBLIC HEALTH STATEMENT

TABLE 1-1. Human Health Effects from Breathing Radium*

	Short-term Exposur (less than or equal to 1					
<u>Levels in Air</u>	<u>Length of Exposure</u>	Description of Effects The health effects result- ing from short-term exposure of humans breathing specific levels of radium are not known.				
	Long-term Exposure (greater than 14 day					
<u>Levels in Air</u>	<u>Length of Exposure</u>	Description of Effects The health effects result- ing from long-term exposure of humans breathing specific levels of radium are not known.				

*See Section 1.2 for a discussion of exposures encountered in daily life.

1. PUBLIC HEALTH STATEMENT

TABLE 1-2. Animal Health Effects from Breathing Radium

	Short-term Exposur (less than or equal to l					
<u>Levels in Air</u>	<u>Length of Exposure</u>	Description of Effects The health effects result- ing from short-term exposure of animals breathing specific levels of radium are not known.				
	Long-term Exposur (greater than 14 da					
<u>Levels in Air</u>	<u>Length of Exposure</u>	Description of Effects The health effects result- ing from long-term exposure of animals breathing specific levels of radium are not known.				

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1. PUBLIC HEALTH STATEMENT

TABLE 1-3. Human Health Effects from Eating or Drinking Radium*

	Short-term Exposu (less than or equal to	
Levels in Food	Length of Exposure	Description_of_Effects
<u>Levels in Water</u>		The health effects result- ing from short-term exposure of humans to food containing specific levels of radium are not known. The health effects result- ing from short-term exposure of humans to water containing specific levels of radium are not known.
	Long-term Exposur (greater than 14 da	re ys)
Levels in Food	Length of Exposure	Description of Effects
Levels in Water		The health effects result- ing from long-term exposure of humans to food containing specific levels of radium are not known.
		The health effects result- ing from long-term exposure of humans to water containing specific levels of radium are not known.

*See Section 1.2 for a discussion of exposures encountered in daily life.

1. PUBLIC HEALTH STATEMENT

TABLE 1-4. Animal Health Effects from Eating or Drinking Radium

Short-term Exposu (less than or equal to 1	
Length of Exposure	Description of Effects
	The health effects result- ing from short-term exposure of animals to food containing specific levels of radium are not known.
	The health effects result- ing from short-term exposure of animals to water containing specific levels of radium are not known.
Long-term Exposur (greater than 14 day	
Length of Exposure	Description of Effects
	The health effects result- ing from long-term exposure of animals to food containing specific levels of radium are not known. The health effects result- ing from long-term exposure of animals to water containing specific levels of radium are not known.
	(less than or equal to Length of Exposure Long-term Exposur (greater than 14 da

1.6 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO RADIUM?

There are few medical tests to determine if you have been exposed to radium. There is a urine test to determine if you have been exposed to a source of radioactivity such as radium. There is also a test to measure the amount of radon, a breakdown product of radium, when it is exhaled. These tests require special equipment and cannot be done in a doctor's office. Another test can measure the total amount of radioactivity in the body; however, this test is not used except in special cases of high exposure.

More information on the methods used to determine levels of exposure to radioactivity can be found in Chapters 2 and 6.

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

The Environmental Protection Agency (EPA) regulates the amount of radium in drinking water so that it will not contain more than 5 pCi of combined radium-226 and radium-228 per liter of water. The amount of radioactivity from all sources that is allowed in drinking water and the amount that workers may be exposed to in nuclear plants is regulated.

1.8 WHERE CAN I GET MORE INFORMATION?

If you have any more questions or concerns not covered here, please contact your State Health or Environmental Department or:

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

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

2.1 INTRODUCTION

This chapter contains descriptions and evaluations of studies and interpretation of data on the health effects associated with exposure to radium. Its purpose is to present levels of significant exposure for radium based on toxicological studies, epidemiological investigations, and environmental exposure data. This information is presented to provide public health officials, physicians, toxicologists, and other interested individuals and groups with an overall perspective of the toxicology of radium and a depiction of significant exposure levels associated with various adverse health effects.

It is important to note that in the various studies reviewed in the preparation of this document, dose levels have been presented by those authors in several ways. In order to facilitate comparisons among studies, these levels have generally been converted to an equivalent dose in microcuries (μ Ci) and kilo-Becquerels (kBq). The historical definition of one curie is the disintegration rate exhibited by one gram of radium. There are 0.027 μ Ci per kBq. In this document, comparisons are usually made between total administered amounts of radioactivity, in μ Ci/kg and kBq/kg, instead of using a daily dosage level.

In the case of radium, as well as any radionuclide, it is important to note that, in addition to the usual routes of exposure that must be considered (inhalation, oral, dermal, and occasionally parenteral) for toxic chemicals, there is also external and internal exposure to emissions of alpha and beta particles and gamma rays; and it is these radioactive emissions which are considered to be responsible for most of the biologically deleterious effects observed in exposed persons. Further information about radionuclides is presented in Appendix B.

2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

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

2.2.1 Inhalation Exposure

Early workers using radium undoubtedly inhaled microscopic particles of the salts of radium as well as the daughter products resulting from their decay, as they worked with these compounds.

Therefore, they must have been continually exposed to alpha and beta particles as well as to the intense penetrating gamma radiation emitted by radium and its daughter products, including radon. Thus, any resulting health effects cannot be attributed to a specific cause but were probably the consequence of a combination of all the radiation insults to that individual.

2.2.1.1 Death

No information has been located regarding the lethal effects of acute exposure to radium via inhalation.

An early case study described a 36-year-old chemist who had worked with radium for 14 years and then suddenly developed acute leukopenia and died of bronchopneumonia within a month after the onset (Reitter and Martland 1926). Autopsy data indicated that 14 PCi of radioactive material, including radium and mesothorium (radium-228), was found in the body, but the observation that 1 µci was found in the lungs (as compared with other internal organs such as the liver, gastrointestinal tract, heart, and kidneys which had no measurable levels of radioactivity) convinced the authors that inhalation was the primary route by which radium had entered the body. Most of the radioactivity was found in the skeleton.

No studies were located regarding lethality in animals after inhalation exposure to radium.

2.2.1.2 Systemic Effects

No studies were located regarding systemic effects in humans or animals after inhalation exposure to radium.

2.2.1.3 Immunological Effects

Acute leukopenia, with almost total absence of granular leukocytes, leukoblastic groups and lymphoid tissue in the bone marrow, was reported in the case of a 36-year-old chemist who had worked with radium for 14 years (Reitter and Martland 1926).

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

2.2.1.4 Neurological Effects

2.2.1.5 Developmental Effects

2.2.1.6 Reproductive Effects

2.2.1.7 Genotoxic Effects

2.2.1.8 Cancer

2.2.2 Oral Exposure

It is important to note that effects observed after the ingestion of radium may be attributed not only to radium itself, but to the presence of any or all of its daughter products produced <u>in vivo</u> and their radioactive emissions.

2.2.2.1 Death

There is no information on the lethal effects of radium due to acute oral exposure. Many deaths, especially from bone cancer, have occurred in humans following long-term oral exposure to radium-226 and radium-228. As described by Rowland et al. (1978), female radium dial painters in the 1920s who "tipped" their paint brushes with their lips or tongues ingested radium in the process. The dial paint usually contained long-lived radium-226 and shorter-lived radium-228. A toxicity ratio has been developed for these isotopes; it has been estimated that radium-228 is about 2.5 times as effective, per $\mu\text{Ci},$ in inducing bone sarcomas as radium-226 (Lloyd et al. 1986; Rowland et al. 1978; Rundo et al. 1986). For various other effects, estimates of the effectiveness of radium-228 relative to radium-226 have ranged from zero to six (Rundo et al. 1986). Estimated systemic intakes for these workers and other exposed persons are listed in the Argonne National Laboratory case tables (Gustafson and Stehney 1985). These estimates are extrapolations based on body radium content at the time of examination (whether from living subjects or exhumed remains), modified by the Norris retention function (Norris et al. 1955) to account for the decrease in body radium content since exposure, and the known or presumed ratios of these isotopes in the materials to which these persons were exposed (Rundo et al. 1986). Radium dose levels have been expressed as: effective systemic radium intake = (μ Ci radium-226) + 2.5 x (μ Ci radium-228).

Some of the radium dial painters ingested amounts of radium sufficient to cause death within a few years of their employment. Martland (1931) described the cases of 18 dial painters who died of cancer at ages 20 to 54 years old. Causes of death were listed as anemia, necrosis of the jaw, and osteogenic sarcoma. The typical period of exposure was about two years.

Radium was also used as a "rejuvenating" tonic in the 1920s and was available to the general public in bottled water. Gettler and Norris (1933) described a case of a 52-year-old man who drank about 1,400 bottles of "Radithor", containing radium at 2 μ g/60 ml bottle, over a

5-year period (total dose: approximately 2,800 μ Ci or 56 μ Ci/kg or 2,074 kBq/kg for a 50-kg man). The cause of death was stated to be a combination of necrosis of the jaw, abscess of the brain, secondary anemia and terminal bronchopneumonia. However, it is important to note that each of these effects can also be attributed to other etiologies.

No studies were located regarding lethality in animals after oral exposure to any of the isotopes of radium.

2.2.2.2 Systemic Effects

Based on case studies of radium dial painters, Martland (1931) stated that anemia, regenerative anemia, aregenerative anemia, or pernicious anemia was listed on the death certificates of ten of 18 persons autopsied as part of this study. The bases of these diagnoses (e.g., clinical impressions of the cadaver, laboratory findings, etc.) were not clearly stated. Sharpe (1974) analyzed detailed hematological data relating to dial painters as well as to persons exposed to radium in other ways (eg., male laborers and equipment operators in radiumrelated industries). He concluded, however, that there were no consistent differences in hematological indices between the radiumexposed patients and closely matched controls. From the limited available data, it is difficult to determine if hematological effects are a concern for humans exposed to radium.

No studies were located regarding hematological effects in animals after oral exposure to radium.

No studies were located regarding the following health effects in humans or animals following oral exposure to radium.

- 2.2.2.3 Immunological Effects
- 2.2.2.4 Neurological Effects
- 2.2.2.5 Developmental Effects
- 2.2.2.6 Reproductive Effects
- 2.2.2.7 Genotoxic Effects
- 2.2.2.8 Cancer

The Center for Human Radiobiology at the Argonne National Laboratory has been conducting a surveillance program to identify persons exposed to radium and to determine the details of their exposure, in some cases through exhumation of their remains (Gustafson and Stehney 1985). Based on their findings, bone sarcomas, carcinomas

of the perinasal sinuses and mastoid air cells (often called head cancers), and deterioration of skeletal tissue are considered to be the only effects that are unequivocally attributable to internal radium (Rundo et al. 1986).

These bone sarcomas and head carcinomas have been seen in many radium dial painters and have appeared from 5 to more than 50 years after first exposure to radium. Of those dial painters for whom radium intakes have been estimated (a total of 1,907), 41 have developed bone sarcomas, 16 developed head carcinomas, and an additional 3 cases developed both types. Among dial painters whose radium intakes were not estimated (a total of 2,928), 20 cases with bone sarcomas and 5 with head carcinomas were identified. Thus 85 out of 4,835 known dial painters developed a malignancy as a consequence of their oral ingestion of radium (Rundo et al. 1986).

Based on data on these dial painters from the 1985 listing of radium cases studied at the Argonne National Laboratory (Gustafson and Stehney 1985) Rundo et al. (1986) have estimated that the lowest total intake level of radium associated with a malignancy was 60 μ Ci (2,222 kBq) or 1.03 μ Ci/kg (38 kBq/kg) based on an estimated 58 kg body weight for a woman. These estimates are based on current radium body content modified by the Norris retention function (to account for the decrease in body radium content with time since exposure) and an estimate of radium-228 from measurements of radium-226 and the known or presumed ratios of these isotopes in the materials to which these persons were exposed (Rundo et al. 1986).

Osteogenic sarcomas were reported in 3 out of 5 rats administered radium for 20 days by dropper (Evans et al. 1944). Each animal was given a different estimated total dose ranging from 10 to 70 μ Ci. The lowest dose to clearly induce a malignancy was 22 μ Ci (approximately 73 μ Ci/kg or 2,703 kBq/kg).

2.2.3 Dermal Exposure

No studies were located regarding the following health effects in humans or animals after dermal exposure to radium. It is important to note, however, that the radium dial painters had chronic dermal exposure to radium on their lips and tongues. Although no recognition of this fact has been located in the literature, it is noteworthy that no local effects on exposed skin have been described in the available case studies of these workers (eg., Martland 1931; Sharpe 1974).

2.2.3.1 Death

- 2.2.3.2 Systemic Effects
- 2.2.3.3 Immunological Effects
- 2.2.3.4 Neurological Effects
- 2.2.3.5 Developmental Effects
- 2.2.3.6 Reproductive Effects
- 2.2.3.7 Genotoxic Effects
- 2.2.3.8 Cancer

2.2.4 Other Routes of Exposure

While parenteral exposure is not a route posing a significant environmental threat to human health from the isotopes of radium, data acquired in studies using this route are presented here because thousands of persons did acquire radium via this route, and most of the toxicity and metabolic studies with experimental animals have used this route. It is again important to note that effects observed after parenteral administration of radium may be attributed not only to radium itself, but to the presence of any or all of its daughter products and their radioactive emissions in vivo.

In the years after World War II (1946 to 1950), repeated injections of radium-224 were given to adults and children in Germany for treatment of tuberculosis, ankylosing spondylitis, and other diseases. Out of about 2,000 persons who received this treatment, 816 of these cases are currently being followed (Spiess et al. 1978). Of the 816, 204 were injected as juveniles (ages 1 to 20 years) and 612 as adults. The average total injected activity was 18 μ Ci/kg (666 kBq/kg) (Mays et al. 1985a).

A second study of persons injected with radium-224 in Germany from 1948 to 1975 included 1,473 ankylosing spondylitis patients who were also treated with repeated intravenous injections of radium, but at lower levels. They typically received a series of 10 to 12 injections at weekly intervals, each containing 28 μ Ci (1,037 kBq). Some patients received two or three such series, and one patient received four. The average total injected activity was 4.8 μ Ci/kg (178 kBq/kg) (Wick and Gossner 1983, 1989).

Pure radium-226 was given intravenously as a medication in the United States from the time it first became available until the mid-1930s. Treatment of patients at the Elgin State Hospital in Illinois was described by Schlundt et al. (1933), where from 1931 to 1933,

32 patients were given 10 μ Ci (370 kBq) injections, usually weekly, for periods ranging from about 2 to 6 months. In the 1950s, these patients were located, their radium body content was measured, and their health status was subsequently followed (Norris et al. 1955).

2.2.4.1 Death

No studies were located regarding acute lethality in humans following parenteral administration of radium isotopes. Early uses of radium-226 by physicians (usually as a treatment for arthritis) involved intravenous injections as large as 1 mg (1,000 μ Ci or 37,037 kBq) of elemental radium (thus approximately 14 μ Ci /kg or 518 kBq/kg), which were claimed to have no ill effects (Proescher 1914). As described in Section 2.2.4.8, patients receiving injections of radium have developed cancer which has resulted in death.

Injection of mice with radium (presumably radium-226) at 2,000 to 4,000 μ Ci/kg (74,000 to 148,000 kBq/kg) was fatal in 7 to 10 days (Proescher and Almquest 1914); however, experimental details were not provided. In 12-week-old mice given a single intraperitoneal injection of radium-224 or a series of 8 such injections over a period of 4 weeks, there was no evidence of a decrease in life span at any level, up to the maximum tested, approximately 60 μ Ci /kg (2,220 kBq/kg) (Humphreys et al. 1985).

2.2.4.2 Systemic Effects

No studies have been located regarding respiratory, cardiovascular, gastrointestinal, musculoskeletal, renal, or dermal effects in humans or animals after parenteral administration of radium.

Hematological Effects. In a follow-up study of the second group of German patients who had received repeated intravenous injections of radium-224, the injected doses averaged 4.8 µCi/kg (178 kBq/kg) total exposure (Wick and Gossner 1983; Wick et al. 1986) for 1,501 patients. Ten cases of bone marrow failure were observed in these patients, as compared with 7 cases in the controls (1,338 similar patients not treated with radiation) (Wick and Gossner 1989). The statistical significance of these findings was not addressed.

In the bone marrow of mice given intraperitoneal injections of radium-226 at 17,820 μ Ci/kg (660,000 kBq/kg), there was a depression in the number of hemopoietic stem cells which lasted until at least 100 days after the injection but returned to normal by 300 days (Schoeters and Vanderborght 1981). Schoeters et al. (1983) reported a marked depression in the number of peripheral white blood cells of mice at 400 days after a 670 μ Ci (24,800 kBq) intraperitoneal injection of

the chloride salt of radium-226 (approximately 22,320 μ Ci /kg or 827,000 kBq/kg). At 530 days post-injection, these levels appeared to be recovering. There were no consistent trends in the peripheral white blood cell levels of the lower dose groups (3,960 and 10,000 μ Ci/kg or 147,000 and 370,000 kBq/kg).

Hepatic Effects. Chronic liver diseases, mostly cirrhosis, were reported in 20 cases (out of 682 adults and 218 children) who were followed for an average of 20 years after repeated injections of radium-224 totaling an average of 18 μ Ci/kg (667 kBq/kg). Eighteen of these patients were injected as adult men, one as an adult woman, and one as a juvenile. The authors suggested that this is a radiation effect; however, statistical significance was not addressed and the total incidence in this group (2.2%) may have been comparable to that of the general population. The higher incidence in men was thought to be related to their higher exposure to liver toxins such as alcohol or industrial chemicals (Spiess and Mays 1979).

Ocular Effects. Cataracts were reported in 6% (12/218) of patients injected with radium-224 as children. The known dosages averaged 28 μ Ci/kg (1,037 kBq/kg). Of these cases with known doses, 14% (11/80) had cataracts after receiving more than 28 μ Ci/kg (1,037 kBq/kg), whereas only 0.8% (1/131) developed cataracts after receiving less than that dose (Stefani et al. 1985). The younger patients received the highest doses in μ Ci/kg in this study, and thus, presumably, the highest radiation dose to the eye. The lowest dose known to be associated with a cataract that developed after a radium-224 treatment in childhood was 15.6 μ Ci/kg (577 kBq/kg) given to a 4.5 year-old-girl (Chmelevsky et al. 1988a).

In beagle dogs, intravenously injected radium-226 was deposited in the melanin granules of pigmented cells and rodlike organelles of the tapetum in the eye (a structure that humans do not have). Retention in the eye varied inversely with dose. At doses from 0.062 to 1.1 μ Ci/kg (2.3 to 41 kBq/kg), loss of pigment at the higher doses and melanosis and intraocular melanoma formation at the lower doses were observed (Taylor et al. 1972).

Other Systemic Effects. Radiation damage to dental tissue, or perhaps to its blood supply, initiates extensive resorption of the dentine, especially at the gum line. These radiation-induced caries weaken teeth and cause them to fracture easily. Such tooth breakage has been reported in 12% (27/218) of patients injected with radium-224 as children (20 years old and younger) and by 2% (17/681) of patients injected as adults (21 years old and older). The highest incidence

occurred in adolescents injected at 16 to 20 years of age (15/61 or 25%). Combining results from all age groups, the incidence of tooth fracture increased significantly with dose (p=0.01) (Sonnabend et al. 1986).

2.2.4.3 Immunological Effects

No studies were located regarding immunological effects in humans after parenteral exposure to radium.

A marked decrease was found in the number of peripheral white blood cells of mice at 400 days after an intraperitoneal injection of the chloride salt of radium-226 at about 22,320 μ Ci/kg (827,000 kBq/kg) (Schoeters et al. 1983). These results suggest that compromised immune function may be a concern for humans exposed to radium.

2.2.4.4 Neurological Effects

No studies were located regarding neurological effects in humans or animals after parenteral exposure to radium.

2.2.4.5 Developmental Effects

In a follow-up study of the first group of German patients injected with radium-224 as therapy for tuberculosis when they were children (see Section 2.2.4), it was found that the adult heights of these persons were markedly lower than the heights of nontreated persons. This effect was attributed to the formation of overcalcified "growth arrest plates" during the radium-224 injections. The reduction was greatest for those individuals who were the youngest at the age of injection; however, the youngest children were given the highest doses of injected radium-224 in μ Ci/kg (Spiess et al. 1985). The authors could not determine if this effect has a threshold but stated that the continued slowing of the growth rate long after irradiation suggests that some growth retardation may occur at very low doses of radium.

2.2.4.6 Reproductive Effects

No studies were located regarding reproductive effects in humans or animals following parenteral exposure to radium.

2.2.4.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans or animals following parenteral exposure to radium.

2.2.4.8 Cancer

Bone tumors, primarily osteogenic sarcomas, have appeared in the first group of German patients injected with radium-224 (see Section 2.2.4) (Spiess et al. 1989). A total of 56 sarcomas have been found; the expected number is 0.2 to 0.3 (Spiess et al. 1989). The lowest total dose associated with a bone tumor was 6.4 μ Ci/kg (237 kBq/kg) given over two months (Mays and Spiess 1984).

An elevated incidence of breast cancer has also been observed in the female patients in this group (14 cases versus 4.1 to 6.1 expected). Eight of these cases occurred among those injected as children, whereas only 0.6 to 0.9 were expected. In patients injected as adults, the 6 observed cases are not significantly different from the 3.5 to 5.2 cases expected (Spiess et al. 1989). This suggests that exposure to radium-224 during childhood poses a much greater risk for the induction of breast tumors than does exposure as an adult.

An elevated incidence of liver cancer has been seen in the first series of German patients (6 versus 1.1 to 1.2 expected). Five cases of kidney cancer have also been observed, compared with 2.4 to 2.6 expected (Spiess et al. 1989); however, this increase is not statistically significant. The authors suggest that these cancers may also have been induced by the radium-224.

In the second group of German patients treated with radium-224 (see Section 2.2.4), at lower injected doses, three malignant tumors in the skeleton have been observed (versus 0.4 to 0.7 expected); two were tumors of the bone marrow (a reticulum cell sarcoma and a plasmocytoma) and one was a fibrosarcoma (Wick and Gossner 1989). One skeletal tumor, a plasmocytoma, was observed among the controls, a group of 1,338 ankylosing spondylitis patients who were not treated with radiation (Wick and Gossner 1989).

Of the Elgin State Hospital patients who received injections of radium-226 (see Section 2.2.4), two patients developed bone sarcomas, four developed head carcinomas, and a seventh patient had both types of malignancy (statistical significance was not addressed) (Gustafson and Stehney 1985).

Large experimental animal studies with parenterally administered radium, primarily using dogs, but some using rats and mice, have demonstrated that radium-224, radium-226, and radium-228 can induce bone cancers and leukemias in these species (Evans et al. 1944; Humphreys et al. 1985; Kofranek et al. 1985; Mays et al. 1987; Taylor et al. 1983). However, head carcinomas, such as those found in humans, were not found in any of the species tested, indicating that this malignancy was not induced under the conditions of these animal studies. The most

unexpected finding was the induction of intraocular melanomas in beagles by radium-226 by Taylor et al. (1972). These tumors have not been seen in any of the human studies.

2.3 TOXICOKINETICS

In radiation biology, the term "dose" has a specific meaning. Dose refers to the amount of radiation absorbed by the organ or tissue of interest per unit mass and is expressed in rads (grays). Estimation of this radiation dose is sometimes accomplished by modeling the sequence of events involved in the acquisition, deposition, clearance, and decay of radium within the body. While based on the current understanding of experimental data on radium toxicokinetics, different models make different assumptions about these processes, thereby resulting in different estimates of dose and risk. These models are described in numerous reports including BEIR IV (1988), ICRP (1979), and Raabe et al. (1983). In this section, the toxicokinetics of radium are described based on the available experimental data rather than on descriptions derived from models.

2.3.1 Absorption

2.3.1.1 Inhalation Exposure

The only study located on human absorption of radium after inhalation exposure involved the accidental rupture of capsules containing radium sulfate (presumed to be primarily radium-226), with the resultant brief exposure of several laboratory workers (Marinelli et al. 1953). Radium was deposited both in the lungs and the skeletons of these individuals, indicating that some of the radium absorbed by the lung had entered the systemic circulation, ultimately depositing in the bones. Some of the radium, however, may have been coughed up and then swallowed during the original exposure and then entered the systemic circulation after being absorbed by the gut. The average half-life of the decrease of gamma ray activity from the thorax was reported to be about 120 days. The possibility of dermal exposure and consequent absorption during this episode was not addressed.

No studies were located regarding the absorption of radium in animals after inhalation exposure.

2.3.1.2 Oral Exposure

Based on a study of elderly human subjects (aged 63 to 83 years) who ingested mock radium dial paint containing $^{224}RaS_4$, Maletskos et al. (1966, 1969) have estimated that about 80% of the ingested radium was promptly excreted via the feces during the first 10 days, and about 20% was retained and distributed systemically. The feces to urine excretion

ratios remained high (about 30:1) during another phase of this study in which similar subjects were given intravenous injections of radium-224. This suggested that biliary excretion is probably involved and that perhaps more than the estimated 20% of ingested radium was actually absorbed. However, this topic was not addressed in the study.

Measurements of body radium acquired by adult and teenage males solely from natural levels of radium in food and water indicated that approximately twice the amount of ingested radium was retained by younger males from one location, Lockport, Illinois (mean age: 16.6 years) than by older males in a penitentiary in Stateville, Illinois (means of age groups: 27, 38 and 44 years) (Stehney and Lucas 1955). Among the prisoners, mean body radium content was increased with the mean age of the men. However, boys from another location, Chicago, Illinois (mean age: 16.6 years) had similar radium body contents to that of the single Chicago adult man participating in this study. The results of this study also suggested that the absorption of radium from water was greater than that from food, based on excretion rates measured in areas where either food or water was the predominant source of radium. The authors acknowledged that these were speculations and not clearly supportable by the results of their limited study.

In rats, the absorption of orally administered radium may be quite low. At 400 to 500 days after administration, they retained 1 to 7% of the ingested radium, primarily in the skeleton. In contrast, rats intradermally injected with radium retained 77% of the administered radium at 140 to 300 days after injection (Evans et al. 1944). Differences seen in the results of these two studies could reflect differences in time frame and/or the route of administration. The probable influence of biliary excretion of orally administered radium and the possibly slow rate of absorption of intradermally administered radium from the site of injection may help account for these differences.

2.3.1.3 Dermal Exposure

No studies were located regarding the absorption of radium in humans or animals after dermal exposure.

2.3.2 Distribution

2.3.2.1 Inhalation Exposure

Based on the observations of Marinelli et al. (1953), immediately after accidental exposure of humans to radium-226 (as the sulfate), the major deposit of radium was in the lungs. This deposition decreased with an average half-life of 118 days (±30 days). Elimination from the lungs via the systemic circulation results in a continuous deposition in

the skeleton as well as distribution to soft tissue and the excretory system. In addition, some of the radium salt may have been coughed up and swallowed during the exposure episode.

It is assumed that radium that has been deposited in the lung as a radium salt enters the systemic circulation either as that salt or as individual radium atoms at a rate dependent upon the solubility and chemical characteristics of the specific radium salt involved. Subsequently, these salts or radium atoms would be systemically transported in the same manner as radium acquired by oral or parenteral administration. However, some of the radium in the lung could be retained for a long time before this process is completed. The ultimate distribution, many years after an inhalation exposure, would probably be very similar to that of other routes of administration; that is, most of the radium that was retained in the body would eventually be deposited in the skeleton (Marinelli et al. 1953).

2.3.2.2 Oral Exposure

No studies have been located that specifically follow the distribution of radium in humans or animals following oral exposure. Distribution to the skeleton is assumed due to the findings of osteosarcomas in the dial painter studies as well as the presence of radium in their exhumed skeletal remains. The affinity for bone is assumed to be related to its similarity to calcium (BIER IV 1988).

2.3.2.3 Dermal Exposure

No studies were located regarding the distribution of radium in humans or animals following dermal exposure.

2.3.2.4 Other Routes of Exposure

Parenteral administration of radium to humans results in short-term distribution to soft tissue which is rapidly followed by deposition of most of the radium in the skeleton (BEIR IV 1988).

Radium, similarly to calcium, deposits in bone within those areas where new bone mineral is being formed and also on all bone surfaces. Radium remains in those areas of new bone formation, but the radium deposits on bone surfaces eventually move into the depths of compact bone as new bone matrix is deposited on top of them. In this deposition process, short-lived radium-224 rapidly decays, leaving no radioactivity within bone; whereas, long-lived radium-226 remains in the skeleton indefinitely (Rowland 1966). Mays et al. (1975) have demonstrated that the radon to radium ratio in bone increased with time after injection in beagles.

Injected radium is deposited in the eye of the dog (Taylor et al. 1972) and to some extent in the human eye (Chmelevsky et al. 1988a).

2.3.3 Metabolism

Radium is an element and cannot be metabolized. In biological systems in which radium salts are deposited, these compounds will dissociate based on their solubility in that media. Radioactive decay of the radium cation occurs over time.

2.3.4 Excretion

2.3.4.1 Inhalation Exposure

Based on a study of persons exposed to radium-226 during an industrial accident which involved the rupture of a capsule containing the insoluble salt radium sulfate (Marinelli et al. 1953), the excretion of radium occurred in two phases. In the initial phase, 2 to 4% of the estimated total body burden was excreted in the urine over a few days and was attributed to the elimination of radium ingested during the incident (due to the coughing up and swallowing of ingested radium). (Fecal excretion was not monitored.) In the second phase, about 100 days after the exposure, the urinary excretion rate was higher than predicted from the authors calculations (based on retention/excretion models on dogs injected with radium chloride). This phase was attributed to the presence of more radium in circulation than expected as a consequence of a continual release of radium sulfate from the lung.

2.3.4.2 Oral Exposure

Following oral exposure to radium, excretion occurs in two phases. In the first phase, approximately 80% of the ingested radium is rapidly eliminated through the feces. In the slower second phase, most of the 20% that was absorbed into systemic circulation, is ultimately excreted from the body via the feces (Maletskos et al. 1966, 1969). These observations suggest that biliary excretion is probably involved; however, no information has been located on that topic.

2.3.4.3 Dermal Exposure

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

2.3.4.4 Other Routes of Exposure

Following intravenous administration of radium-224 to elderly human subjects (63 to 83 years), the excretion of radium was primarily via the feces, with fecal to urinary ratios of about 30-to-1 usually observed

(Maletskos et al. 1966, 1969). Although these observations suggest that biliary excretion is involved, no data are available to verify that assumption. The whole body retention was about 15% after 20 days.

The excretion of parenterally acquired radium from the human body occurs in two phases; the first phase is very rapid, but the small fraction that remains in the body is ultimately released very slowly, presumably due to the turnover of bone matrix. An equation to describe the retention of radium in the human body, derived by Norris et al. (1955), predicts that the retention of radium 10 days after acquisition will be 16%, dropping to 2.5% at 1 year, 0.76% at 10 years, and 0.43% at 30 years. A similar equation has been developed for dogs.

Seil et al. (1915) studied the excretion pattern of radium that had been subcutaneously injected as the chloride salt into two dogs. The resulting measurements varied widely over the next few days; however, it was clear that there was a rapid initial elimination of radium in the feces and that fecal to urinary excretion ratios were typically about 10-to-1.

In a study in dogs, it was shown that long-term retention of radium is dependent upon age at injection, with younger dogs (3 months old) that were still undergoing skeletal growth retaining more of the injected activity than older dogs (18 months to 2 years old). However, very young dogs (2 to 5 days old), undergoing major skeletal growth and changes in bone shape lost most of their injected radium in the course of these processes (Bruenger et al. 1983).

2.4 RELEVANCE TO PUBLIC HEALTH

Death. Death and decreased longevity have been reported in persons who have had long-term exposure (approximately one or more years) to radium. A 52-year-old man died following 5 years of consumption of about 1,400 bottles of water containing radium at 2 µg per bottle, resulting in the total ingestion of approximately 2,800 µCi or 56 µCi/kg (2,074 kBq/kg) for a 50-kg man (Gettler and Norris 1933). However, the causes of death (jaw necrosis, brain absess, secondary anemia, and bronchopneumonia) can also be attributed to other etiologies. Case studies of women who died following ingestion of radium in dial paint were reported by Martland (1931). Deaths were attributed to anemia, necrosis of the jaw, and osteogenic sarcomas. A typical exposure duration was about two years. A 36-year-old chemist who had worked with radium for 14 years died of bronchopneumonia (Reitter and Martland 1926). Autopsy results suggested to the authors that inhalation was the main route of radium intake.

No deaths of patients (being treated mostly for arthritis) were reported to result from intravenous injections of radium at amounts up to 1,000 μ Ci or 14 μ Ci/kg (518 kBq/kg) (Proescher 1914). However, these patients may not have been followed clinically for more than a few months after these injections.

Studies using mice have shown life-shortening effects of intravenously injected radium-226 at high dose levels (2,000 to 4,000 μ Ci/kg or 74,074 to 148,148 kBq/kg) (Proescher and Almquest 1914). Injection of mice with radium-224 at lower levels (up to 60 μ Ci/kg or 2,222 kBq/kg) did not result in life-shortening effects (Humphreys et al. 1985).

Based on the results in humans and animals, lethality is a major public health concern associated with long-term low-level or short-term high-level exposure to radium. As discussed previously, total cumulative intake appears to be the most important factor in relation to health effects related to radium exposure.

Systemic Effects. Diseases of the hematopoietic tissues have been reported in patients given repeated injections of radium-224. Anemia, panmyelophthisis, and chronic myeloid leukemia were seen in excess of the control levels in these cases (compared with a higher incidence of acute leukemia in the control group) (Wick et al. 1986). Anemia has also been reported in case studies of the radium dial painters (Martland 1931), but the disease patterns have not been clearly established (Sharpe 1974).

Studies with mice injected with radium-226 at 24 μ Ci/kg (889 kBq/kg) have demonstrated reductions in the hemopoietic stem cells of the bone marrow for at least 100 days after radium acquisition (Schoeters and Vanderborght 1981).

Ocular effects have not been reported in humans or animals exposed to radium via inhalation, oral, or dermal routes. However, ocular effects have been observed in both humans and animals injected with radium. Cataracts were reported in 6% of the German patients who had been injected with radium-224 as children (Chmelevsky et al. 1988a; Stefani et al. 1985). In contrast, the incidence of cataracts in female dial painters was not correlated with total radium intake or age at first exposure, nor was there a difference in appearance times between high and low total radium intakes (Adams et al. 1983). However, the dial painters were exposed orally, the isotope was mainly radium-226, and very few of these dial painters were exposed when younger than 15 years of age. Any of these factors may account for the difference between the results observed in these two studies.

In beagle dogs, intravenously injected radium-226 resulted in melanosis and intraocular melanoma formation at the lower doses and a loss of pigment at the higher doses (Taylor et al. 1972). In this study, deposition of radium was found in the melanin granules of pigmented cells and rodlike organelles of the tapetum of the eye (a structure that humans do not have). Although this process cannot take place in humans, these results further suggest that the eye may be a target for absorbed radium in exposed humans.

Other Systemic Effects. Information on other systemic effects is not available for humans or animals exposed to radium via inhalation, oral, or dermal exposure. However, tooth breakage has been reported to occur in the German patients who were injected with radium-224 (Sonnabend et al. 1986). The incidence of these dental fractures was highest (25%) in persons who had been injected at 16 to 20 years of age, as compared with 12% in the total group of persons injected at age 20 years and younger, and 2% in persons injected when they were 21 years old and older.

Immunological Effects. Evidence of radium's potential effects on the human immune system was presented by Reitter and Martland (1926) in the case study of a chemist who developed acute leukopenia after working with radium for 14 years. Autopsy revealed almost total absence of granular leukocytes, leukoblastic groups, and lymphoid tissue in the bone marrow. Similarly, Martland (1931) described the development of leukopenia in the radium dial painters.

Schoeters et al. (1983) showed a reduction in the number of peripheral white blood cells of mice at 400 days after an intraperitoneal injection of radium-226. These observations suggest that immunological effects may be an important area of concern for persons occupationally exposed to radium.

Cancer. In humans, radium-224 is known to induce bone sarcomas, and it is strongly suspected of inducing breast cancer in females who received this isotope when younger than 21 years of age at total doses greater than 12 μ Ci/kg (444 kBq/kg). Liver and kidney cancers are also possibly induced by radium-224 (Spiess et al. 1989).

Bone sarcomas are known to be induced by both radium-226 and radium-228, while carcinomas of the bones enclosing the mastoid air cells and paranasal sinuses are known to be induced by exposure to radium-226. These carcinomas are believed to be caused by radon, a gaseous daughter product of radium-226, which migrates from the location where it was formed and becomes trapped within air cells in these structures. Here the subsequent decay products of radon irradiate the sensitive cells on the surfaces, and this irradiation is thought to

induce the malignant change. Breast cancer and multiple myeloma were found to be elevated in female dial painters, but these effects may be the consequence of the external radiation from the radioactive paint that was used by these workers (Rowland et al. 1989; Stebbings et al. 1984).

In Great Britain, radium dial painters with higher total radium-226 intakes and who were younger than 30 years of age at the start of painting showed an excess of breast cancers (Baverstock and Papworth 1989). External gamma ray exposure to the radioactive paint could also have been the cause of cancer in this population.

In experimental animals, bone cancer has been the most prominent consequence of radium incorporation and has been found in all species tested.

It should be noted that leukemia, which is often induced in humans by irradiation of marrow cells, has not been observed to occur in excess in the studies of the radium-irradiated populations (i.e., dial painters; patients receiving intravenous injections) above the numbers expected for nonirradiated populations (Baverstock and Papworth 1985; Spiers et al. 1983; Spiess et al. 1989).

2.5 BIOMARKERS OF EXPOSURE AND EFFECT

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

A biomarker of exposure is a xenobiotic substance or its metabolite(s) or the product of an interaction between a xenobiotic agent and some target molecule or cell 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 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 (e.g., high urinary levels of phenol can result from exposure to several different aromatic compounds). Depending on the properties of the substance (e.g., biologic half-life) and environmental conditions (e.g., duration and route of exposure), the substance and all of its metabolites may have left the body by the time biologic samples can be taken. It may be difficult to identify

individuals exposed to hazardous substances that are commonly found in body tissues and fluids (e.g., essential mineral nutrients such as copper, zinc and selenium). Biomarkers of exposure to radium are discussed in Section 2.5.1.

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

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

2.5.1 Biomarkers Used to Identify or Quantify Exposure to Radium

Exposure to radium can be determined by use of a whole body counter to measure the presence of gamma radiation emitted by radium (Toohey et al. 1983). Radium levels can also be measured in urine, feces, and other biological media by means of gamma-ray spectroscopy (Lloyd et al. 1983).

2.5.2 Biomarkers Used to Characterize Effects Caused by Radium

Humans have not been shown to develop specific adverse effects as a result of exposure to radium. Osteogenic sarcoma and cataracts are associated with radium exposure but can also result from other causes. Similarly, chromosomal aberrations may result from radium exposure as well as from other factors such as cigarette smoking or occupational exposure to solvents.

Attempts to correlate the estimated total intake of radium with observed health effects, especially bone cancer, have been conducted at the Argonne National Laboratory (Gustafson and Stehney 1985). For example, Rundo et al. (1986) have estimated that the lowest total intake level of radium associated with a malignancy (bone sarcoma) was 60 µCi (2,222 kBq) or 1.03 µCi/kg (38 kBq/kg) based on an estimated 58-kg body

weight for a woman. If data associated with exposed populations were fully analyzed, levels of radium in human tissue might be a good predictor of at least the potential for developing bone cancer. However, there is expected to be some degree of uncertainty, as in cases of persons with high levels of exposure to radium (such as some of the dial painters, the case of the chemist described by Reitter and Martland and the man who drank 1,400 bottles of "Radithor"), who did not develop bone cancer (Gettler and Norris 1933; Martland 1931; Reitter and Martland 1926).

2.6 INTERACTIONS WITH OTHER CHEMICALS

No data have been located which evaluate the health effects of radium in any of its isotopic forms in combination with any other chemicals or radionuclides.

2.7 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

The available studies suggest that persons who are exposed to radium during childhood or adolescence may be at greater risk from the potential health effects of radium, especially tooth breakage (Section 2.2.4.2), reduction in bone growth (Section 2.2.4.5), and breast tumors (Section 2.2.4.8). There may also be a subpopulation of humans who are genetically more susceptible to the development of bone cancer (Floyd et al. 1983). Patients with Paget's disease have 10 to 100 times the risk of bone sarcoma than the general population.

2.8 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, 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 radium 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 these health effects (and techniques for developing methods to determine such health effects) of radium.

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

2.8.1 Existing Information on the Health Effects of Radium

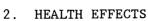
The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to radium are summarized in Figure 2-1. The purpose of this figure is to illustrate the existing information concerning the health effects of radium. Each dot in the figure indicates that one or more studies provide information associated with that particular effect. The dot does not imply anything about the quality of the study or studies. Gaps in this figure should not be interpreted as "data needs" information.

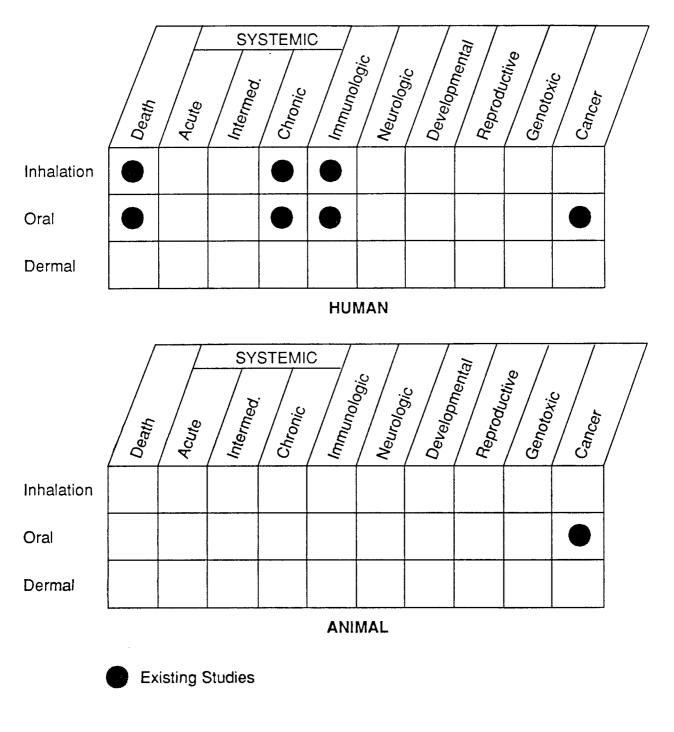
Figure 2-1 indicates whether information on the endpoint of a particular health effect is available for a specific route and duration of exposure for radium. Some information was located concerning human inhalation or oral exposure to radium, and no information was located concerning effects following dermal exposure to radium by humans. The only information available for animals is an intermediate-duration study in rats conducted via the oral route that resulted in cancer. There is virtually no information on noncancer endpoints from animal studies. As discussed in previous sections, most available information on radium is the result of studies using parenteral administration.

In general, the adverse effects of radium are believed to be the consequence of the radiation emitted from the element itself and its daughter products. Because there is already a considerable amount of information on the effects of radiation on humans and animals deri-ved from studies on the effects of the atomic bomb and of therapeutic x-ray and gamma-ray treatments of malignancies, the experimental animal studies with radium have made no attempt to duplicate this information. They have instead concentrated on radium's most sensitive endpoint, cancer. For example, it can be predicted that the beta and gamma rays emitted by a radium source will produce local radiation burns and tissue damage when the source is placed on human or animal skin, hence there have been no valid reasons to conduct such studies with radium.

2.8.2 Identification of Data Needs

Acute-Duration Exposure. There is no information available on the effects of acute-duration exposure to radium by humans or animals via inhalation, oral, or dermal exposure. The available toxicokinetic data suggest that radium can be absorbed and retained after inhalation and oral exposure. Although there are some toxicokinetic data that provide information on the retention of inhaled radium sulfate in the lung, it is not clear whether this compound and other salts of radium would remain in the lung long enough after acute-duration exposure to cause local effects such as lung cancer or other carcinogenic or noncarcinogenic systemic effects.







Animal studies conducted via the inhalation, oral, and dermal routes of exposure for this duration period would be useful since the potential short-term effects of such exposure as well as effects that could emerge years later, such as cancer, are not known.

Intermediate-Duration Exposure. There are no data on intermediateduration exposure of humans to radium via the inhalation, oral, or dermal routes. There are no data on animals exposed via inhalation or the dermal route. The only information located was a very limited 20-day oral study in rats that resulted in osteogenic sarcomas. The data were not sufficient to calculate an MEL by any route. The available toxicokinetic data show that radium can be absorbed and retained after inhalation or oral exposure, although quantitative data are lacking. It would be useful to have information on the effects of intermediate-duration exposure to radium via inhalation, oral, and dermal routes in order to help assess the potential health effects of exposure to radium in the vicinity of hazardous waste sites and other settings, and to evaluate the possibility of long-range effects such as cancer that may emerge years later.

Chronic-Duration Exposure and Cancer. A case report is available on human chronic-duration exposure to radium via inhalation and indicates that acute leukopenia, bronchopneumonia, and death occurred in a chemist after 14 years of exposure. A case report is also available on a man who regularly consumed bottles of a "rejuvenating" tonic containing radium for about 5 years, resulting in effects described as necrosis of the jaw, abscess of the brain, secondary anemia, bronchopneumonia, and death. (Each of these causes of death can also be attributed to other etiologies.) Numerous studies have followed the dial painters who ingested radium, and effects reported in these studies include anemia, bone sarcomas, head carcinomas, and death. Although dermal exposure to radium also occurred in these cases, skin effects have not been reported. No data are available on chronic-duration exposure to radium by animals via any route of exposure. The available data were not considered to be adequate to calculate an MEL for any route of exposure. Animal studies on the noncarcinogenic effects of chronic-duration exposure to radium via inhalation, oral, and dermal exposure would be useful in assessing the potential health risks of humans chronically exposed to low levels of radium in the vicinity of hazardous waste sites and other settings.

Bone cancer has occurred in humans after chronic-duration oral exposure to radium and in rats that were orally exposed in an intermediate duration study (20 days). It would be useful to have carcinogenicity information from animal studies conducted via

inhalation, oral, and dermal exposure since humans in the vicinity of hazardous waste sites and other settings would be exposed to radium via all routes of exposure.

Genotoxicity. Neither <u>in vitro</u> nor <u>in vivo</u> genotoxicity studies have been located for radium. A battery of <u>in vitro</u> genotoxicity tests may provide useful information on the mechanism of carcinogenicity for radium.

Reproductive Toxicity. No studies were located on reproductive effects of radium in humans or animals via inhalation, oral, or dermal exposure. Animal studies using the oral route would be especially useful in evaluating the potential for these effects in human populations exposed to high levels of radium in drinking water (eg., more than 5 pCi). Studies using dermal and inhalation exposure would also be useful, since these are also probable routes of human exposure to radium in the vicinity of hazardous waste sites and other settings.

Developmental Effects. No information has been located on developmental effects in humans or animals resulting from inhalation, oral, or dermal exposure to radium. It was observed that radium-224 injected into young children markedly reduced their adult height due to radiation damage to the growth plate in the long bones. Animal studies via inhalation, oral, and dermal exposure would be useful in determining if radium, like calcium, can cross the placenta and enter fetal circulation, and can have adverse effects upon fetal development.

Immunotoxicity. Studies that assess the potential effects of radium on the immune system of orally or dermally exposed humans have not been located. The case report of a chemist exposed to radium primarily via inhalation for 14 years reported leukopenia and the almost total absence of granular leukocytes, leukoblastic groups, and lymphoid tissue in the bone marrow. No studies on animals exposed via inhalation, oral, or dermal routes have been located. A study reporting a reduction in peripheral white blood cells in intraperitoneally injected rats has been located. The reported observations suggest that immunological effects may be a concern for humans exposed to radium. A battery of immune function tests conducted in animals via inhalation and the oral and dermal routes would provide useful information relative to this concern.

Neurotoxicity. No reports of neurotoxicity resulting from inhalation, oral, or dermal exposure were located in the available human and animal studies. No further information appears to be needed at this time.

Epidemiological and Human Dosimetry Studies. Two large studies in Germany that follow radium-224 injected patients are being conducted by Spiess and by Wick and Gossner, and the radium study being conducted at Argonne National Laboratory has developed a large data base with information on the radium dial painters, patients who were medically treated with radium, and other persons exposed to radium. These studies will be of value in determining any effects that may be experienced by these aging populations. Additional data are not needed at this time.

Biomarkers of Exposure and Effect. Currently, human exposure to radium can be assessed by the presence of radioactivity in the body as measured by a whole body counter and in biological fluids such as blood or urine by gamma spectroscopy.

Effects specifically related to radium exposure have not been identified. Studies to identify potential biomarkers of radium's subtle effects would be useful as indicators that immediate mitigation of exposure to radium is warranted or that serious effects such as bone cancer may follow.

Absorption, Distribution, Metabolism, and Excretion. Quantitative data on the absorption of radium after intake via any exposure route are very limited. No data were located on the absorption of radium after dermal exposure. Information on laboratory workers exposed to radium during an industrial accident indicates that absorption can occur via the inhalation route. A study in elderly human subjects indicated that at least 20% of the ingested radium-224 in mock radium dial paint was absorbed and retained. No studies were located on the absorption of radium by animals after inhalation or dermal exposure. A study of orally exposed rats indicated that retention of radium at 400 to 500 days was 1% to 7% of the administered dose. Further studies to investigate the absorption and retention of radium after inhalation, oral, and dermal exposure would be helpful in elucidating the relative risks associated with exposure by each route.

No studies have been located regarding the distribution of radium in humans after oral or dermal exposure. Due to the findings of osteosarcomas in the radium dial painters and in a study in rats and the presence of radium in the exhumed skeletal remains of the dial workers, it is assumed to deposit in the bone after oral exposure. Data from a study of laboratory workers exposed via inhalation during an accident and a case report of a chemist exposed for 14 years also indicate that most radium was deposited in the skeleton. In the case of the chemist, no measurable levels of activity were found in the liver, gastrointestinal tract, heart, or kidneys. Information on radium

distribution following inhalation, oral and dermal exposure would be useful in helping to determine the potential target organs in persons exposed via each route.

Radium salts, such as radium sulfate, can be dissociated to Ra2+ and the corresponding anion. However, radium is an element and cannot be metabolized. It is changed over time by the decay of its isotopic forms, each at its own rate. Therefore, no information is needed in this area.

Excretion data in orally and parenterally exposed humans indicate that feces is the major route of radium excretion and that biliary excretion is probably also involved. Some urinary elimination also takes place in persons exposed via inhalation, oral, and dermal routes. Continued excretion for months after exposure has been attributed to the release of radium from the lungs in persons exposed via inhalation and from the turnover of bone matrix in persons exposed orally or via parenteral administration. It would be useful to have quantitative information on the excretion patterns of radium administered to animals via inhalation, oral, and dermal administration and to more clearly elucidate the role of biliary excretion in the elimination process.

Comparative Toxicokinetics. There are currently not enough data to evaluate any potential species-related differences in response to radium exposure by any route. It would be useful to have information on which animal models most closely approximate humans in this regard in order to help interpret the relevance to humans of any toxicity findings in animal studies. Studies on the toxicokinetics of radium following inhalation, oral, and dermal exposure are needed to compare the different routes of exposure.

2.8.3 On-going Studies

In Germany, Spiess is following about 900 patients who were injected with radium-224 immediately after World War II. Wick and Gossner are following a larger group of about 1,500 patients injected more recently with lower doses of radium-224. These studies are currently active, and summaries of their data are published periodically.

The Center for Human Radiobiology at the Argonne National Laboratory is the repository for all data accumulated in the United States on radium-exposed persons. This study has recently been severely reduced in magnitude, but the records on 5784 cases remain available at the laboratory (Rundo et al. 1986).

Two large studies of radium and other bone-seeking radionuclides in dogs were conducted at the University of Utah (Wrenn et al. 1986) and at the University of California at Davis (Raabe et al. 1981, 1983). Results of both projects are still being analyzed.

3. CHEMICAL AND PHYSICAL INFORMATION

3.1 CHEMICAL IDENTITY

The chemical formula and available identification numbers for radium are listed in Table 3-1.

3.2 PHYSICAL AND CHEMICAL PROPERTIES

Table 3-2 lists important physical properties of radium and selected radium compounds. Radioactive properties of the four naturally-occurring radium isotopes are listed in Table 3-3. In addition to the naturally occurring isotopes, there are 12 other known isotopes of radium. The principal decay schemes of the uranium and thorium decay series that produce the naturally-occurring radium isotopes are presented in Figure 3-1.

3. CHEMICAL AND PHYSICAL INFORMATION

	Value	Reference		
Chemical name	Radium	NLM 1988		
Natural isotopes	Radium-223; Radium-224; Radium-226; Radium-228	Windholz 1983		
Trade name	No data			
Chemical formula	Ra	NLM 1988		
Chemical structure	Ra ⁺²	NLM 1988		
Valence state	+2	Windholz 1983		
Identification numbers:				
CAS Registry NIOSH RTECS EPA Hazardous Waste OHM/TADS	7440-14-4 No data No data No data	NLM 1988		
DOT/UN/NA/IMCO Shipping HSDB NCI	No data 2146 No data	HSDB 1988		

TABLE 3-1. Chemical Identity of Radium

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

Property	Radium	Radium Bromide	Radium Carbonate	Radium Chloride	Radium Hydroxide	Radium Iodate	Radium Nitrate	Radium Sulfate
Chemical formula	Ra	RaBr ₂	RaCO3	RaCl ₂	Ra(OH) ₂	RaIO ₃	RaNO ₃	RaSO ₄
Molecular weight	226.03	385.83	286.03	296.93	No data	575.83	350.04	382.08
Synonyms	No data	No data	Carbonic acid, radium salt	No data	No data	No data	Nitric acid, radium salt	Sulfuric acid, radium salt
CAS number	7440-14-4	10031-23-9	7116-98-5	10025-66-8	98966-86-0	No data	10213-12-4	7446-16-4
Color	Silver- white	White	White	Yellowish- white	No data	No data	No data	White
Physical state	Solid	Solid	Solid	Solid	No data	No data	Solid	Solid
Melting point	700°C	728°C	No data	1000°C	No data	No data	No data	No data
Boiling point	<1140°C	900°C (sublimes)	No data	No data	No data	No data	No data	No data
Density at 20°C	5	5.79	No data	4.91	No data	No data	No data	No data
Odor Odor threshold:	No data	No data	No data	No data	No data	No data	No data	No data
Water	No data	No data	No data	No data	No data	No data	No data	No data
Air Solubility:	No data	No data	No data	No data	No data	No data	No data	No data
Water at 20°C	Decays	Soluble	Insoluble	Soluble	No data	Solub le	Soluble	Insoluble
Other solvents	Decays	Soluble	Decomposes	Soluble	No data	No data	No data	Insoluble
	in acids	in alcohol	in acids	in alcohol				in acids
Partition coefficients:	L							
Log octanol/water	na ^b	NA	NA	NA	NA	NA	NA	NA
Log Koc	NA	NA	NA	NA	NA	NA	NA	NA
Vapor pressure at 20°C	No data	No data	No data	No data	No data	No data	No data	No data
Henry's law constant: Autoignition	NA	NA	NA	NA	NA	NA	NA	NA
temperature	No data	No data	No data	No data	No data	No data	No data	No data
Flashpoint	No data	No data	No data	No data	No data	No data	No data	No data
Flammability limits	No data	No data	No data	No data	No data	No data	No data	No data
Conversion factors	No data	No data	No data	No data	No data	No data	No data	No data

TABLE 3-2.	Physical and	Chemical Properties	of Selected	Radium Compounds ^a

^aSources: CHEMNAME 1989; Sax and Lewis 1987; Weast 1985; Windholz 1983. $^{\rm b}{\rm NA}$ = not applicable

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CHEMICAL AND PHYSICAL INFORMATION

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3. CHEMICAL AND PHYSICAL INFORMATION

TABLE 3-3. Selected Radioactive Properties of Naturally Occurring Isotopes of Radium^a

Isotope	Decay Mode	Decay Energy (MeV ^b)	Half-life
Radium-223	alpha	5.979	11.4 days
Radium-224	alpha	5.789	3.6 days
Radium-226	alpha	4.870	1600 years
Radium-228	beta	0.045	5.7 years

^aSource: Weast 1985. ^bMillion electron volts

Uranium-238 series				Thorium-232 series				Uranium-235 series									
Np																	
U	²³⁸ U 4.5 x 10 ⁹ years		²³⁴ U 2.5 x 10 ⁵ years										²³⁵ U 7.1 x 10 ⁸ years				
Pa	↓	²³⁴ Pa / 1.18 min	ł										•	²³¹ Pa 3.2 x 10 ⁴ years			
Th	²³⁴ Th 24.1 days		²³⁰ Th 7.5 x 10 ⁴ years					²³² Th 1.4 x 10 ¹⁰ years		²²⁸ Th 1.90 years			²³¹ Th 25.6 h	•	²²⁷ Th 18.6 days		
Ac									²²⁸ Ac 6.13 h					²²⁷ Ac 22.0 years			
Ra			²²⁶ Ra 1622 years					²²⁸ Ra 5.75 years		²²⁴ Ra 3.64 days					²²³ Ra 11.4 days		
Fr			•							•					•		
٦n			²²² Rn 3.825 days							²²⁰ Rn 54.5 s					²¹⁹ Rn 3.92 s		
At			+							Ļ					↓		
⁵ 0			²¹⁸ P0 3.05 min		²¹⁴ Po 1.6 x 10 ⁻⁴ ✓ sec		²¹⁰ Po 138.4 ✔ days			²¹⁶ Po 0.158 s	65 percent	²¹² Po 3.0 x 10 ⁷ s			215Po 1.8 msec		
Bi			↓	²¹⁴ Bi 19.7 min	↓	²¹⁰ Bi 5.0 days	↓			Ļ	²¹² Bi 60.5 min				•	²¹¹ Bi 2.16 min	
ър			²¹⁴ РЪ 26.8 min		²¹⁰ Pb / 22.3 years		²⁰⁶ Pb stable			²¹² Pb 10.6 h	35 percent	stable			211Pb 36.1 min	•	³⁰⁷ Pb stable
Ti											²⁰⁸ Ti 3.1 min	1				²⁰⁷ Ti 4.79 min	

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FIGURE 3-1. Uranium and Thorium Isotope Decay Series Showing the Sources and Decay Products of the Four Naturally-Occurring Radium Isotopes

Adapted from: Aieta et al. 1987.

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4. PRODUCTION, IMPORT, USE, AND DISPOSAL

4.1 PRODUCTION

Between 1913 and 1920, about 70 g of radium were produced by Pittsburgh refineries (Blaufox 1988). No current information on production of radium has been located.

4.2 IMPORT

No current information has been located on the importation of radium. In the late 1970's, Zaire and Canada were the world's principal producers of radium (HSDB 1988). No quantitative data regarding U.S. imports of radium from those countries have been located.

4.3 USE

Radium has been used as a radiation source for treating neoplastic diseases, as a radon source, in radiography of metals, and as a neutron source for research (Weast 1985; Windholz 1983).

Until the 1960s, radium was a component of the luminous paints used for watch and clock dials, instrument panels in airplanes, military instruments, and compasses (Blaufox 1988).

During the early years of this century, radium was used in potions with supposed curative properties. This practice was discontinued by the early 1930's (Blaufox 1988; Macklis 1990).

4.4 DISPOSAL

Because radium is a radioactive substance, disposal of wastes containing radium is controlled by a number of federal and state regulations (see Chapter 7). Both the EPA and the Nuclear Regulatory Commission have promulgated regulations for land disposal of these wastes detailing containment requirements and permissible exposure levels based on radioactivity.

On a global level, the amount of radium released to the environment OK disposed of through industrial use is considered to be insignificant compared to the natural occurrence of radium in the environment. Radium is present in the wastes of uranium mining and refining processes, and disposal of these wastes is regulated.

5.1 OVERVIEW

Radium is a naturally-occurring metal that is almost ubiquitous in soils, water, geologic materials, plants, and foods at low concentrations. The utilization of radium, uranium, and fossil fuels has resulted in the redistribution of radium in the environment by way of air, water, and land releases. The concentration of radium in natural water is usually controlled by adsorption-desorption reactions with minerals and rocks and by the solubility of radium-containing minerals. In addition, radium is constantly being produced by the radioactive decay of its precursors, uranium, and thorium. Radium does not degrade other than by radioactive decay at rates which are specific to each of four naturally-occurring isotopes. The concentrations of radium-226 and radium-228 in drinking water are generally low, but there are specific geographic regions where high concentrations of radium occur due to geologic sources. Radium may be bioconcentrated and bioaccumulated by plants and animals, and it is transferred through food chains from lower trophic levels to humans.

The frequency of NPL hazardous waste sites in the United States at which radium has been found at higher than background levels can be seen in Figure 5-1.

5.2 RELEASES TO THE ENVIRONMENT

5.2.1 Air

The combustion of coal may be the most important mechanism for releasing radium into the atmosphere. The mean concentration of radium-226 in coal is on the order of 1 pCi/g (0.04 Bq/g). When combusted, radium may volatilize, then condense onto coal fly ash particles, which in turn may be released from power plants as fugitive emissions. The concentrations of radium-226 in fly ash have ranged from 1 to 10 pCi/g (0.04 to 0.4 Bq/g) (Coles et al. 1978; Eisenbud and Petrow 1964; Morris and Bobrowski 1979).

The radium-228 content of fly ash has varied from 1.8 to 3.1 pCi/g (0.07 to 0.12 Bq/g) (Eisenbud and Petrow 1964). If it is assumed that the total radium content of fly ash is 5 pCi/g (0.19 Bq/g), and that 1% of the ash generated at all coal-fired power plants in the United States escapes into the atmosphere, then an order-of-magnitude estimate of the amount of radium released each year would be 2.2 Ci (81,000,000 kBq) (Roy et al. 1981). Eisenbud and Petrow (1964) estimated that a single 1000-megawatt coal-fired power plant will discharge about 28 mCi (1,037,000 kBq) of total radium per year. Radium-226 has been detected in soils in industrial regions at levels up to 8.1 pCi/g (0.30 Bq/g) (Jaworowski and Gryzbowska 1977).

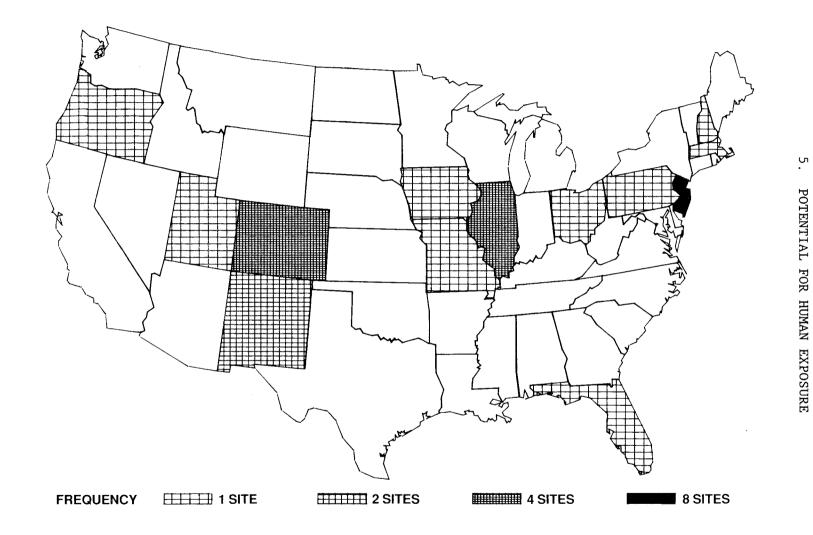


FIGURE 5-1. Frequency of Sites with Radium Contamination

Global releases of radium-226 by the combustion of coal have been estimated as 150 Ci (5,550,000,000 kBq) per year (Jaworowski et al. 1971). It has also been observed that radium-226 concentrations in glacial ice samples collected in Europe have increased by a factor of 100 during the last 80 years. The source of these elevated levels of radium may have been emissions from fossil fuels (Jaworowski et al. 1971).

Another potential source of atmospheric radium is particulate matter created by uranium mining and milling operations. However, no information was located on estimated releases or atmospheric concentrations.

5.2.2 Water

The most significant water-related releases of radium may be from the leaching of uranium mine tailings and from the release of ore -processing effluents generated by leaching, decantation, and filtration processes. Approximately 97 million tons of mine tailings that contain an estimated 60,000 Ci $(2.2 \times 10^9 \text{ kBg})$ of radium-226 have been stockpiled at the surface in the western United States (Kaufmann et al. 1976). It has been estimated that 10 million tons of uranium mine tailings are generated each year in Canada (Kalin 1988). Laboratory extraction studies (Havlik et al. 1968a, 1968b) have demonstrated that radium-226 may leach from solid wastes, particularly by acidic wastewaters. Surface runoff and leachate from uranium mine tailings have contained radium-226 ranging from 38 to 116 pCi/L (1.4 to 4.3 Bq/L) (Kalin 1988; Swanson 1985). Untreated uranium milling effluent has contained radium-226 at up to 2.2 μ Ci/L (81 kBq/L) (Sebesta et al. 1981). In the past, leachate from mine tailings containing radium-226 concentrations of 53 to 292 pCi/L (2 to 11 Bq/L) has been deep-well injected (Kaufmann et al. 1976). Approximately 2,000 to 3,000 Ci (74,000,000,000 to 111,000,000,000 kBq) of total radioactivity were released to the subsurface by two uranium mills in New Mexico. No information was located on the total amount of radium released to the environment by water-related discharges. As discussed in Section 5.4.2, however, concentrations of radium-226 and radium-228 found in surface and ground water sources have generally been low.

5.2.3 Soils

Land releases of radium are related to atmospheric fallout of coal fly ash (see Section 5.2.1). For example, elevated radium-226 concentrations in snow have been detected near a coal-fired power plant in Poland (Jaworowski et al. 1971). Other land releases may include the disposal of coal fly ash, lime slurry derived from water softening processes, and uranium mine tailings and associated wind-blown dusts.

However, no information was located on the total amount of land-released radium.

5.3 ENVIRONMENTAL FATE

Radium may be transported in the atmosphere in association with particulate matter. It exists primarily as a divalent ion in water, and its concentration is usually controlled by adsorption-desorption mechanisms at solid-liquid interfaces and by the solubility of radiumcontaining minerals. Radium does not degrade in water other than by radioactive decay at rates that are specific to each isotope. Radium may be readily adsorbed by earth materials; consequently, it is usually not a mobile constituent in the environment. It may be bioconcentrated and bioaccumulated by plants and animals, and it is transferred in food chains from lower trophic levels to humans.

5.3.1 Transport and Partitioning

5.3.1.1 Air

Radium may be transported in the atmosphere by the movement of particulate matter derived from uranium and coal utilization (see Section 5.2.1). These fugitive emissions would be subject to atmospheric dispersion, gravitational settling and wash-out by rain.

No data were located on the residence time of radium in the atmosphere or its deposition rate. However, data for other elements adsorbed to particulate matter indicate that the residence time for fine particles is about 1 to 10 days (EPA 1982b; Keitz 1980). Radium may, therefore, be subject to long-range transport in the atmosphere.

5.3.1.2 Water

Radium in water exists primarily as a divalent ion (Ra^{2^+}) and has chemical properties that are similar to barium, calcium, and strontium. The solubility of radium salts in water generally increases with increased pH levels. The solubilities of radium sulfate and carbonate are low; the solubility constants for crystalline RaSO, and RaCO, have been estimated as 5.495 x 10^{-11} mole/L and 5.01 x 10^{-9} mole/L,respectively (Langmuir and Riese 1985). Radium nitrate, chloride, and iodate are very soluble in water (Ames and Rai 1978). However, the concentration of radium in water is usually controlled by adsorptiondesorption reactions at solid-liquid interfaces which are in turn influenced by pH (see Section 5.3.1.3) or by the dissolution and coprecipitation of minerals that contain radium (EPA 1985a; Langmuir and Riese 1985). The tendency for radium to coprecipitate with barite, and sparingly soluble barium sulfate, as (BaRa)SO₄ is well known. Moreover, water treatment by adsorption and water-softening techniques are thought

to be effective in reducing radium in untreated drinking water (Watson et al. 1984). Therefore, it is likely that radium in water does not migrate significantly from the area where it is released or generated (EPA 1985a). Limited field data also support the generalization that radium is not mobile in groundwater (Kaufmann et al. 1976; Swanson 1985).

5.3.1.3 Aquifers, Sediments, and Soils

Radium in water may be readily adsorbed by sediments, soils, and aquifer components. It has been experimentally demonstrated that radium can be adsorbed by soils and sediments (Benes and Strejc 1986; Landa and Reid 1982), ferric hydroxide and quartz (Benes et al. 1984; Valentine et al. 1987), kaolinite and montmorillonite (Benes et al. 1985), and muscovite and albite (Benes et al. 1986).

Partition coefficients such as adsorption constants (K_d) describe the tendency of chemicals to partition to solid phases from water. Adsorption constants for inorganic ions such as Ra^{2+} cannot be predicted a priori because they depend on the type of adsorbent, the pH of the water, and the presence of other ions in solution. K_d values for sand have varied from 18 to 1,742 mL/g in the pH range of 7.4 to 8.3 (Benes et al. 1984; Valentine et al. 1987). K_d values for clay minerals and other common rock-forming minerals have ranged from 2,937 to 90,378 mL/g in alkaline solutions (Benes et al. 1985, 1986). Similarly, K_{ds} for soils in alkaline solutions have ranged from 214 to 467 mL/g (Ames and Rai 1978). Adsorption constants based on field studies with lake sediments have varied from 205 to 15,833 mL/g (Swanson 1985). The magnitude of these adsorption constants indicate that partitioning to solid surfaces is a major removal mechanism of radium from water. Swanson (1985) concluded that about 90% of the radium-226 released by uranium-mine effluent to two small lakes was adsorbed by the lake sediments and algae-detrital material.

The removal of Ra^{2^+} by adsorption has been attributed to ion exchange reactions, electrostatic interactions with potential determining ions at mineral surfaces, and surface-precipitation with $BaSO_4$. The adsorptive behavior of Ra^{2^+} is similar to that of other divalent cationic metals in that it decreases with an increase in pH and is subject to competitive interactions with other ions in solution for adsorption sites. In the latter case, Ra^{2^+} is more mobile in groundwater that has a high total dissolved solids (TDS) content. It also appears that the adsorption of Ra^{2^+} by soils and rocks may not be a completely reversible reaction (Benes et al. 1984, 1985; Landa and Reid 1982). Hence, once adsorbed, radium may be partially resistant to removal, which would further reduce the potential for environmental release and human exposure.

5.3.1.4 Plants and Animals

Transfer from soil to plants. Radium in the soil may be readily absorbed by plants, depending on the specific plant type and soil (Rayno 1983). Elevated concentrations of radium-226 above background levels have been detected in areas where radium and/or uranium was mined or processed (Kalin 1988; Rayno 1983; Tracy et al. 1983; Watson et al. 1984). The partitioning of radium-226 to plants from soils has been estimated by measuring the ratio of radium activity (or concentration) in the plant mass to that in the host soil. Soil-plant transfer coefficients or concentration factors have ranged from 1.1 x 10^{-3} to 6.5 (Rayno 1983; Tracy et al. 1983). Watson et al. (1984) concluded that a reasonable radium-226-concentration factor for fruits is 3 x 10^{-3} and that 0.1 describes the partitioning of radium-226 to forage and hay. An unweighted mean concentration factor for grain was 0.63. No information was located on soil-to-plant transfers for radium-228; however, its properties in this regard may be similar to those of radium-226.

Transfer from plants to cattle. There is a potential for human exposure to radium by the consumption of beef and milk derived from cattle who graze on forage grown in soils containing radium. The mean ratio of radium-226 in milk to that in the animal's diet has been estimated to be 3.8×10^{-3} (Watson et al. 1984). A similar ratio or transfer coefficient for flesh was 6.8×10^{-3} .

Transfer from water to aquatic organisms. Aquatic organisms such as fish, snails, clams, and algae can bioaccumulate radium from water. Bioconcentration factors (BCFs) for fish living in streams or lakes receiving uranium-processing waste effluent have ranged from 1 to 60 for flesh portions, and from 40 to 1,800 in bone samples (Markose et al. 1982; Swanson 1985). It has been proposed that bottom-feeding organisms ingest suspended solids containing adsorbed radium, then are in turn consumed by larger predatory fish.

5.3.2 Transformation and Degradation

5.3.2.1 Air

Pure metallic radium oxidizes when exposed to air, but radium compounds suspended in air are not subject to transformation or degradation mechanisms.

5.3.2.2 Water

Radium in water exists as a stable divalent ion; it probably does not hydrolyze nor is it significantly influenced by oxidation-reduction reactions (Ames and Rai 1978). The solubility of radium salts is increased with increasing pH levels.

5.3.2.3 Soil

Radium in soils and sediment does not biodegrade nor participate in any chemical reactions that transform it into other forms. The only degradation mechanism operative in air, water, and soil is radioactive decay. Radium has 16 known isotopes (see Chapter 3), but only 4 occur naturally (Radium-223, -224, -226, and -228). The half-life of radium-226 is 1,620 years. The half-lives of radium-228, radium-223, and radium-224 are 5.77 years, 11.4 days, and 3.64 days, respectively.

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

Radium is a naturally-occurring metal and is almost ubiquitous at low concentrations in air, water, soil, rocks, and food. The median concentrations of radium-226 and radium-228 in drinking water are generally low, but there are geographic areas where higher concentrations of radium are known to occur. The utilization of coal and uranium has resulted in re-distributing radium in the environment, but the overall effects appear to be small. Estimated levels of average human exposure to radium of non-occupational populations are presented in Table 5-1.

5.4.1 Air

Dust samples collected from the atmosphere of New York City were found to contain radium-226 at 8 x $10^{-5}~\rm pCi/m^3$ (3.0 x $10^{-6}~\rm Bq/m^3)$ and radium-228 at 1.5 x $10^{-4}~\rm pCi/m^3$ (5.6 x $10^{-6}~\rm Bq/m^3)$ (Eisenbud and Petrow 1964). No other published data on ambient concentrations of radium in the atmosphere were located.

5.4.2 Water

Radium is a naturally-occurring and fairly ubiquitous metal at low concentrations in water and rock-forming minerals. It has been estimated that the total mass of radium-226 in the earth's oceans is about 150 tons (Fremlin and Abu Jarad 1980). The occurrence of radium in ground, surface, and finished (treated) drinking water has been assessed (Aieta et al. 1987; Cech et al. 1988; EPA 1985a; Hess et al. 1985; Longtin 1988; Lucas 1985; Michel and Cothern 1986; Watson et al. 1984). In general, shallow wells tend to have lower radium-226 concentrations than deeper wells, and the total content in municipal

TABLE 5-1. Estimated Levels of Average Human Exposure to Radium by Nonoccupational Populations

Isotope	Medium	Typical Concentration In Medium	Assumed Rate of Intake of Medium	Assumed Fraction Absorbed	Estimated Intake ^a (pCi/kg/day)	Estimated Intake ^a (mBq/kg/day)
Radium-226	Air	8 x 10 ⁻⁵ pCi/m ^{3b}	20 m ³ /day	0.2	5 x 10 ⁻⁶	1.9 x 10 ⁻⁴
Radium-228	Air	1.5 x 10 ⁻⁴ pCi/m ^{3b}	20 m ³ /day	0.2	9 x 10 ⁻⁶	3.3×10^{-4}
Radium-226	Water	0.9 pCi/L ^C	2 L/day	0.2 ^d	0.005	0.19
	Water	10 pCi/L ^e	2 L/day	0.2	0.057	2.1
Radium-228	Water	1.4 pCi/L ^C	2 L/day	0.2	0.008	0.30
	Water	6.4 pCi/L ^f	2 L/day	0.2	0.037	1.4
Radium-226	Food	0.6 pCi/kg ^g	2 kg/day	0.2	0.003	0.11

^aAssuming a 70-kg adult.

^bEisenbud and Petrow (1964). Air samples collected in New York City.

^CMean concentration from Longtin (1988).

^dSee Section 2.3.1.2

^eMean concentration of noncompliance water (Hess et al. 1985).

 $f_{\text{Estimated mean of noncompliance water assuming that the ratio <math>^{228}\text{Ra}/^{226}\text{Ra}$ is 0.64 (Lucas 1985).

^gEstimated from Eisenbud (1973) and Bortoli and Gaglione (1972).

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(treated) water supplies is lower than that in raw well water (Watson et al. 1984). The radium content of surface water is usually very low. Radium-226 generally ranges from 0.1 to 0.5 pCi/L (0.004 to 0.019 Bq/L) (Hess et al. 1985). Based on 990 random samples of drinking water from ground water sources, the average population-weighted concentrations of radium-226 and radium-228 in the United States (excluding Hawaii) were about 0.91 pCi/L (0.034 Bq/L) and 1.41 pCi/L (0.052 Bq/L), respectively (Longtin 1988). Approximately 90% of these samples contained radium-226 at less than 1 pCi/L (0.04 Bq/L); similarly, about 90% contained radium-228 at less than 1 pCi/L (0.04 Bq/L). (These were not necessarily the same water sources.) However, there were approximately 200 public water supplies with radium-226 activities after treatment that were in excess of the regulatory maximum contaminant level (MCL) of 5 pCi (0.19 Bq) total radium/L (Hess et al. 1985). The mean radium-226 activity of the supplies in excess of the MCL was about 10 pCi/L (0.37 Bq/L).

A survey on the occurrence of radium-228 in municipal water supplies in Illinois, Iowa, Missouri, and Wisconsin indicated that the activity of this isotope may range from 0.3 to 32.0 pCi/L (11.1 to 1,180 mBq/L) (Lucas 2985), while Michel and Cothern (1986) reported that typical concentrations are less than 1 pCi/L (37 mBq/L).

There are few data on the occurrence of radium-224 in water. It has been speculated that the activity of this isotope could approach 30 to 40 pCi/L (1,110 to 1,480 mBq/L) (EPA 1985a).

Data on the presence of radon in groundwater can be used as a guide to the presumably corresponding presence of radium in the same source. Based on descriptions of aquifer composition or lithology and data from state water-resource agencies, counties with potentially high levels of radon in groundwater have been identified by Michel (1987). These estimates indicate that the U.S. counties with the highest levels of radium would be found in many areas of the Western third of the country, including large areas of California, Nevada, Idaho, and Montana. Wisconsin and Minnesota would also have high levels. In the East, the Appalachian Mountain region including almost all of Maine and New Hampshire would have high levels, as well as a large section of central Florida. It is important to note that quantitative estimates are not available, and the potentially "high" values for radon and radium imply only a comparison to other areas, not necessarily a risk to human health or the environment.

5.4.3 Soil

The mean concentration of radium-226 in 356 surface soil samples collected from 0 to 6 cm in 33 states was 1.1 pCi/g (0.041 Bq/g) (Myrick et al. 1981). This mean concentration is very similar to those reported

for typical igneous rocks (1.3 pCi/g or 0.048 Bq/g), sandstone (0.71 pCi/g or 0.026 Bq/g), shale (1.1 pCi/g or 0.041 Bq/g), and limestone (0.42 pCi/g or 0.016 Bq/g) (Eisenbud 1973). The concentration of radium-226 in soils in Northern Italy was reported to average 0.72 pCi/g [range: 0.08 to 3.8 pCi/g (0.003 to 0.14 Bq/g)] (DeBortoli and Gaglione 1972), excluding regions with extremely high levels of natural radioactivity (no data presented).

The concentrations of radium-226 in soils that were contaminated by mining or milling activities have ranged from less than 1 to 3,700 pCi/g (0.037 to 137 Bq/g) (Kalin 1988; Landa 1984; Tracy et al. 1983). No information was located on the occurrence of the other radium isotopes in soil or rocks.

The presence of uranium in soil can be used as an indication of occurrence of radium and radon in the same location. Based on geological reports and data synthesized from the National Uranium Resource Evaluation (NURE) program, areas with potentially high radon levels in soil gas have been identified by Michel (1987). These areas would have correspondingly high soil radium levels, although quantitative estimates are not available. These uranium "hot spots" occur with more frequency in the Western third of the United States, and include large areas of California and Idaho. High concentrations have been found in Wisconsin and Minnesota and a very dense area has been identified in western Missouri/eastern Kansas. In the East, high levels appear generally along the Appalachian mountains and near industrialized sites. High levels have also been found in the northern to central sections of Florida.

5.4.4 Other Media

Radium-226 may occur in many different foods, and reported activities have varied considerably. The mean radium-226 contents of diets in 11 cities in the United States were estimated to be 0.52 to 0.73 pCi/kg of food consumed (0.019 to 0.027 Bq/kg) (Eisenbud 1973). Estimates of the mean concentrations of radium-226 in milk and beef are 0.23 pCi/L (0.009 Bq/L) and 0.22 pCi/kg (0.008 Bq/kg) (fresh weight), respectively, in the United States (Watson et al. 1984). No information was located on the occurrence of radium-228 in food.

5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

Major sources of exposure to radium by the general population are the consumption of drinking water and food (Table 5-1). Of the many radionuclides found in nature, radium is considered to be one of the most important because of its wide occurrence in groundwater, and because it, like calcium, is retained in bone tissues (Aieta et al. 1987). Bone cancer is the greatest health risk from exposure to radium.

Based on assumptions about the concentration of radium in drinking water provided by utilities, the size of the population consuming this water, and the associated risk of cancer, Hess et al. (1985) estimated that the average concentration of radium in drinking water may cause cancer in 941 persons per year in the United States. The risk of exposure to radium in food is uncertain because of the variability in diets and in the radium-226 content of foods. It has been estimated that the yearly intake of radium-226 for food in New York City is on the order of 640 pCi (24 Bq) (Eisenbud 1973).

Levels of occupational exposure to radium are difficult to assess. Workers who are occupationally exposed to radium through the mining and processing of uranium are also probably exposed simultaneously to uranium itself, thorium, and radon by inhalation and probably dermal exposure. Nielson and Rogers (1981) suggested that inhalation exposures during uranium mining and milling operations involving crushing, grading, or blasting are the most significant routes of exposure. There is also some concern about ingesting dust at processing plants (Dixon 1985). It has also been suggested that inhalation of fugitive emissions from mine tailings could be locally significant (Ruttenber et al. 1984), but radium-specific data were not located.

5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

The populations at greatest risk of exposure from the consumption of drinking water with a high radium content are located in the Piedmont and Coastal Plain province in New Jersey, North Carolina, South Carolina, and Georgia and parts of Minnesota, Iowa, Illinois, Missouri, and Wisconsin (Hess et al. 1985; Longtin 1988). It has been estimated that about 600,000 people consume water with radium-226 concentrations in excess of the MCL (5 pCi/L or 0.19 Bq/L) in Illinois, Iowa, Missouri, and Wisconsin. Isolated occurrences of high radium-226 have also been detected in Arizona, New Mexico, Texas, Mississippi, Florida, and Connecticut. There is also a high probability of exposure to high radium-228 concentrations in many of the states listed above in addition to parts of California, Colorado, Idaho, Montana, New Mexico, and Wyoming (Michel and Cothern 1986).

It has been suggested that uranium miners and millers who are in chronic contact with dust are at risk. However, such workers are simultaneously exposed to several radionuclides and no generalization specific to radium can be made.

5.7 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCIA, 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 radium 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 radium.

The following categories of 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 known, would reduce or eliminate the uncertainties of human health assessment. Each data need discussion highlights the availability, or absence, of the relevant exposure information. A statement that reflects the importance of identified data needs is also included. In the future, these data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

5.7.1 Identification of Data Needs

Physical and Chemical Properties. Although some of the physical and chemical properties of radium and radium compounds have not been determined, many of those that are needed to evaluate its behavior in the environment are known. The adsorption-desorption behavior of radium with geologic materials depends on the specific system under study and should be determined on a case-by-case basis. Also, thermodynamic and kinetic data for solid solution formation are scarce. Research in this area would facilitate modeling the fate of radium in water.

Production, Import, Use, and Disposal. Radium is apparently used only in small quantities (e.g., in laboratories) in the United States. The quantities discharged to the environment from this source are probably insignificant compared to naturally-occurring radium. However, data on actual amounts of radium currently in use and amounts disposed of as waste would be useful in estimating human exposure potential.

Environmental Fate. Studies of releases of radium that result from uranium mining and processing would be helpful to fully assess the total amount and environmental fate of radium released to the environment. Field data on the mobility of radium in groundwater would also be helpful in attempts to predict its potential for occurrence in sources of drinking water at remote sites.

Bioavailability from Environmental Media. Data on the absorption of radium from environmental media via inhalation, oral, and dermal exposure would be useful in determining potential risks for organisms (humans, animals and plants) that have been exposed to radium in air, soil, or natural waters.

Food Chain Bioaccumulation. The existing information indicates that radium may be transferred through the food chain from lower trophic levels to humans. Additional monitoring studies in areas where radium occurs naturally at high concentrations in soil would be helpful to determine if this pathway is a significant route of exposure. The transfer of radium-228 from soils through the food chain has not been assessed.

Exposure Levels in Environmental Media. The concentration of radium-226 in drinking water has been the subject of numerous studies, and average values are reasonably well known. It appears that emphasis could be given to monitoring radium-226 concentrations in regions where high concentrations are expected to occur ("hot spots"), such as regions with high levels of natural radioactivity, in the vicinity of uranium mining and milling operations, and at NPL and other hazardous waste sites. Information on the occurrence of radium in the atmosphere would also be useful in helping to predict exposure via inhalation.

The occurrence of radium-228 has not been as well established, and additional data would be helpful, particularly in geologic regions where high concentrations are likely. There is virtually no information on the occurrence and levels of radium-223 and radium-224 in drinking water. The occurrence and levels of any of the isotopes of radium in food are highly variable, and additional data would facilitate exposure estimates.

Exposure Levels in Humans. There is no information available on the general background levels of radium in human tissue. Information on these levels, especially in the skeleton, would be especially useful as a means to monitor continuing exposure to radium.

Exposure Registries. A national exposure registry for persons exposed to radium was not located but would be useful in relating factors such as age, sex, season, geography, regulations, environment and other factors to measured exposure concentrations and health outcomes.

5.7.2 On-going Studies

The EPA is presently conducting a survey called the National Inorganics and Radionuclides Survey (NIRS). This study has been ongoing since 1981, and preliminary reports have been published. These data are still being analyzed for the establishment of revised interim drinking water regulations.

6. ANALYTICAL METHODS

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

6.1 BIOLOGICAL MATERIALS

The presence of radium in biological materials or environmental samples is generally determined by virtue of its radioactivity. Except in the laboratory where radium compounds have been isolated and determined for a certain purpose, determination of radium compounds in biological and environmental samples is relatively rare. As a Group IIA alkaline earth element, radium is similar in its chemical behavior to other members of that group, especially its nearest neighbor, barium. For example, radium tends to precipitate as the sulfate, which is the basis for its isolation for chemical analysis by coprecipitation with barium sulfate. Furthermore, radium associates with calcium in living systems and accumulates in bone. The determination of radium compounds or specific isotopes is usually accomplished by a separation procedure, followed by quantitative analysis of total radium based on its radioactivity.

Radium is determined in both biological and environmental samples by the emission of ionizing radiation from its radioisotopes (alphaeemitting radium-223, radium-224, and radium-226, as well as beta-emitting radium-228) and from its daughter products. Gamma-ray spectrometry of the gamma rays emitted by decay products of radium can also be used to measure radium. One of the most important examples is the measurement of gamma rays emitted by ²¹⁴Bi (Davis et al. 1987). Intermediate loss of radon gas in the decay chain can be troublesome in this kind of measurement. One method of radium measurement in bone collects the radioactive radon-222 gas product of the decay of radium-226, and its radioactivity is measured and extrapolated back to the concentration of radium-226 (Walton et al. 1959).

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A method has been developed to measure the rate of elimination of radon in exhaled breath (Stehney et al. 1955). Based on the assumption that 70% of the radon from fixed body radium is exhaled, this test can be used to calculate approximate levels of the body burden of radium. Some analytical methods for the determination of radium in biological materials are given in Table 6-1. It is important to note that the major contributions of these studies are descriptions of sample preparation techniques rather than advances in alpha or gamma spectrometry.

6.2 ENVIRONMENTAL SAMPLES

Because small amounts of radium radionuclides in environmental samples may be regarded as hazardous, it is usually necessary to detect very small quantities of radium which may require processing large quantities of sample (Quinby-Hunt et al. 1986). This introduces possibilities for contamination and sample loss. Specifically, in the case of water samples, sorption of the radionuclide to container walls and to suspended matter may be important sources of error.

Significant concentrations of contaminant radium may be submicromolar. Therefore, radiochemical separations are commonly employed that make use of a carrier, a nonradioactive element with chemical properties similar to those of radium. For radium, barium is the element of choice, and radium is coprecipitated from solution with barium sulfate, BaSO₄. Correction for losses in the precipitation procedure may be made by adding a tracer consisting of an isotope of radium not expected in the sample and noting its recovery at the end of the analytical procedure. The isotope radium-223 can be used for this purpose.

Radium is commonly determined in environmental samples by the emission of alpha particles from the radium-226 radioisotope. Betaemitting radium-228 can also be measured. Measurement of the radioactive radon-222 gas product of the decay of radium-226 can be used to give the concentration of radium-226. Gamma-ray spectroscopy of daughter radioisotopes such as ²¹⁴Bi can also be used to determine radium.

Because of the low penetrating power of alpha particles, special counters are required to assay alpha activity. These include gas-filled counters (thin window or internal, proportional counters), scintillation counters, and semiconductor detectors. In addition, a very thin sample is required to prevent the sample itself from absorbing alpha particles.

Sample Matrix	Sample Preparation	Analytical Method	Sample Detection Limit ^a	Accuracy ^a	Reference
Fish, whole, skin, bone	Skin, bone, flesh separated, bones ashed, dissolved, copre- cipitated with barium sulfate	Alpha spec- trometry	<0.8 pCi/g (0.03 Bq/g)	No data	Swanson 1983
Vole skeletal bones	Flesh separated from bones, bones ashed, dissolved, radium coprecipitated with barium sulfate	Alpha spec- trometry	No data	98 ± 10%	Burns et al. 1987
Biological sam- ples (fish tissue)	Freeze dry, grind, seal in count- ing vials to ensure equilibrium with daughter nuclides	Gamma spec- trometry	0.14-0.27 pCi/g ^b (5-10 mBq/g)	No data	Joshi 1987
Human, whole body	Count total activity with a whole body counter	Gamma spec- trometry	No data	No data	Toohey et al. 1983
Plant tissue	Collection of plant material, ashing	Gamma spec- trometry	No data	No data	Teixeira and Franco 1986
Plant shoots	Collection of plant material, ashing	Gamma spec- trometry	No data	No data	D'Souza and Mistry 1970
Human skeletal bones	Bone ashed, dissolved in hot, dilute hydrochloric acid, filtered. (Radon emanation is measured)	Gamma spec- trometry	No data	No data	Walton et al. 1959
log urine, feces	Urine and feces each sealed in cans, frozen for one month, then counted	Gamma spec- trometry	No data	No data	Lloyd et al. 1983

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

^aMost studies presented in this table were generally chosen because they present information on sample preparation rather than on advances in alpha or gamma spectrometry.

^bBased on dry mass.

< = less than; pCi = picocurie; g = gram; mBq = milliBecquerel.

ANALYTICAL METHODS

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6. ANALYTICAL METHODS

A promising method has been developed for measuring radium-226 concentrations in water samples of one liter size (Whittaker 1986). All nongaseous alpha-emitting radionuclides are coprecipitated with barium sulfate and iron hydroxide, followed by counting alpha emissions from the precipitate. A count at 3 hours followed by one at 7 days is used to measure radium-226.

Some analytical methods for the determination of radium in environmental samples are given in Table 6-2.

6.3 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, 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 radium 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 radium.

The following categories of 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 known, would reduce or eliminate the uncertainties of human health assessment. Each data need discussion highlights the availability, or absence, of the relevant exposure information. A statement that reflects the importance of identified data needs is also included. In the future, these data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

6.3.1 Identification of Data Needs

Methods for Determining Biomarkers of Exposure and Effect. As discussed above, the presence of radium in biological materials is usually determined by virtue of its radioactivity. Methods available for the determination of radioactivity in biological materials include alpha spectroscopy and gamma spectrometry, which is more convenient, but generally less sensitive, than alpha spectroscopy (Joshi 1987). It would be useful to have additional data on the sensitivity and accuracy of the methods that are currently in use.

Effects specifically associated with radium exposure have not been identified. The development of methods for detecting biomarkers of radium's effects would be useful.

Sample Matrix	Sample Preparation	Analytical Method	Sample Detection Limit	Accuracy	Reference
Soils	Samples collected to 0.3 m with a coring tool	No data	No data	No data	ASTM 1988a
coils	Samples collected from soil, reduced to small, homogen- eous sample	Gamma spec- trometry sug- gested ^a	No data	No data	ASTM 1988b
later	Precipitate with barium sulfate and iron hydroxide	Alpha counting	No data	94.2%	Whittaker 1980
Vater	Precipitate with barium sulfate and lead sulfate	Alpha counting	No data	94.9- 99.4%	APHA 1985a
Vater	Precipitate with barium sulfate, redissolve, evolve radon	Alpha counting of radon daughter	0.03 pCi	97.1- 98.0%	АРНА 1985Ъ
Water (for Radium-228)	Precipitate with barium sulfate and lead sulfate, separate actinium-228	Beta counting of actinium -228	No data	94.2%	APHA 1985c
Vater	Precipitate with barium sulfate and lead sulfate	Alpha count- ing of radium isotopes	l pCi/L	No data	ASTM 1988c
Water, soils, sediments	Collection of radium by resin	Gamma spec- trometry	0.5 pCi/L Ra-226	100 ± 2%	Lucas 1987
Water, soils, sediments	Collection of water samples	Gamma spec- trometry	No data	No data	Davis et al. 1987
Water ^b	Samples collected from soil reduced homogenous sample	Alpha and beta counting	<3 pCi/L	85 ± 24%	EPA 1986a
dater	Precipitate with barium sulfate and lead sulfate	Alpha count- ing of radium isotopes	No data	No data	EPA 1986b

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

^aThis is a sample processing and homogenization technique with which various analysis methods can be used. ^bMethod for gross alpha and beta activity, which may be indicative of radium content.

m = meter; pCi = picocurie; L = liter; Ra = Radium; < = less than.</pre>

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ANALYTICAL METHODS

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6. ANALYTICAL METHODS

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. It would be useful to have data on the sensitivity and accuracy of methods that are currently used to determine radium in environmental media. In addition, continued development of sensitive and accurate methods and instrumentation that would minimize problems with background and contamination would be useful in determining radium levels in environmental media. It would also be useful to develop portable, compact instruments to conduct field analyses with optimum sensitivity and accuracy.

6.3.2 On-going Studies

Refinements continue to be made in detecting radioactivity from radium isotopes and their daughter products. These developments include better, more sensitive detectors and more efficient data handling systems. Substantial improvements may be anticipated in the area of high resolution gamma spectroscopy. Research is underway to improve sample preparation and separation to give more sensitive analysis and better speciation. Because of the demands of cleanup programs including Superfund II, the Formerly Utilized Sites Remedial Action Program, and the Uranium Mill Tailings Remedial Action Program, research is underway to increase sample output and to decrease time and costs per sample (Donivan et al. 1987).

7. REGULATIONS AND ADVISORIES

International and national regulations and guidelines pertinent to human exposure to radium are summarized in Table 7-1. Recommendations for radiation protection for people in the general population as a result of exposure to radiation in the environment are found in the Federal Radiation Guidance (FRC 1960) and ICRP No. 26 (ICRP 1977). National guidelines for occupational radiation protection are found in the "Federal Radiation Protection Guidance for Occupational Exposure" (EPA 1987). This guidance for occupational exposure supercedes recommendations of the Federal Radiation Council for occupational exposure (FRC 1960). The new guidance presents general principles for the radiation protection of workers and specifies the numerical primary guides for limiting occupational exposure. These recommendations are consistent with the ICRP (ICRP 1977).

The basic philosophy of radiation protection is the concept of AURA (As Low As Reasonably Achievable). As a rule, all exposure should be kept as low as reasonably achievable, and the regulations and guidelines are meant to give an upper limit to exposure. Based on the primary guides (EPA 1987a), guides for Annual Limits on Intake (ALIs) and Derived Air Concentrations (DACS) have been calculated (EPA 1988). The AL1 is defined as "that activity of a radionuclide which, if inhaled or ingested by Reference Man (ICRP 1975), will result in a dose equal to the most limiting primary guide for committed dose" (EPA 1988; ICRP 1979) (see Appendix B). The DAC is defined as "the concentration of radionuclide in air which, if breathed by Reference Man (ICRP 1975) for a work-year, would result in the intake of one AL1 (EPA 1988). The ALIs and DACs refer to occupational situations but may be converted to apply to exposure of persons in the general population by application of conversion factors (Table 7-1).

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7. REGULATIONS AND ADVISORIES

TABLE 7-1. Regulations and Guidelines Applicable to Radium

Agency	Description	Value ^a *	Reference
	Internatio	onal	
Guidelin	25:		
ICRP	Occupational - whole body exposure	5 rem/yr (50 mSv/yr)	ICRP 1977
	Individual – short-term, to critical populations	0.5 rem/yr (5 mSv/yr)	
	Individual - chronic exposure	0.1 rem/yr (1 mSv/yr)	
WHO	Guideline values recommended Gross alpha activity Gross beta activity	<u>_pC1/L (Bq/L)</u> 2.7 (0.1) 27 (1)	WHO 1984
	National	1	
	·····	-	
Regulatio a. Air:	5015 :		
EPA OAQI	Hazardous Air Pollutant S NESHAPS (Radionuclides) (proposed)	NA	EPA 1989a
b. Water			
EPA OWRS	Effluent limitations guidelines	NA	EPA 1982a 40 CFR 440
EPA	MCL	pCi/L (Bg/L)	EPA 1986 c (40
ODW	Radium-226, radium-228	$5(2 \times 10^{-1})$	CFR 141.15,
	Gross alpha particle activity (excluding radon and uranium)	$15 (6 \times 10^{-1})$	141.16)
e. Nonsp	ecific media:		
EPA	Reportable quantity		EPA 1989b 40 CFR 302
	Radium-223	$\frac{\text{Ci} (Bq)}{1 (4 \times 10^{10})}$	
	Radium-224	$1 (4 \times 10^{-1})$ 10 (4 \times 10^{11})	
	Radium-225	$1 (4 \times 10^{10})$	
	Radium-226	0.1 (4x10 ⁹)	
	Radium-227	$1000 (4 \times 10^{13})$	
	Radium-228	0.1 (4x10 ⁹)	
EPA	Radiation protection:		
ORP	Standards for nuclear power	25 mrem	40 CFR
	operations. Annual radiation dose equivalent to whole body		190.10
	Standards for management and	100 Ci	40 CFR 191
	disposal of spent fuel and	$(4 \times 10^{12} \text{ Bq})$	Appendix A
	wastes. Release limit,	- • •	Table 1
	radium-226 ^b		

7. REGULATIONS AND ADVISORIES

gency	Description	Value ^a *	Reference
	Standards for uranium and thorium		40 CFR
	mill tailings. Radium-226:	pCi/g (Bq/g)	192.12
	First 15 cm of soil	$5(2 \times 10^{-1})$	
	More than 15 cm below soil	$15(6 \times 10^{-1})$	
	Groundwater protection	<u>pCi/L (Bg/L)</u>	40 CFR
	Combined radium-226 and -228	$5(2\times10^{-1})$	192.32
	Gross alpha particle activity	15 (6x10 ⁻¹)	
	(excluding radon and uranium)		
FDA	Levels in bottled water.	pCi/L (Bg/L)	21 CFR
	Radium-226 and -228	$5(2 \times 10^{-1})$	103.35
	Gross alpha particle activity	15 (6x10 ⁻¹)	
NRC	Radiation standards for exposure	NA	NRC 1988 ^C
	levels, discharge, disposal		10 CFR 20
	Radium-226	0.01 µCi	NRC 1988 ^C
		(4x10 ² Bq)	10 CFR 20
			Appendix C
uidelines:		đ	
EPA	Carcinogenic classification	Group A ^d	IRIS 1988, 1989
EPA	Occupational - the committed	5 rem/yr	EPA 1987a
	effective dose equivalent	(50 mSv)	
	(internal) and annual effective		
	dose equivalent (external) combined		
FRC	Individual - whole body exposure	0.5 rem/yr (5 mSv)	FRC 1960 ^e
FRC	Individual – operational guide for	0.17 rem/yr	FRC 1960 ^e
	"suitable sample of population" when	(1.7 mSv)	110 1700
	individual whole body doses are not known	, , , ,	
EPA	Lung clearance class ^f , ^g :		EPA 1988
	All forms	W	_
EPA	Occupational ALI for inhalation		EPA 1988
	of class W forms of ^h :	pCi (Bq)	
	Radium-223	7×10^5 (3 × 10 ⁴)	
	Radium-224	2×10^6 (7 × 10 ⁴)	
	Radium-225	7x10 ⁵ (3x10 ⁴)	
	Radium-226	6×10^5 (2×10 ⁴)	
	Radium-227	$1 \times 10^{10} (4 \times 10^8)$	
	Radium-228	1x10 ⁶ (4x10 ⁴)	
EPA	Occupational ALI for ingestion of ¹ :	pCi (Bq)	EPA 1988
	Radium-223	5×10^6 (2 × 10 ⁵)	
	Radium-224	8x10 ⁶ (3x10 ⁵)	
	Radium-225	8x10 ⁶ (3x10 ⁵)	
	Radium-226	2×10^6 (7 × 10 ⁴)	
	Radium-227	$2 \times 10^{10} (7 \times 10^8)$	
	Radium-228	2×10^{6} (7 × 10 ⁴)	

TABLE 7-1 (Continued)

 $\sum_{i=1}^{n-1} \frac{1}{i} \sum_{i=1}^{n-1} \frac{1}{i$

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7. REGULATIONS AND ADVISORIES

TABLE 7-1 (Continued)

Agency	Description	Value ^a *	Reference
EPA	Occupational DAC for inhalation		EPA 1988
	of class W forms of j:	pCi/cm^3 (Bg/m ³)	
	Radium-223	3×10^{-4} (1×10 ¹)	
	Radium-224	$7 \times 10^{-4} (3 \times 10^{1})$	
	Radium-225	$3 \times 10^{-4} (1 \times 10^{1})$	
	Radium-226	$3 \times 10^{-4} (1 \times 10^{1})$	
	Radium-227	$6 (2x10^5)$	
	Radium-228	$5 \times 10^{-4} (2 \times 10^{1})$	
FRC = Federa ICRP = Inter MCL = Maximm NRC = Nuclea OAQPS = Offic ODW = Office NESHAPS = Na	and Drug Administration al Radiation Council rnational Commission on Radiological Protection um Contaminant Level plicable ar Regulatory Commission ice of Air Quality Planning and Standards e of Drinking Water e of Radiation Programs ational Emissions Standards for Hazardous Air Po Health Organization	llutants	
	ry and Appendix B for definition of units		
^a Numerical v	values are provided in this column, when availab	le. However, many regulat	ions list chemicals

^aNumerical values are provided in this column, when available. However, many regulations list chemicals and/or involve requirements too complex for inclusion here. In these case, NA (Not Applicable) is inserted in this column. The cited references provide details of the regulations.

^bCumulative release to the accessible environment for 10,000 years after disposal per 1,000 metric tons of Heavy Metal or other units of waste.

^CThe Nuclear Regulatory Commission limits in 10 CFR 20 are in the process of revision.

dGroup A: Human carcinogen.

 e FRC guidance for occupational exposure is superseded by EPA (1987) Federal Radiation Protection Guidance. fLung clearance class indicates the rate at which the element is cleared from the lung: D (days), W (weeks), Y (years).

^gThe ALIs and DACs recommended by the EPA are numerically identical to those recommended by the ICRP Publication 30 (ICRP 1979).

^hConversion of the ALI for occupational settings to apply to exposure of persons in the general population is:

$ALI_i = ALI * 0.1$

where ALI_i is the intake for the general population, ALI is the intake for occupational exposures and 0.1 is the ratio of the dose limit to the individual (0.5 rem/yr) and the dose limit for occupational workers (5 rem/yr).

ⁱBased on a fractional uptake from the small intestine to blood (f₁) of 0.2.

 $^{
m j}$ Conversion of the DAC for occupational exposure to apply to the general public is:

$DAC_1 = DAC * 0.03$

where DAC_i refers to the "Derived Air Concentration" for exposure to the general population and 0.03 represents the adjustment for hours of exposure (168 hrs per month occupational vs. 720 hrs per month of continuous exposure), breathing rate (29 m³/day for occupational vs. 22 m³/day for the general population) and dose limits (0.5 rem/yr for individuals vs. 5 rem/yr for occupational settings).

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Absorbed Dose -- The mean energy imparted to the irradiated medium, per unit mass, by ionizing radiation. Units: gray (GY), rad.

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 radiation imparts some or all of its energy to any material through which it passes.

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.

Absorption Coefficient -- Fractional decrease in the intensity 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 deposition of energy in the absorber. The total absorption coefficient is the sum of individual energy absorption processes. (See Compton Effect, Photoelectric Effect, and Pair Production.)

Linear Absorption Coefficient -- A factor expressing the fraction of a beam of x or gamma radiation absorbed in a unit thickness of material. In the expression $I=I_0e^{\mu x}$, I_0 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.

Mass Absorption Coefficient -- The linear absorption coefficient per cm divided by the density of the absorber in grams per cubic centimeter. It is frequently expressed as μ/\bullet , where μ is the linear absorption coefficient and p 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 inducing radioactivity by irradiation.

Activity -- The number of nuclear transformations occurring in a given quantity of material per unit time. (See Curie.)

Activity Median Aerodynamic Diameter (AMAD) -- The diameter of a unitdensity sphere with the same terminal settling velocity in air as that of the aerosol particulate whose activity is the median for the entire aerosol.

Acute Exposure -- Exposure to a chemical for a duration of 14 days or less, as specified in the toxicological profiles.

Acute Radiation Syndrome -- The symptoms which taken together characterize a person suffering from the effects of intense radiation. The effects occur within hours or weeks.

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

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

Alpha Particle -- A charged particle emitted from the nucleus of an atom. An alpha particle has a mass charge equal in magnitude to that of a helium nucleus; i.e., two protons and two neutrons and has a charge of +2.

Annihilation (Electron) -- An interaction between a positive and a negative electron in which they both disappear; their energy, including rest energy, being converted into electromagnetic radiation (called annihilation radiation) with two 0.51 Mev gamma photons emitted at an angle of 180° to each other.

Atomic Mass -- 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} gm. (Symbol: u)

Atomic Number -- The number of protons in the nucleus of a neutral atom of a nuclide. 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 atoms of an element expressed in atomic mass units.

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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 -- Radiation arising from radioactive material other than that under consideration. Background radiation due to cosmic rays and natural radioactivity is always present. There may also be background radiation due to the presence of radioactive substances in building materials.

Becquerel (Bq) -- International System of Units unit of activity and equals one transformation (disintegration) per second. (See Units.) Beta Particle -- Charged particle emitted from the nucleus of an atom. A beta particle has a mass and charge equal in magnitude to that of the electron. The charge may be either +1 or -1.

Biologic Effectiveness of Radiation -- (See Relative Biological Effectiveness)

Bone Seeker -- Any compound or ion which migrates in the body preferentially into bone.

Branching -- The occurrence of two or more modes by which a radionuclide can undergo radioactive decay. For example, radium C can undergo • or β^- decay, ⁶⁴Cu can undergo β^- , β^+ , 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 -- The production of electromagnetic radiation (photons) by the negative acceleration that a fast, charged particle (usually an electron) undergoes from the effect of an electric or magnetic field, for instance, from the field of another charged particle (usually a nucleus).

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

Capture, Electron -- A mode of radioactive decay involving the capture of an orbital electron by its nucleus. Capture from a particular electron shell is designated as "K-electron capture," "L-electron capture,II etc.

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 capable of inducing cancer.

Carcinoma -- Malignant neoplasm composed of epithelial cells, regardless of their derivation.

Cataract -- A clouding of the crystalline lens of the eye which obstructs the passage of light.

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

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

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 of energy less than the incident photon.

Containment -- The confinement of radioactive material in such a way that it is prevented from being dispersed into the environment or is released only at a specified rate.

Contamination, Radioactive -- Deposition of radioactive material in any place where it is not desired, particularly where its presence may be harmful.

Cosmic Rays -- High-energy particulate and electromagnetic radiations which originate outside the earth's atmosphere.

Count (Radiation Measurements) -- The external indication of a radiation-measuring device designed to enumerate ionizing events. It may refer to a single detected event to the total number registered in a given period of time. The term often is erroneously used to designate a disintegration, ionizing event, or voltage pulse.

Counter, Geiger-Mueller -- Highly sensitive, gas-filled radiation-measuring device. It operates at voltages sufficiently high to produce avalanche ionization.

Counter, Scintillation -- The combination of phosphor, photmultiplier tube, and associated circuits for counting light emissions produced in the phosphors by ionizing radiation.

Curie - A unit of activity. One curie equals 3.7×10^{10} nuclear transformations per second. (Abbreviated Ci.) Several fractions of the curie are in common usage.

Megacurie -- One million curies. Abbreviated MCi.

Microcurie -- One-millionth of a curie $(3.7 \times 10^4 \text{ disintegrations})$ per sec). Abbreviated µCi.

Millicurie -- One-thousandth of a curie $(3.7 \times 10^7 \text{ disintegrations})$ per set). Abbreviated mCi.

Nanocurie -- One-billionth of a curie. Abbreviated nCi.

Picocurie -- One-millionth of a microcurie (3.7×10^{-2}) disintegrations per second or 2.22 disintegrations per minute). Abbreviated pCi; replaces the term µµc.

Decay, Radioactive -- Transformation of the nucleus of an unstable nuclide by spontaneous emission of charged particles and/or photons.

Decay Chain or Decay Series -- A sequence of radioactive decays (transformations) beginning with one nucleus. The initial nucleus, the parent, decays into a daughter 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. Sometimes, to distinguish the sequence, the daughter of the first daughter is called the granddaughter, etc.

Decay Constant -- The fraction of the number of atoms of a radioactive nuclide which decay in unit time. (Symbol •). (See Disintegration Constant).

Decay Product, Daughter Product -- A new isotope 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) may be either radioactive or stable.

Delta Ray -- Energetic or swiftly moving electrons ejected from an atom during the process of ionization. Delta rays cause a track of secondary ionizations along their path.

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

Disintegration Constant -- The fraction of the number of atoms of a radioactive nuclide which decay in unit time; 3, is the symbol for the decay constant in the equation $N=N_oe^{-\lambda t}$ where N_o is the initial number of atoms present, and N is the number of atoms present after some time, t. (See Decay Constant.)

Disintegration, Nuclear -- A spontaneous nuclear transformation (radioactivity) characterized by the emission of energy and/or mass from the nucleus. When large numbers of nuclei are involved, the process is characterized by a definite half-life. (See Transformation, Nuclear.)

Dose -- A general term denoting the quantity of radiation or energy absorbed. For special purposes it must be appropriately qualified. If unqualified, it refers to 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 protection. It expresses all radiations on a common scale for calculating the effective absorbed dose. It is defined as the product of the absorbed dose in rad and certain modifying factors. (The unit of dose equivalent is the rem. In SI units, the dose equivalent is the sievert, which equals 100 rem.)

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, 100 rad=l gray (Gy). (See Absorbed Dose.)

Maximum Permissible Dose Equivalent (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, 50 percent of the individuals in a large group of animals or organisms. Also called the LD_{50} .

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 and Rad.)

Dose, Fractionation -- A method of administering radiation, in which relatively small doses are given daily or at longer intervals.

Dose, Protraction -- A method of administering radiation by delivering it continuously over a relatively long period at a low dose rate.

Dose-distribution Factor -- A factor which accounts for modification of the dose effectiveness in cases in which the radionuclide distribution is nonuniform.

Dose Rate -- Absorbed dose delivered per unit time.

Dosimetry -- Quantification of radiation doses to individuals or populations resulting from specified exposures.

Early Effects (of radiation exposure) -- Effects which appear within 60 days of an acute exposure.

Electron -- A stable elementary particle having an electric charge equal to $\pm 1.60210 \times 10^{-19} \text{ C}$ (Coulombs) and a rest mass equal to $9.1091 \times 10^{-31} \text{ kg}$. 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. (Abbreviated: eV, 1 eV=1.6x10⁻¹² 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 <u>in utero</u> death.

Energy -- Capacity for doing work. "Potential energy" is the energy inherent in a mass because of its spatial relation to other masses. "Kinetic energy" is the energy possessed by a mass because of its motion; MKSA unit: $kg-m^2/sec^2$ or joules.

Binding Energy -- The energy represented by the difference in mass between the sum of the component parts and the actual mass of the nucleus.

Excitation Energy -- The energy required to change a system from its ground state to an exited state. Each different excited state has a different excitation energy.

Ionizing Energy -- The average energy lost by ionizing radiation in producing an ion pair in a gas. For air, it is about 33.73 eV.

Radiant Energy -- The energy of electromagnetic radiation, such as radio waves, visible light, x and gamma rays.

Enriched Material -- (1) Material in which the relative amount of one or more isotopes of a constituent has been increased. (2) Uranium in which the abundance of the 235 U isotope is increased above normal.

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.

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 radium and its series to Radium D. The half-life of radium is about 1,600 years; of radon, 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.

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. An example of this is radon (half-life of approximately 3.82 days) and successive members of the series to Radium D. Equilibrium, Radiation -- The condition in a radiation field where the energy of the radiations entering a volume equals the energy of the radiations leaving that volume.

Equilibrium Fraction (F) -- In radon-radon daughter equilibrium, the parents and daughters have equal radioactivity, that is, as many decay into a specific nuclide as decay out. However, if fresh radon is continually entering a volume of air or if daughters are lost by processes other than radioactive decay, e.g., plate out or migration out of the volume, a disequilibrium develops. The equilibrium fraction is a measure of the degree of equilibrium/disequilibrium. The working-level definition of radon does not take into account the amount of equilibrium. The equilibrium fraction is used to estimate working levels based on measurement of radon only.

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 a metastable state and will return to ground state by radiation of the excess energy.

Exposure -- A measure of the ionization produced in air by x or gamma radiation. It is the sum of the electrical charges on all ions of one sign produced in air when all electrons liberated by photons in a volume element of air are completely stopped in air, divided by the mass of the air in the volume element. The special unit of exposure is the roentgen.

Fission, Nuclear -- A nuclear transformation characterized by the splitting of a nucleus into at least two other nuclei and the release of a relatively large amount of energy.

Gamma Ray -- Short wavelength electromagnetic radiation of nuclear origin (range of energy from 10 keV to 9 MeV).

Genetic Effect of Radiation -- Inheritable change, chiefly mutations, produced by the absorption of ionizing radiation by germ cells. On the basis of present knowledge these effects are purely additive; there is no recovery.

Gray (Gy) -- SI unit of absorbed dose. One gray equals 100 rad. (See Units.)

Half-Life, Biological -- The time required for the body to eliminate one-half of any absorbed substance by regular processes of elimination. Approximately the same for both stable and radioactive isotopes of a particular element. This is sometimes referred to as half-time.

Half-Life, Effective -- Time required for a radioactive element in an animal body to be diminished 50% as a result of the combined action of radioactive decay and biological elimination.

Effective half-life: = <u>Biological half-life x Radioactive half-life</u> Biological half-life + Radioactive half-life

Half-life, Radioactive -- Time required for a radioactive substance to lose 50% of its activity by decay. Each radionuclide has a unique halflife.

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.

<u>In Vitro</u> -- Isolated from the living organism and artificially maintained, as in a test tube.

In Vivo -- Occurring within the living organism.

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 to 364 days as specified in the Toxicological Profiles.

Internal Conversion -- One of the possible mechanisms of decay from the metastable state (isomeric transition) in which the transition energy is transferred to an orbital electron, causing its ejection from the atom. 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.II

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 radiation energy.

Ionization Density -- Number of ion pairs per unit volume.

Ionization Path (Track) -- The trail of ion pairs produced by ionizing radiation in its passage through matter.

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.

Isotones -- Nuclides having the same number of neutrons in their nuclei.

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. Almost identical chemical properties exist between isotopes of a particular element. The term should not be used as a synonym for nuclide.

Stable Isotope -- A nonradioactive isotope of an element.

Joule -- The unit for work and energy, equal to one newton expended along a distance of one meter (lJ=lNxlm).

Labeled Compound -- A compound consisting, in part, of labeled molecules. That is molecules including radionuclides in their 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.

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

Lethal Concentration $_{(50)}(LC_{50})$ -- The 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 laboratory animal population.

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.

Lethal Dose $_{(50)}(LD_{50})$ -- The dose of a chemical which has been calculated to cause death in 50% of a defined laboratory animal population.

Lethal Time $_{(50)}$ (LT₅₀) -- A calculated period of time within which a specific concentration of a chemical is expected to cause death in 50% of a defined laboratory animal population.

Linear Energy Transfer (LET) -- The average amount of energy transferred locally to the medium per unit of particle track length.

Low-LET -- Radiation characteristic of electrons, x-rays, and gamma rays.

High-LET -- Radiation characteristic of protons or fast neutrons.

Average LET -- is specified to even out the effect of a particle that is slowing down near the end of its path and to allow for the fact that secondary particles from photon or fast-neutron beams are not all of the same energy.

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.

Linear Hypothesis -- The assumption that a dose-effect 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.

Malformations -- Permanent structural changes in an organism that may adversely affect survival, development, or function.

Mass Numbers -- The number of nucleons (protons and neutrons) in the nucleus of an atom. (Symbol: A)

Minimal Risk Level -- An estimate of daily human exposure to a chemical that is likely to be without an appreciable risk of deleterious effects (noncancerous) over a specified duration of exposure.

Mutagen -- A substance that causes mutations. A mutation is a change in the genetic material in a body cell. Mutation can lead to birth defects, miscarriages, or cancer.

Neurotoxicity -- The occurrence of adverse effects on the nervous system following exposure to chemical.

Neutrino -- A neutral particle of very small rest mass originally postulated to account for the continuous distribution of energy among particles in the beta-decay process.

No-Observed-Adverse-Effect Level (NOAEL) -- The dose of chemical at which there were no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

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 (Kow) -- The equilibrium ratio of the concentrations of a chemical in n-octanol and water, in dilute solution.

Pair Production -- An absorption process for x and gamma radiation in which the incident photon is annihilated in the vicinity of the nucleus of the absorbing atom, with subsequent production of an electron and positron pair. This reaction only occurs for incident photon energies exceeding 1.02 MeV.

Parent -- A radionuclide which, upon disintegration, yields a spec ified nuclide--either directly or as a later member of a radioactive series.

Photon -- A quantity of electromagnetic energy (E) whose value in joules is the product of its frequency (v) in hertz and Planck constant (h). The equation is: E=hv.

Photoelectric Effect -- An attenuation process observed for x- and gamma- radiation in which an incident photon interacts with an orbital electron of an atom delivering all of its energy to produce a recoil electron, but with no scattered photon.

Positron -- Particle equal in mass to the electron $(9.1091 \times 10^{-31} \text{ kg})$ and having an equal but positive charge (+1.60210x10⁻¹⁹ Coulombs). (See Electron).

Potential Ionization -- The potential necessary to separate one electron from an atom, resulting in the formation of an ion pair.

Power, Stopping -- A measure of the effect of a substance upon the kinetic energy of a charged particle passing through it.

Progeny -- The decay products resulting after a series of radioactive decays. 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 1.007277 mass units.

 q_1^* -- The upper-bound estimate of the low-dose slope of the doseresponse curve as determined by the multistage procedure. The q_1^* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually μ g/L for water, mg/kg/day for food, and μ g/m³ for air).

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 (QF) -- 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 effectiveness of the absorbed dose.

 ${\bf Rad}$ -- The unit of absorbed dose equal to 0.01 J/kg in any medium. (See Absorbed Dose.)

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Radiation -- (1) The emission and propagation of energy through space or through a material medium in the form of waves; for instance, the emission and propagation of electromagnetic waves, or of sound and elastic waves. (2) The energy propagated through space or through a material medium as waves; for example, energy in the form of electromagnetic waves or of elastic waves. The term radiation or radiant energy, when unqualified, usually refers to electro-magnetic radiation. Such radiation commonly is classified, according to frequency, as Hertzian, infra-red, visible (light), ultra-violet, X-ray and gamma ray. (See Photon.) (3) By extension, corpuscular emission, such as alpha and beta radiation, or rays of mixed or unknown type, as cosmic radiation.

Annihilation Radiation -- 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.

Background Radiation -- Radiation arising from radioactive material other than the one directly under consideration. Background radiation due to cosmic rays and natural radioactivity is always present. There may also be background radiation due to the presence of radioactive substances in other parts of the building, in the building material itself, etc.

Characteristic (Discrete) Radiation -- Radiation originating from an atom after removal of an electron of excitation of the nucleus, The wavelength of the emitted radiation is specific, depending only on the nuclide and particular energy levels involved.

External Radiation -- Radiation from a source outside the body -- the radiation must penetrate the skin.

Internal Radiation -- Radiation from a source within the body (as a result of deposition of radionuclides in body tissues).

Ionizing Radiation -- Any electromagnetic or particulate radiation capable of producing ions, directly or indirectly, in its passage through matter.

Monoenergetic Radiation -- Radiation of a given type (alpha, beta, neutron, gamma, etc.) in which all particles or photons originate with and have the same energy.

Scattered Radiation -- Radiation which during its passage through a substance, has been deviated in direction. It may also have been modified by a decrease in energy.

Secondary Radiation -- Radiation that results from absorption of other radiation in matter. It may be either electromagnetic or particulate.

Radioactivity -- The property of certain nuclides to spontaneously emit particles or gamma radiation or x radiation following orbital electron capture or after undergoing spontaneous fission.

Artificial Radioactivity -- Man-made radioactivity produced by particle bombardment or electromagnetic irradiation, as opposed to natural radioactivity.

Induced Radioactivity -- 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.

Natural Radioactivity -- The property of radioactivity exhibited by more than 50 naturally occurring radionuclides.

Radioisotopes -- A radioactive atomic species of an element with the same atomic number and usually identical chemical properties.

Radionuclide -- A radioactive species of an atom characterized by the constitution of its nucleus.

Radiosensitivity -- Relative susceptibility of cells, tissues, organs, organisms, or any living substance to the injurious action of radiation. Radiosensitivity and its antonym, radioresistance, are currently used in a comparative sense, rather than in an absolute one.

Reaction (Nuclear) -- An induced nuclear disintegration, i.e., a process occurring when a nucleus comes in contact with a photon, an elementary particle, or another nucleus. In many cases the reaction can be represented by the symbolic equation: $X+a\rightarrow Y+b$ or, in abbreviated form, X(a,b) Y. X is the target nucleus, a is the incident particle or photon, b is an emitted particle or photon, and Y is the product nucleus.

Reference Dose (RfD) -- An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the NOAEL (from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a

professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

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 required to produce an identical biological effect in a particular experimental organism or tissue. NOTE: This term should not be used in radiation protection. (See Quality Factor.)

Rem -- A unit of dose equivalent. The dose equivalent in rem is numerically equal to the absorbed dose in rad multiplied by the quality factor, the distribution factor, and any other necessary modifying factors.

Reportable Quantity (RQ) -- The quantity of a hazardous substance that is considered reportable under CERCIA. Reportable quantities are (1) 1 lb or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Section 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 for photon radiation. One roentgen equals 2.58×10^{-4} Coulomb per kilogram of air.

Short-Term Exposure Limit (STEL) -- The maximum concentration to which workers can be exposed continually for up to 15 minutes. 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, Radiation -- (Radiation Therapy): A self-limited syndrome characterized by nausea, vomiting, diarrhea, and psychic depression following exposure to appreciable doses of ionizing radiation,

particularly to the abdominal region. Its mechanism is unknown and there is no satisfactory remedy. It usually appears a few hours after irradiation and may subside within a day. It may be sufficiently severe to necessitate interrupting the treatment series or to incapacitate the patient. (General): The syndrome associated with intense acute exposure to ionizing radiations. The rapidity with which symptoms develop is a rough measure of the level of exposure.

Sievert -- The SI unit of radiation dose equivalent. It is equal to dose in grays times a quality factor times other modifying factors, for example, a distribution factor; 1 sievert equals 100 rem.

Specific Activity -- Total activity of a given nuclide per gram of an element.

Specific Energy -- The actual energy per unit mass deposited per unit volume in a given event. This is a stochastic quantity as opposed to the average value over a large number of instance (i.e., the absorbed dose).

Standard Mortality Ratio (SMR) -- Standard mortality ratio is the ratio of the disease or accident mortality rate in a certain specific population compared with that in a standard population. The ratio is based on 200 for the standard so that an SMR of 100 means that the test population has twice the mortality from that particular cause of death.

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 is deposited and remains on the surface for a long period of time. 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 structural defects that affect the development of a fetus.

Threshold Limit Value (TLV) -- An allowable exposure concentration averaged over a normal 8-hour workday or 40-hour workweek.

Toxic Dose (TD_{50}) -- A calculated dose of a chemical, introduced by a route other than inhalation, which is expected to cause a specific toxic effect in 50% of a defined laboratory animal population.

Transformation, Nuclear -- The process by which a nuclide is transformed into a different nuclide by absorbing or emitting a particle.

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/or internal conversion electron emission.

Tritium -- The hydrogen isotopes with one proton and two neutrons in the nucleus (Symbol: ${}^{3}\text{H}$ or T).

Unattached Fraction -- That fraction of the radon daughters, usually ²¹⁸Po (Radium A), which has not yet attached to a particle. As a free atom, it has a high probability of being retained within the lung and depositing alpha energy when it decays.

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,	Rad	liolo	ogical	
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Units	Equivalents
Becquerel* Curie Bq	1 Bq = 1 disintegration per second = 2.7×10^{-11} Ci 1 Ci = 3.7×10^{10} disintegrations per second = 3.7×10^{10}
Gray* Rad Rem Sievert*	1 Gy = 1 J/kg = 100 rad 1 Rad = 100 erg/g = 0.01 Gy 1 Rem = 0.01 Sievert 1 Sv = 100 rem

*International Units are 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 $1.3 \times 10^5 \, \text{MeV}$ of potential alpha energy.

Working Level Month (WLM) -- 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 shorter than those of visible light. They are usually produced by bombarding a metallic target with fast electrons in a high vacuum. In nuclear reaction, it is customary to refer to photons originating in the extranuclear part of the atom as X-rays. These rays are sometimes called roentgen rays after their discoverer, W.C. Roentgen.

APPENDIX A

PEER REVIEW

A peer review panel was assembled for radium. The panel consisted of the following members: Dr. Carmia Borek, Professor of Pathology, Columbia University; Dr. Douglas Crawford-Brown, Assistant Professor in the Department of Environmental Science, University of North Carolina; Dr. Haluk Ozkaynak, Lecturer, Harvard School of Public Health, Research Fellow, Energy and Environmental Policy Center, Kennedy School of Government, Harvard University; Dr. Ray Lloyd, Research Professor, Radiobiology Division, University of Utah. These experts collectively have knowledge of radium'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.

A joint panel of scientists from ATSDR and EPA has reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply their approval of the profile's final content. The responsibility for the content of this profile lies with the Agency for Toxic Substances and Disease Registry.

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), and Early et al. (1979).

B.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 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 atom is said to be stable; however, if there are too few or too many neutrons, the nucleus of the atom is unstable. Unstable nuclides undergo a process referred to as radioactive transformation in which energy is emitted. 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 man-made. Naturally-occurring radionuclides 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 man-made sources of ionizing radiation.

Man-made radioactive atoms are produced either as a by-product of fission of uranium atoms in a nuclear reactor or by bombarding stable atoms with particles, such as neutrons, 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 man-made 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.

B.2 RADIOACTIVE DECAY

B.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 (electrons, neutrons, neutrinos, alpha particles, beta particles, protons, and fission products) or electromagnetic radiation (gamma rays and X-rays). Table B-1 summarizes the basic characteristics of the more common types of radiation encountered.

B.2.2 Half-Life and Activity

For any given radionuclide, the rate of decay is a first-order process that depends on the number of radioactive atoms present and is

TABLE B-1. Characteristics of Nuclear Radiations

			Typical		Length <u>Magnitude)</u>	
Radiation	Rest Mass	Charge	Energy Range	<u>Air</u>	Solid	General Comments
α	4.00 amu	2+	4-10 MeV	5-10 cm	25-40 µ m	Identical to ionized He nucleus
ß (negatron)	5.48x10 ⁻⁴ amu 0.51 MeV	-	0-4 MeV	0-1 m	0-1 cm	Identical to electron
Positron (ß positive)	5.48x10 ⁻⁴ amu 0.51 MeV	+	-	0-1 m	0-1 cm	Identical to electron except for charge
Proton	938.26 MeV 1.0073 amu	+	-	-	-	-
Neutron	1.0086 amu 939.55 MeV	0	0-15 MeV	0-100 m	0-100 cm	Free half life: 16 min
X (e.m. photon)	-	0	eV∽100 keV	0.1-10 mª	0-1 m ^a	Photons from electron transitions
γ (e.m. photon)	-	0	10 KeV-3 MeV	0.1-10 mª	1 mm-1 m	Photons from nuclear transitions

^aExponential attenuation in the case of electromagnetic radiation.

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 the average, how many atoms will transform during any interval of time.

The source strength is a measure of the rate of emission of radiation. For these radioactive materials it is customary to describe the source strength in terms of the source activity, which is defined as the number of disintegrations (transformations) per unit time occurring in a given quantity of this material. The unit of activity is the <u>curie</u> (Ci) which was originally related to the activity of one gram of radium, but is now defined as:

1 curie (Ci) = 3.7×10^{10} disintegrations (transformations)/second (dps) or

2.22x10¹² disintegrations (transformations)/minute (dpm).

The SI unit of activity is the becquerel (Bq); 1 Bq = 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 rate of transformation 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, $T_{\rm R}$, i.e., the time it takes for a specified source material to decay to half its initial activity.

The activity of a radionuclide at time t may be calculated by:

 $A = A_0 e^{-0.693t/T}$

where A is the activity in dps, A is the activity at time zero, t is the time at which measured, and T_{rad} is the radiological half-life of the radionuclide. It is apparent that activity exponentially decays with 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.

The specific activity is the radioactivity per unit weight of material. This activity is usually expressed in curies per gram and may be calculated by

curies/gram = $1.3 \times 10^8 / (T_{rad})$ (atomic weight)

where $T_{\rm rad}$ 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

<u>biological half-life</u> $(T_{\rm biol})$ 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 half-life:

 $T_{eff} = (T_{biol} \times T_{rad})/(T_{biol} + T_{rad}).$

Table B-2 presents representative effective half-lives of particular interest.

B.2.3 Interaction of Radiation with Matter

Both ionizing and nonionizing radiation will interact with materials, that is, it 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 secondarily may react with a target molecule. 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 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.

B-2.4 Characteristics of Emitted Radiation

B.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

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APPENDIX B

TABLE B-2. Half-Lives of Some Radionuclides in Adult Body Organs

			Half-Life ^a	
Radionuclide	Critical Organ	Physical	Biological	Effective
Hydrogen-3 ^b (Tritium)	Whole body	12.3 y	12 d	11.97d
Iodine-131	Thyroid	8 d	138 d	7.6 d
Strontium-90	Bone	28 y	50 y	18 y
Plutonium-239	Bone	24,400 y	200 y	198 y
	Lung	24,400 y	500 d	500 d
Cobalt-60	Whole body	5.3 y	99.5 d	9.5 d
Iron-55	Spleen	2.7 у	600 d	388 d
Iron-59	Spleen	45.1 d	600 d	41.9 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.

atomic mass number by four and reduction of the atomic number by 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. Alpha particles have a large mass as compared to electrons. Decay of alpha-emitting radionuclides may result in the emission of several different alpha particles. A radionuclide has an alpha emission with a discrete alpha energy and characteristic pattern of alpha energy emitted.

The alpha particle has an electrical charge of +2. Because of this double positive charge, alpha particles have great ionizing power, but their large size results in very little penetrating power. In fact, an alpha particle cannot penetrate a sheet of paper. The range of an alpha particle, that is, 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 ingested, inhaled, or otherwise absorbed).

B.2.4.2. Beta Emission. Nuclei which are excessively neutron rich decay by B-decay. A beta particle (B) is a high-velocity electron ejected from a disintegrating nucleus. The particle may be either a negatively charged electron, termed a negatron (B-) or a positively charged electron, termed a positron (R+). Although the precise definition of "beta emission" refers to both fi- and D+, common usage of the term generally applies only to the negative particle, as distinguished from the positron emission, which refers to the 13+ particle.

B.2.4.2.1 Beta Negative Emission. Beta particle $(\beta$ -) emission is another process by which a radionuclide, usually those 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 remains unchanged. 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 in tissue is much less. Beta negative emitting radionuclides can cause injury to the skin and superficial body tissues but mostly present an internal contamination hazard.

B-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 $(\beta+)$ is emitted, accompanied by a neutrino (see glossary). This increases the number of neutrons by one, decreases the number of protons by one, and again leaves the atomic mass 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 13 emitters of equal energy.

B.2.4.2.3 Gamma Emission. Radioactive decay by alpha, beta, 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 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.

B.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.

B.3.1 Dose Units

B.3.1.1 Roentgen. The roentgen (R) is a unit of exposure related to the amount of ionization caused in air by gamma or x-radiation. One roentgen equals 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.

B.3.1.2 Absorbed Dose and Absorbed Dose Rate. Since different types of radiation interact differently with any material through which they pass, any

attempt to assess their effect on humans or animals should take into account these differences. The absorbed dose is defined as the energy imparted by the incident 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. 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.

B.3.1.3 Working Levels and Working Level Months. Working levels are units that have been used to describe the radon decay-product activities in air in terms of potential alpha energy. It 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 (WIN). One WLM corresponds to exposure to a concentration of 1 WL for the reference period of 170 hours.

B.3.2 Dosimetry Models

Dosimetry models are used to estimate the internally deposited dose from exposure to radioactive substances. The models for internal dosimetry consider the quantity 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 models for external dosimetry consider only the photon doses to organs of individuals who are immersed in air or are exposed to a contaminated ground surface. 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 man-produced radionuclides from nuclear weapons testing.

B.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.

B.3.2.2 Inhalation. The inhalation route of exposure has long been recognized as being of major importance 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. Giliary clearance acts only in the upper 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 particulates are absorbed into the blood and translocated to other organs and Roy (1987).

B.3.3 Internal Emitters

The absorbed dose from internally deposited radioisotopes is the energy absorbed by the surrounding tissue. For a radioisotope distributed uniformly throughout an infinitely large medium, the concentration of absorbed energy must be equal to the concentration of energy emitted by the isotope. 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 isotope emissions are penetrating radiation and a substantial fraction may travel great distances within tissue, leaving the tissue without interacting. 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.

B.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 (Hobbs and McClellan 1986; ICRP 1984; Mettler and Moseley 1985; Rubin and Casarett 1968).

B.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 to 500 rad (0.5 to 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 essentially 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 Bergonig-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 mutations.

B.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 - HHB), 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 HHB fibrosis and occlusion of the microcirculation.

B.4.3 Acute and Chronic Somatic Effects

B.4.3.1 Acute Effects. The result of acute exposure to radiation is commonly referred to as acute radiation syndrome. This effect is seen only after exposures to relatively high doses (>50 rad), which would only be expected to occur in the event of a serious nuclear accident. The four stages of acute radiation syndrome are prodrome, latent stage, manifest illness stage, recovery or death. The initial phase is characterized by nausea, vomiting, malaise and fatigue, increased temperature, and blood changes. The latent stage is similar to an incubation period. Subjective symptoms may subside, but changes may be taking place within the blood-forming organs and elsewhere which will subsequently give rise to the next stage. The manifest illness stage gives rise to symptoms are hair loss, fever, infection, hemorrhage, severe diarrhea, prostration, disorientation, and cardiovascular collapse. The symptoms and their severity depend upon the radiation dose received.

B.4.3.2 Delayed Effects. The level of exposure to radioactive pollutants that may be encountered in the environment is expected to be too low to result in the acute effects described above. When one is exposed to radiation in the environment, the amount of radiation absorbed is more likely to produce long-term effects, which manifest themselves years after the original exposure, and may be due to a single large over-exposure or continuing low-level exposure.

Sufficient evidence exists in both human populations and laboratory animals to establish that radiation can cause cancer and that the incidence of cancer increases with increasing radiation dose. Human data are extensive and include epidemiological studies of atomic bomb survivors, many types of radiation-treated patients, underground miners, and radium dial painters. Reports on the survivors of the atomic bomb explosions at Hiroshima and Nagasaki, Japan (with whole-body external radiation doses of 0 to more than 200 rad) indicate that cancer mortality has increased (Kato and Schull 1982). Use of X-rays (at doses of approximately 100 rad) in medical treatment for ankylosing spondylitis or other benign conditions or diagnostic purposes, such as breast conditions, has resulted in excess cancers in irradiated organs (BEIR 1980, 1990; UNSCEAR 1977, 1988). Cancers, such as leukemia, have been observed in children exposed <u>in utero</u> to doses of 0.2 to 20 rad (BEIR, 1980, 1990; UNSCEAR 1977, 1988). Medical use of Thorotrast (colloidal thorium dioxide) resulted in increases in the incidence of cancers of the liver, bone,

and lung (ATSDR 1990a; BEIR 1980, 1990; UNSCEAR 1977, 1988). Occupational exposure to radiation provides further evidence of the ability of radiation to cause cancer. Numerous studies of underground miners exposed to radon and radon daughters, which are alpha emitters, in uranium and other hard rock mines have demonstrated increases in lung cancer in exposed workers (ATSDR 1990b). Workers who ingested radium-226 while painting watch dials had an increased incidence of leukemia and bone cancer (ATSDR 1990c). These studies indicate that depending on radiation dose and the exposure schedule, ionizing radiation can induce cancer in nearly any tissue or organ in the body. Radiation-induced cancers in humans are found to occur in the hemopoietic system, the lung, the thyroid, the liver, the bone, the skin, and other tissues.

Laboratory animal data indicate that ionizing radiation is carcinogenic and mutagenic at relatively high doses usually delivered at high dose rates. However, due to the uncertainty regarding the shape of the dose-response curve, especially at low doses, the commonly held conservative position is that the cancer may occur at dose rates that extend down to doses that could be received from environmental exposures. Estimates of cancer risk are based on the absorbed dose of radiation in an organ or tissue. The cancer risk at a particular dose is the same regardless of the source of the radiation. A comprehensive discussion of radiation-induced cancer is found in BEIR IV (1988), BEIR V (1990), and UNSCEAR (1982, 1988).

B.4.4 Genetic Effects

Radiation can induce genetic damage, such as gene mutations or chromosomal aberrations, by causing changes in the structure, number, or genetic content of chromosomes in the nucleus. The evidence for the mutagenicity of radiation is derived from studies in laboratory animals, mostly mice (BEIR 1980, 1988, 1990; UNSCEAR 1982, 1986, 1988). Evidence for genetic effects in humans is derived from tissue cultures of human lymphocytes from persons exposed to ingested or inhaled radionuclides (ATSDR 1990c, 1990d). Evidence for mutagenesis in human germ cells (cells of the ovaries or testis) is not conclusive (BEIR 1980, 1988, 1990; UNSCEAR 1977, 1986, 1988). Chromosome aberrations following radiation exposure have been demonstrated in man andn in experimental animals (BEIR 1980, 1988, 1990; UNSCEAR 1982, 1986, 1988).

B.4.5 Teratogenic Effects

There is evidence that radiation produces teratogenicity in animals. It appears that the developing fetus is more sensitive to radiation than the mother and is most sensitive to radiation-induced damage during the early stages of organ development. The type of malformation depends on the stage of development and the cells that are undergoing the most rapid differentiation at the time. Studies of mental retardation in children exposed in utero to radiation from the atomic bomb provide evidence that radiation may produce

teratogenic effects in human fetuses (Otake and Schull 1984). The damage to the child was found to be related to the dose that the fetus received.

B.5 UNITS IN RADIATION PROTECTION AND REGULATION

B.5.1 Dose Equivalent and Dose Equivalent Rate. Dose equivalent or rem is a special radiation protection quantity that is used to express the absorbed dose in a manner which considers the difference in biological effectiveness of various kinds of ionizing radiation. The ICRU has defined the dose equivalent, H, as the product of the absorbed dose, D, the quality factor, Q, and all other modifying factors, N, at the point of interest in biological tissue. This relationship is expressed as follows:

 $H = D \times Q \times N.$

The quality 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. By definition it is independent of tissue and biological end point and, therefore, of little use in risk assessment now. Originally Relative Biolotical 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 for various radiation types are provided in Table B-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.

B.5.2 Relative Biological Effectiveness. The term relative biologic 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 to 250 KeV X-rays have been used as reference standards. The term RBE has been widely used in experimental radiobiology, and the term quality factor used in calculations of dose equivalents for radiation protection purposes (ICRP 1977; NCRP 1971; UNSCEAR 1982). The generally accepted values for RBE are provided in Table B-4.

B.5.3 Effective Dose Equivalent and Effective Dose Equivalent Rate. The absorbed dose is usually defined as the mean absorbed dose within 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 nonuniformly 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.

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1	2	5	

TABLE B-3. Quality Factors (QF)

1. X-rays, electrons, and positrons of any specific ionization

QF = 1.

2. Heavy ionizing particles

Average LET in Wate	r		
(MeV/cm)			QF
35 or less		1	
35 to 70		1	to 2
70 to 230			to 5
230 to 530		5	to 10
530 to 1750		10	to 20
r practical nurnoses	a OF of 10 is often	hapin n	for alpha na

For practical purposes, a QF of 10 is often used for alpha particles^a and fast neutrons and protons up to 10 MeV. A QF of 20 is used for heavy recoil nuclei.

^aThe ICRP (1977) recommended a quality factor of 20 for alpha particles.

LET = Linear energy transfer MeV/cm = Megaelectron volts per centimeter MeV = Megaelectron volts

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TABLE B-4. Representative LET and RBE Values*

	Energy	Av. LET $(1-X)$	DDE	Quality Factor
Radiation	(MeV)	(keV/µ)	<u>RBE</u>	ractor
X-rays, 200 kVp	0.01-0.2	3.0	1.00	1
Gamma rays	1.25	0.3	0.7	1
	4	0.3	0.6	1
Electrons (ß)	0.1	0.42	1.0	1
	0.6	0.3	1.3	1
	1.0	0.25	1.4	
Protons	0.1	90.0		6
	2.0	16.0	2	10
	5.0	8.0	2	10
Alpha particle	0.1	260.0		
mpna parororo	5.0	95.0	10-20	10
Heavy ions	10-30	~150.0	~25	20
Neutrons	thermal		4-5	3
noutlons	1.0	20.0	2-10	10

*These values are general and approximate. RBE and QF values vary widely with different measures of biological injury.

The effective dose equivalent, $H_{_{\rm R}}$ is

 $H_E =$ (the sum of) $W_t H_t$

where H_t is the dose equivalent in the tissue, W_t is the weighting factor, 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). Weighting factors for selected tissues are listed in Table B-5. 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 B-6.

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TABLE B-5. Weighting Factors for Calculating Effective Dose Equivalent for Selected Tissues

Tissue	Weighting Factor
Gonads	0.25
Breast	0.15
Red bone marrow	0.12
Lung	0.12
Thyroid	0.03
Bone surface	0.03
Remainder	0.30

TABLE B-6. Comparison of Common and SI Units for Radiation Quantities

Quantity	Customary Units	Definition	SI Units	Definition
Activity (A)	Curie (Ci)	3.7x10 ¹⁰ transforma- tions s ⁻¹	becquerel (Bq)	s ⁻¹
Absorbed Dose (D)		rad (rad)	10 ⁻² Jkg ⁻¹	gray (Gy)Jkg ⁻¹
Absorbed Dose Rate (D)	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 (rem)	10 ⁻² Jkg ⁻¹	sievert (Sv)	Jkg ⁻¹
Dose Equivalent Rate (H)	rem per second (rem s ⁻¹)	10 ⁻² Jkg ⁻¹ s ⁻¹	sievert per second (Sv s ⁻¹)	Jkg ⁻¹ s ⁻¹
Linear Energy Transfer (L∞)	kiloelectron volts per micrometer (keVµM ⁻¹)	1.602x10 ⁻¹⁰ Jm ⁻¹	kiloelectron volts per micrometer (keVµm ⁻¹)	1.602x10 ⁻¹⁰ Jm ⁻¹

S⁻¹ = per second Jkg⁻¹ = Joules per kilogram Jkg⁻¹s⁻¹ = Joules per kilogram per second Jm⁻¹ = Joules per meter

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