TOXICOLOGICAL PROFILE FOR RADON

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

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DISCLAIMER

Use of trade names is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry, the Public Health Service, or the U.S. Department of Health and Human Services.

UPDATE STATEMENT

A Toxicological Profile for Radon, Draft for Public Comment was released in September 2008. This edition supersedes any previously released draft or final profile.

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

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FOREWORD

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

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

The profiles focus on health and toxicologic information; therefore, each toxicological profile begins with a public health statement that describes, in nontechnical language, a substance's relevant toxicological properties. Following the public health statement is information concerning levels of significant human exposure and, where known, significant health effects. A health effects summary describes the adequacy of information to determine a substance's health effects. ATSDR identifies data needs that are significant to protection of public health.

Each profile:

(A) Examines, summarizes, and interprets available toxicologic information and epidemiologic evaluations on a toxic substance to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects;

(B) Determines whether adequate information on the health effects of each substance is available or being developed to determine levels of exposure that present a significant risk to human health of acute, subacute, and chronic health effects; and

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

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

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

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*Legislative Background

The toxicological profiles are developed under the Comprehensive Environmental Response, Compensation, and Liability Act of 1980, as amended (CERCLA or Superfund). CERCLA section 104(i)(1) directs the Administrator of ATSDR to "…effectuate and implement the health related authorities" of the statute. This includes the preparation of toxicological profiles for hazardous substances most commonly found at facilities on the CERCLA National Priorities List and that pose the most significant potential threat to human health, as determined by ATSDR and the EPA. Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list. In addition, ATSDR has the authority to prepare toxicological profiles for substances not found at sites on the National Priorities List, in an effort to "…establish and maintain inventory of literature, research, and studies on the health effects of toxic substances" under CERCLA Section 104(i)(1)(B), to respond to requests for consultation under section 104(i)(4), and as otherwise necessary to support the site-specific response actions conducted by ATSDR.

QUICK REFERENCE FOR HEALTH CARE PROVIDERS

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

Primary Chapters/Sections of Interest

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

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

Chapter 3: Health Effects: Specific health effects of a given hazardous compound are reported by type of health effect (death, systemic, immunologic, reproductive), by route of exposure, and by length of exposure (acute, intermediate, and chronic). In addition, both human and animal studies are reported in this section.
NOTE: Not all health effects reported in this section are necessarily observed in the clinical setting. Please refer to the Public Health Statement to identify general health effects observed following exposure.

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

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

Other Sections of Interest:

Section 3.8 Biomarkers of Exposure and Effect
Section 3.11 Methods for Reducing Toxic Effects

ATSDR Information Center

Phone: 1-800-CDC-INFO (800-232-4636) or 1-888-232-6348 (TTY) ***Fax:*** (770) 488-4178
E-mail: cdcinfo@cdc.gov ***Internet***: http://www.atsdr.cdc.gov

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

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

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

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

Other Agencies and Organizations

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

The National Institute for Occupational Safety and Health (NIOSH) conducts research on occupational diseases and injuries, responds to requests for assistance by investigating problems of health and safety in the workplace, recommends standards to the Occupational Safety and Health Administration (OSHA) and the Mine Safety and Health Administration (MSHA), and trains professionals in occupational safety and health. Contact: NIOSH, 200 Independence Avenue, SW, Washington, DC 20201 • Phone: 800-CDC-INFO (800-232-4636) or NIOSH Technical Information Branch, Robert A. Taft Laboratory, Mailstop C-19, 4676 Columbia Parkway, Cincinnati, OH 45226-1998 • Phone: 800-35-NIOSH.

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

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

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Referrals

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

The American College of Occupational and Environmental Medicine (ACOEM) is an association of physicians and other health care providers specializing in the field of occupational and

environmental medicine. Contact: ACOEM, 25 Northwest Point Boulevard, Suite 700, Elk Grove Village, IL 60007-1030 • Phone: 847-818-1800 • FAX: 847-818-9266.

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THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:

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

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

3. Data Needs Review. The Environmental Toxicology Branch (proposed) reviews data needs sections to assure consistency across profiles and adherence to instructions in the Guidance.

4. Green Border Review. Green Border review assures the consistency with ATSDR policy.

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PEER REVIEW

A peer review panel was assembled in 2008 for radon. The panel consisted of the following members:

1. R. William Field, Ph.D., M.S., Professor, College of Public Health, Department of Occupational and Environmental Health and Department of Epidemiology, University of Iowa, Iowa City, Iowa;

2. Naomi H. Harley, Ph.D., Research Professor, Department of Environmental Medicine, New York University School of Medicine, New York, New York; and

3. Jonathan Samet, M.D., Professor and Chairman, Department of Epidemiology, Bloomberg School of Public Health, The Johns Hopkins University, Baltimore, Maryland.

These experts collectively have knowledge of radon's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(I)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended.

Scientists from the Agency for Toxic Substances and Disease Registry (ATSDR) have reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound.

The citation of the peer review panel should not be understood to imply its approval of the profile's final content. The responsibility for the content of this profile lies with the ATSDR.

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CONTENTS

DISCLAIMER ii
UPDATE STATEMENT iii
FOREWORD v
QUICK REFERENCE FOR HEALTH CARE PROVIDERS vii
CONTRIBUTORS xi
PEER REVIEW xiii
CONTENTS xv
LIST OF FIGURES xix
LIST OF TABLES xxi

1. PUBLIC HEALTH STATEMENT 1
1.1 WHAT IS RADON? 2
1.2 WHAT HAPPENS TO RADON WHEN IT ENTERS THE ENVIRONMENT? 3
1.3 HOW MIGHT I BE EXPOSED TO RADON AND RADON PROGENY? 3
1.4 HOW CAN RADON AND RADON PROGENY ENTER AND LEAVE MY BODY? 4
1.5 HOW CAN RADON AND RADON PROGENY AFFECT MY HEALTH? 5
1.6 HOW CAN RADON AND RADON PROGENY AFFECT CHILDREN? 5
1.7 HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO RADON AND RADON PROGENY? 6
1.8 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO RADON AND RADON PROGENY? 6
1.9 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH? 6
1.10 WHERE CAN I GET MORE INFORMATION? 8

2. RELEVANCE TO PUBLIC HEALTH 9
2.1 BACKGROUND AND ENVIRONMENTAL EXPOSURES TO RADON IN THE UNITED STATES 9
2.2 SUMMARY OF HEALTH EFFECTS 10
2.3 MINIMAL RISK LEVELS (MRLs) 12

3. HEALTH EFFECTS 15
3.1 INTRODUCTION 15
3.2 DISCUSSION OF HEALTH EFFECTS OF RADON BY ROUTE OF EXPOSURE 18
3.2.1 Inhalation Exposure 20
3.2.1.1 Death 31
3.2.1.2 Systemic Effects 32
3.2.1.3 Immunological and Lymphoreticular Effects 34
3.2.1.4 Neurological Effects 34
3.2.1.5 Reproductive Effects 34
3.2.1.6 Developmental Effects 35
3.2.1.7 Cancer 35
3.2.2 Oral Exposure 42
3.2.2.1 Death 42
3.2.2.2 Systemic Effects 42
3.2.2.3 Immunological and Lymphoreticular Effects 42
3.2.2.4 Neurological Effects 42
3.2.2.5 Reproductive Effects 42
3.2.2.6 Developmental Effects 42

3.2.2.7 Cancer 42
3.2.3 Dermal Exposure 43
3.2.3.1 Death 43
3.2.3.2 Systemic Effects 43
3.2.3.3 Immunological and Lymphoreticular Effects 43
3.2.3.4 Neurological Effects 43
3.2.3.5 Reproductive Effects 43
3.2.3.6 Developmental Effects 43
3.2.3.7 Cancer 43
3.3 GENOTOXICITY 45
3.4 TOXICOKINETICS 49
3.4.1 Absorption 51
3.4.1.1 Inhalation Exposure 51
3.4.1.2 Oral Exposure 54
3.4.1.3 Dermal Exposure 55
3.4.2 Distribution 56
3.4.2.1 Inhalation Exposure 56
3.4.2.2 Oral Exposure 57
3.4.2.3 Dermal Exposure 58
3.4.3 Metabolism 58
3.4.4 Elimination and Excretion 58
3.4.4.1 Inhalation Exposure 58
3.4.4.2 Oral Exposure 59
3.4.4.3 Dermal Exposure 60
3.4.4.4 Other Routes of Exposure 60
3.4.5 Physiologically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Models 60
3.5 MECHANISMS OF ACTION 82
3.5.1 Pharmacokinetic Mechanisms 82
3.5.2 Mechanisms of Toxicity 84
3.5.3 Animal-to-Human Extrapolations 88
3.6 TOXICITIES MEDIATED THROUGH THE NEUROENDOCRINE AXIS 88
3.7 CHILDREN'S SUSCEPTIBILITY 89
3.8 BIOMARKERS OF EXPOSURE AND EFFECT 91
3.8.1 Biomarkers Used to Identify or Quantify Exposure to Radon and Radon Progeny 92
3.8.2 Biomarkers Used to Characterize Effects Caused by Radon and Radon Progeny 92
3.9 INTERACTIONS WITH OTHER CHEMICALS 93
3.10 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE 96
3.11 METHODS FOR REDUCING TOXIC EFFECTS 96
3.11.1 Reducing Peak Absorption Following Exposure 97
3.11.2 Reducing Body Burden 97
3.11.3 Interfering with the Mechanism of Action for Toxic Effects 97
3.12 ADEQUACY OF THE DATABASE 98
3.12.1 Existing Information on Health Effects of Radon 98
3.12.2 Identification of Data Needs 100
3.12.3 Ongoing Studies 105

4. CHEMICAL, PHYSICAL, AND RADIOLOGICAL INFORMATION 107
4.1 CHEMICAL IDENTITY 107
4.2 PHYSICAL, CHEMICAL, AND RADIOLOGICAL PROPERTIES 107

5. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL 115
5.1 PRODUCTION 115
5.2 IMPORT/EXPORT 117
5.3 USE 117
5.4 DISPOSAL 118

6. POTENTIAL FOR HUMAN EXPOSURE 121
6.1 OVERVIEW 121
6.2 RELEASES TO THE ENVIRONMENT 124
6.2.1 Air 124
6.2.2 Water 126
6.2.3 Soil 127
6.3 ENVIRONMENTAL FATE 127
6.3.1 Transport and Partitioning 127
6.3.2 Transformation and Degradation 130
6.3.2.1 Air 130
6.3.2.2 Water 131
6.3.2.3 Sediment and Soil 131
6.3.2.4 Other Media 131
6.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT 131
6.4.1 Air 131
6.4.2 Water 133
6.4.3 Sediment and Soil 135
6.4.4 Other Environmental Media 136
6.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE 137
6.6 EXPOSURES OF CHILDREN 141
6.7 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES 142
6.8 ADEQUACY OF THE DATABASE 143
6.8.1 Identification of Data Needs 143
6.8.2 Ongoing Studies 146

7. ANALYTICAL METHODS 147
7.1 BIOLOGICAL MATERIALS 147
7.2 ENVIRONMENTAL SAMPLES 149
7.3 ADEQUACY OF THE DATABASE 157
7.3.1 Identification of Data Needs 158
7.3.2 Ongoing Studies 158

8. REGULATIONS, ADVISORIES, AND GUIDELINES 159

9. REFERENCES 165

10. GLOSSARY 205

APPENDICES
A. ATSDR MINIMAL RISK LEVELS AND WORKSHEETS A-1
B. USER'S GUIDE B-1
C. ACRONYMS, ABBREVIATIONS, AND SYMBOLS C-1
D. OVERVIEW OF BASIC RADIATION PHYSICS, CHEMISTRY, AND BIOLOGY D-1
E. INDEX E-1

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LIST OF FIGURES

3-1. Cumulative Absolute Risk of Death from Lung Cancer by Age 75 Years Versus Long-Term Average Radon Concentration at Home for Continuing Smokers, Ex-Smokers, and Lifelong Nonsmokers in the United Kingdom 40

3-2. Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a Hypothetical Chemical Substance 62

3-3. Compartment Model to Represent Particle Deposition and Time-Dependent Particle Transport in the Respiratory Tract 66

3-4. Reaction of Gases or Vapors at Various Levels of the Gas-Blood Interface 68

3-5. The Human Respiratory Tract Model: Absorption into Blood 74

3-6. Simplified Version of the Human Respiratory Tract Model (HRTM) 76

3-7. Schematic Diagram of the NAS (1999b) PBPK Model Developed to Describe the Fate of Radon within Systemic Tissues 78

3-8. Khursheed (2000) PBPK Model for Inhalation and Ingestion of Radon Gas 81

3-9. Conceptual Model of the Biology Leading From Alpha Irradiation of Cells by Radon and Radon Progeny to Tumor Development 86

3-10. Existing Information on Health Effects of Radon 99

4-1. ^{238}U Decay Series Showing Sources and Decay Products 112

4-2. ^{232}Th Decay Series Showing Sources and Decay Products 113

4-3. ^{235}U Decay Series Showing Sources and Decay Products 114

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LIST OF TABLES

3-1. Selected Characteristics and Exposure Data for Individual Miner Cohort Studies Included in the Analysis of Pooled Data from the Individual Studies, and Lung Cancer Mortality Rates and Relative Risks by Cumulative WLM for Pooled Data 24

3-2. Selected Results from Analysis of Pooled Data from 11 Mining Cohorts, Based on Deciles of Case Exposures That Were Each Under 100 WLM 25

3-3. ORs for Lung Cancer from Combined Analysis of Two China Residential Case-Control Studies (Using a 5–30-Year Exposure Time Window) 27

3-4. Selected Characteristics of Study Subjects, Exposure Estimates, and ORs for Lung Cancer from Combined Analysis of Seven North American Residential Case-Control Studies (Using a 5–30-Year Exposure Time Window) 29

3-5. Relative Risk and Excess Relative Risk of Lung Cancer by Radon Level in Homes 5–34 Years Previously, Estimated from the Pooled Data for 13 European Residential Case-Control Studies 30

3-6. Genotoxicity of Radon and Radon Progeny *In Vivo* 46

3-7. Genotoxicity of Radon and Radon Progeny *In Vitro* 47

3-8. Reference Respiratory Values for a General Caucasian Population at Different Levels of Activity 67

3-9. Reference Values of Parameters for the Compartment Model to Represent Time-Dependent Particle Transport from the Human Respiratory Tract 70

3-10. Parameters in the NAS (1999b) PBPK Model 80

3-11. Parameters in Khursheed (2000) PBPK Model for Radon Gas 83

4-1. Chemical Identity of Radon 108

4-2. Physical, Chemical, and Radiological Properties of Radon 109

4-3. Radioactive Properties of ^{222}Rn and Its Short-lived Progeny 111

7-1. Analytical Methods for Determining Radon Progeny in Biological Samples 148

7-2. Analytical Methods for Determining Radon and Progeny in Environmental Samples 154

8-1. Regulations, Advisories, and Guidelines Applicable to Radon 161

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1. PUBLIC HEALTH STATEMENT

This public health statement tells you about radon and the effects of exposure to it.

The Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites are then placed on the National Priorities List (NPL) and are targeted for long-term federal clean-up activities. The presence of radon at any site could be a consequence of its natural occurrence in the environment; its production from substances in anthropogenic hazardous waste; or both. These sites may be sources of exposure and exposure to this substance may be harmful.

When a substance is released from a large area, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment. This release does not always lead to exposure. You are exposed to a substance when you come in contact with it. You may be exposed by breathing, eating, or drinking the substance, or by skin contact. External exposure to radiation may occur from natural or man-made sources. Radon is a naturally-occurring radioactive gas that changes into other radioactive substances, called progeny. Since radon and its progeny are present together in rock, soil, water, air, and construction materials, you will be exposed to the low-level radiation they give off just by being near them. Naturally occurring sources of radiation include radon and other radioactive elements in air, water, soil, or building materials, as well as cosmic radiation from space. Man-made radioactive materials are found in consumer products, industrial equipment, nuclear medicine patients, and to a smaller extent from atomic bomb fallout, hospital waste, and nuclear reactors.

The results of the 1992 EPA National Residential Radon Survey estimated that 1 in 15 homes had an elevated radon level (i.e., a level at or above the EPA action level of 4 picocuries per liter of air). At the time, an estimated 5.8 million homes had an elevated radon level. The source of radon in homes is from naturally occurring (geologic) sources.

When you are exposed to radon many factors will determine whether you will be harmed. These factors include the dose (how much), the duration (how long), and how you come in contact with

it. You must also consider any other chemicals you are exposed to and your age, sex, diet, family traits, lifestyle, and state of health.

1.1 WHAT IS RADON?

Radioactive gas	Radon (Rn) is a naturally occurring colorless, odorless, tasteless radioactive gas that occurs in differing atomic structure with the same atomic number but different atomic mass, called isotopes. As radon undergoes radioactive decay, it gives off radiation and becomes another radioactive element. This is repeated several times until it becomes stable lead. The elements that radon changes into are called radon daughters or radon progeny. The radiation given off is alpha particles, beta particles, and gamma rays. This radiation gives a radiation dose to people when they are exposed to radon. Radon is measured in terms of its activity (curies or becquerels). Both the curie (Ci) and the becquerel (Bq) tell us how much a radioactive material decays every second (1 Ci = 37 billion Bq = 37 billion decays per second). The radiation dose from radon and its progeny is measured in terms of the energy that they impart to tissue (in units called gray or rem for public exposure, or working levels for occupational exposure).
Natural product of the environment	Radon isotopes are formed naturally through the radioactive decay of uranium or thorium. Uranium and thorium (solids) are found in rocks, soil, air, and water. Uranium and thorium decay to other elements such as radium (a solid), which in turn decays into radon (a gas). Uranium and thorium have been present since the earth was formed and have very long half-lives (4.5 billion years for uranium and 14 billion years for thorium). The half-life is the time it takes for half of the atoms of a radionuclide (radioactive element) to undergo radioactive decay and change it into a different element, some of which are radioactive and some are stable. Because of the long half-lives of uranium, thorium, and radium, and since they constantly decay into radon, all of these elements will continue to exist indefinitely at about the same levels as they do now. Radon has no commercial uses other than as a radiation standard for calibrating radon monitoring equipment in support of environmental surveys of homes and other buildings.

Exists in various forms called isotopes and decays to other radioactive isotopes	The most common radon isotope is radon-222 (^{222}Rn). An atom of ^{222}Rn gives off an alpha particle (which is the size of a helium atom without electrons), transforming into an atom of polonium-218 (^{218}Po), which later gives off an alpha particle of its own, transforming into an atom of radioactive lead (^{214}Pb). The final step in the radioactive decay of radon progeny results in the formation of an atom of stable lead which is not radioactive. The half-life of ^{222}Rn is 3.82 days. Some of the radon decay products have the following half-lives: ^{218}Po is 3.05 minutes; ^{214}Pb is 26.8 minutes; and ^{210}Pb is 22.2 years.

More information about the properties of radon can be found in Chapters 4, 5, and 6.

1.2 WHAT HAPPENS TO RADON WHEN IT ENTERS THE ENVIRONMENT?

Moves to air, groundwater, and surface water	Radon gas in rocks and soil can move to air, groundwater, and surface water. Decay products of ^{222}Rn, such as ^{218}Po and ^{214}Pb, are solids that can attach to particles in the air and be transported this way in the atmosphere. They can be deposited on land or water by settling or by rain. Radon will undergo radioactive decay in the environment.

For more information on radon in the environment, see Chapter 6 (Potential for Human Exposure).

1.3 HOW MIGHT I BE EXPOSED TO RADON AND RADON PROGENY?

Air	Since radon progeny are often attached to dust, you are exposed to them primarily by breathing them in. They are present in nearly all air. Depending on the size of the particles, the radioactive particulates can deposit in your lungs and impart a radiation dose to the lung tissue. Background levels of radon in outdoor air are generally quite low (0.4 picocuries/L average activity of radon in outdoor air in the United States), but can vary based on time of day, location, and the underlying soil geology. Background levels also vary as a result of meteorological conditions, such as precipitation and temperature inversions. Temperature inversions occur when the air temperature increases with elevation above the ground. In indoor locations, such as homes, schools, or office buildings, levels of radon and radon progeny are generally higher than outdoor levels. House construction can affect radon levels; however, radon levels can be elevated in homes of all types: old homes, new homes, drafty homes, insulated

	homes, homes with basements, and homes without basements. Local geology, construction materials, and how the home was built are among the factors that can affect radon levels in homes. Radon typically moves up through the ground to the air above and into the home through cracks and other holes in the foundation, in part due to convective flow. Your home traps radon inside, where it can build up. Any home may have elevated radon levels. The only way to know if you are exposed to elevated household radon levels is to have your home tested.
Water	You may be exposed to radon and radon progeny by coming into contact with surfacewater or groundwater that contains radon or by drinking water from wells that contain radon. Radon in water can become airborne. In general, domestic water from a well with a concentration of 10,000 pCi/L of radon is estimated to contribute about 1 pCi/L of radon to the indoor air.

Further information on how you might be exposed to radon and radon progeny is given in Chapter 6.

1.4 HOW CAN RADON AND RADON PROGENY ENTER AND LEAVE MY BODY?

When they are inhaled or swallowed	Radon and its radioactive progeny can enter your body when you breathe them in or swallow them. Most of the inhaled radon gas is breathed out again. Some of the radon progeny, both unattached and attached to dust, may remain in your lungs and undergo radioactive decay. The radiation released during this process passes into lung tissue and can cause lung damage. Some of the radon that you swallow with drinking water passes through the walls of your stomach and intestine. After radon enters your blood stream most of the radon quickly moves to the lungs where you breathe most of it out. Radon that is not breathed out goes to other organs and fat tissue where it may remain and undergo decay.

Further information on how radon and radon progeny enter and leave the body is given in Chapter 3.

1.5 HOW CAN RADON AND RADON PROGENY AFFECT MY HEALTH?

This section looks at studies concerning potential health effects in animal and human studies.

Lung cancer	Lung cancer is essentially the only health effect associated with exposure to radon and radon progeny. Many scientists believe that long-term exposure to elevated levels of radon and radon progeny in air increases your chance of getting lung cancer. Smoking cigarettes greatly increases your chance of developing lung cancer if you are exposed to radon and radon progeny at the same levels as people who do not smoke. The greater your exposure to radon, especially if you smoke cigarettes, the greater your chance of developing lung cancer.

More information on the health effects of radon and radon progeny is presented in Chapters 2 and 3.

1.6 HOW CAN RADON AND RADON PROGENY AFFECT CHILDREN?

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

Differences between children and adults	Smaller lungs and faster breathing rates in children may result in higher estimated radiation doses to the lungs of children relative to adults. However, limited information from children employed as miners in China do not provide evidence of increased susceptibility to the effects of exposure to radon and radon progeny.

1.7 HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO RADON AND RADON PROGENY?

Reduce indoor exposure levels	Indoor radon levels can be reduced by the installation of a sub-slab suction (depressurization) system, also known as an active soil depressurization system (ASD). A radon vent fan connected to the suction pipe(s) draws the radon gas from below the house and releases it into the outdoor air, while simultaneously creating a negative pressure (vacuum) beneath the slab. Sealing of openings to the soil can improve the operation and efficiency of the ASD system. Certified radon mitigation experts can be located by contacting your state health or environmental program. If the ASD does not reduce levels sufficiently, consider reversing the fan direction to pressurize the subslab, and then compare the results and use the more effective method. Measures to prevent high radon levels in new home construction are expected to be effective at reducing radon-related lung cancer deaths, but remediating old homes with high radon levels may be less effective. If you smoke in your home, stopping will reduce the radiation dose from radon since smoke particles help increase the radiation dose.

1.8 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO RADON AND RADON PROGENY?

Radon progeny in urine and in lung and bone tissues	Radon in human tissues is not detectable by routine medical testing. Some radon progeny can be detected in urine and in lung and bone tissue. Tests for these products are not generally available to the public and are of limited value since they cannot be used to accurately determine how much radon you were exposed to, nor can they be used to predict whether you will develop harmful health effects.

Further information on how radon and radon progeny can be measured in exposed humans is presented in Chapters 3 and 7.

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

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

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

Regulations and recommendations can be expressed as "not-to-exceed" levels, that is, levels of a toxic substance in air, water, soil, or food that do not exceed a critical value that is usually based on levels that affect animals; they are then adjusted to levels that will help protect humans. Sometimes these not-to-exceed levels differ among federal organizations because they used different exposure times (an 8-hour workday, a 24-hour day, or a work-year), different animal studies, or other factors.

Recommendations and regulations are also updated periodically as more information becomes available. For the most current information, check with the federal agency or organization that provides it.

Air	EPA recommends actions that can be taken to reduce radon levels if measured indoor levels of radon are 4 or more pCi per liter (pCi/L) of air. This is the same as 148 Becquerels per cubic meter [Bq/m^3] of air in the international system. EPA also notes that radon levels less than 4 pCi/L still pose a health risk and can be reduced in many cases, and that smoking increases the risk from radon. The EPA recommends using a certified radon mitigation specialist if indoor radon levels need to be reduced to ensure that appropriate methods are used to reduce radon levels. The Mine Safety and Health Administration (MSHA) has adopted an exposure limit of 4 Working Level Months (WLM) per year for people who work in underground mines (WLMs basically combine the concentration of radon progeny in mine air with the portion that is attached to dust in the air and the length of exposure inside the mine). The Nuclear Regulatory Commission published a table of allowable exposure to radon by workers and allowable releases of radon to the environment by its licensees.
Water	EPA does not have a drinking water limit for radon.

EPA maintains a website (http://www.epa.gov/radon) that provides extensive information on radon for the general public. Additional information on governmental regulations regarding radon and radon progeny can be found in Chapter 8.

1.10 WHERE CAN I GET MORE INFORMATION?

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

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

Toxicological profiles are also available on-line at www.atsdr.cdc.gov and on CD-ROM. You may request a copy of the ATSDR ToxProfiles™ CD-ROM by calling the toll-free information and technical assistance number at 1-800-CDCINFO (1-800-232-4636), by e-mail at cdcinfo@cdc.gov, or by writing to:

Agency for Toxic Substances and Disease Registry
Division of Toxicology and Human Health Sciences (proposed)
1600 Clifton Road NE
Mailstop F-62
Atlanta, GA 30333
Fax: 1-770-488-4178

Organizations for-profit may request copies of final Toxicological Profiles from the following:

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

2. RELEVANCE TO PUBLIC HEALTH

2.1 BACKGROUND AND ENVIRONMENTAL EXPOSURES TO RADON IN THE UNITED STATES

Radon is a noble gas formed from the natural radioactive decay of uranium (U) and thorium (Th), natural components of the earth's crust, which decay to radium (Ra) and then to radon (Rn). Decay chains include ^{226}Ra and ^{222}Rn for ^{238}U; ^{223}Ra and ^{219}Rn for ^{235}U; and ^{224}Ra and ^{220}Rn for ^{232}Th. As radium decays, radon is formed and released into pores in the soil. Fissures and pores in the substrate allow the radon to migrate to the surface, where it can be released to the air. Radon may also be released into surface and groundwater from the surrounding soil. Though radon is chemically inert, it decays by normal radioactive processes to other radon progeny. The alpha emitting progeny of radon (primarily polonium isotopes ^{218}Po and ^{214}Po) are the ones that can damage the lungs and potentially cause cancer.

Radon may be useful in helping to detect seismic activity, for radiation therapy (as a decay product of ^{223}Ra), as a tracer for leak detection, for flow rate measurements, in radiography, and is used in some chemical laboratory research. It can also be used in the exploration of petroleum or uranium, as a tracer in the identification of NAPL (non-aqueous phase liquid) contamination of the subsurface, in atmospheric transport studies, and as a radiation standard for calibrating radon monitoring equipment in support of environmental surveys of homes and other buildings.

The primary source of radon is its precursors in soil where it is formed and released. On a global scale, it is estimated that 2,400 million curies of radon are released from soil annually. Groundwater provides a secondary source of radon, with an estimated 500 million curies released globally per year. Additional sources of radon include surface water, metal mines (uranium, phosphorus, tin, silver, gold, etc.), coal residues and combustion products, natural gas, and building materials. Global radon releases from oceans, phosphate residues, uranium mill tailings, coal residues, natural gas emissions, coal combustion, and human exhalation are estimated at 34, 3, 2, 0.02, 0.01, 0.009, and 0.00001 millions of curies per year, respectively. Geology, soil moisture conditions, and meteorological conditions can affect the amount of radon released from soil.

The primary pathway for human exposure to radon is inhalation, both indoors and outdoors. Ambient outdoor levels are the result of radon emanating from soil or released from coal, oil, or gas power plants, which can vary temporally and spatially. Outdoor radon levels are typically much lower than indoor radon levels. Soil gas intrusion into buildings accounts for the majority of indoor radon. However,

indoor radon also can originate from water used for domestic purposes, outdoor air, and building materials.

Exposure to high concentrations can occur in any location with geologic radon sources. Relatively high-level occupational exposure can occur through employment at underground mines (uranium, phosphorus, tin, silver, gold, hard rock, and vanadium), sites contaminated with radon precursors (radium, uranium, or thorium), natural caverns, phosphate fertilizer plants, oil refineries, utility and subway tunnels, excavators, power plants, natural gas and oil piping facilities, "health" mines and spas, fish hatcheries, and, historically, hospitals that used radium needles for therapy.

2.2 SUMMARY OF HEALTH EFFECTS

The most compelling evidence of radon-induced health effects in humans derives from numerous studies of underground miners, particularly uranium miners exposed in the middle part of the twentieth century in the United States and several European countries. These cohort mortality studies typically involved long-term estimates of exposure to high levels of radon based on available measurements in the working environment and contained inherent uncertainty due to confounding factors such as smoking status and coexposure to known or suspected carcinogens (diesel exhaust, arsenic, and silica dust). Nevertheless, the results consistently demonstrate increased risk of lung cancer with increasing exposure to radon in the working environment. The mining cohorts have been followed for several decades or more. Continued follow-up and refined assessments of the most widely-studied mining cohorts have resulted in improved exposure estimates (except for silica dust, which was not considered) and more complete categorization of individuals according to cause of death, mining history, and smoking status. Assessments did not account for actual confounding due to exposure to silica dust (which has since been identified as a known human carcinogen), nor did they necessarily include adjustments for potential confounding exposures to arsenic and diesel exhaust, although considerations for arsenic were made in several studies. One in-depth analysis included assessment of results pooled from 11 of the most widely-studied mining cohorts using the most recent and comprehensive follow-up results available at the time for each individual cohort. The results provide evidence for increasing risk of lung cancer mortality with increasing cumulative exposure to radon and its progeny, and the risk is significantly increased when there is coexposure to cigarette smoke, arsenic, or silica dust.

Reported associations between radon and lung cancer in the mining cohorts raised concern regarding the potential health effects of radon in homes, particularly at levels lower than those experienced in

mining cohorts. Numerous residential case-control studies of lung cancer have been performed in the United States and in many other countries, including Canada, China, Finland, Germany, Sweden, and the United Kingdom. Some of these studies reported positive or weakly positive associations between lung cancer risk and residential indoor radon concentrations, whereas significant associations were not observed in others. One recent residential case-control study reported a borderline statistically significant negative association between lung cancer risk and exposure to radon at levels in the range of 25–150 Bq/m^3 (1.4–4.1 pCi/L), which are near or below the 4.0 pCi/L EPA action limit. Numbers of cases and controls in the individual residential case-control studies limited the statistical power to identify a significant association between radon exposure and an adverse health outcome such as lung cancer. In order to increase the statistical power, investigators involved in most of the studies pooled the results in three separate assessments that included: (1) a combined analysis of 2 China case-control studies, (2) a combined analysis of 7 North American case-control studies, and (3) a combined analysis of 13 European case-control studies. In addition, an overall assessment of the China, North American, and European analyses was conducted by the United Kingdom. Independent results of the pooled analyses provide convincing evidence of an association between residential radon and lung cancer risk in cigarette smokers and recent ex-smokers as demonstrated by increased lung cancer risk with increasing cumulative exposure. The risk to nonsmokers was found to be 25-fold lower. Thus, the risk of radon-induced lung cancer decreases more by reducing or stopping smoking than by reducing residential radon concentration, and both can be used in conjunction for further risk reduction. Collectively, these studies show appreciable health hazard from residential radon, particularly for smokers and recent ex-smokers. An overall pooling of the China, North American, and European case-control studies is in progress.

Associations between radon and health effects other than lung cancer have been made by some investigators. Excess mortality from noncancer diseases reported in some of the mining cohorts include all noncancer respiratory diseases, pneumoconioses, emphysema, interstitial pneumonitis, other (unspecified) chronic obstructive respiratory diseases, and tuberculosis. However, confounding factors such as exposure to crystalline silica dust and other respiratory toxicants, smoking history, and work experience were likely major contributors to mortalities from noncancer respiratory diseases. Alterations in respiratory function in U.S. uranium miners have been reported. Analyses among U.S. uranium miners indicated a loss of pulmonary function associated with increasing cumulative exposure to radon and radon progeny and with the duration of underground mining. Evaluations of these respiratory end points did not include adjustment for effects other mine pollutants, such as ore crystalline silica and diesel engine exhaust particles, which were not recognized as human carcinogens at the time the studies were conducted.

Some information is available regarding lung cancer in animals exposed to radon and its progeny at concentrations considered relevant to human health. Significantly increased incidences of lung tumors were reported in rats repeatedly exposed to radon and its progeny at cumulative exposures as low as 20–50 Working Level Months (WLM). These results are consistent with the demonstrated associations between lung cancer risk and exposure to radon and radon progeny in occupationally-exposed miners and residentially-exposed individuals.

2.3 MINIMAL RISK LEVELS (MRLs)

Inhalation MRLs

No acute-, intermediate-, or chronic-duration inhalation MRLs were derived for radon due to a lack of suitable human or animal data regarding health effects following inhalation exposure to radon and its progeny. The strongest evidence for radon exposure-response and radiation dose-response relationships in humans is for lung cancer; however, cancer is not an appropriate end point for MRL derivation. Nonneoplastic lesions have been reported in animals exposed to radon and its progeny for acute, intermediate, and chronic exposure durations; however, these effects were consistently observed only at lethal or near lethal exposure levels, which were several orders of magnitude higher than those associated with lung cancer in chronically-exposed humans.

Oral MRLs

No acute-, intermediate-, or chronic-duration oral MRLs were derived for radon due to a lack of suitable human or animal data regarding health effects following oral exposure to radon and its progeny. Available human data are limited. In an ecological study, radon levels were measured in 2,000 public and private wells in 14 counties in Maine (Hess et al. 1983). The county averages were compared to cancer rate by county to determine any degree of correlation. Significant correlation was reported for all lung cancer and all cancers combined, when both sexes were combined, and for lung tumors in females. Confounding factors (e.g., smoking) were not considered in this analysis. In addition, exposure to radon in these water supplies could have been by the inhalation route as well as the oral route. No significant associations were observed between cases of bladder or kidney cancer, relative to controls, where mean concentrations of radon in the drinking water were 170, 140, and 130 Bq/L in bladder cancer cases, kidney cancer cases, and controls, respectively (Kurttio et al. 2006). The U.K. Health Protection Agency

2. RELEVANCE TO PUBLIC HEALTH

(HPA 2009) reviewed available studies that assessed possible associations between radon and cancer end points and concluded that there is insufficient evidence to suggest that radon is associated with increased risk of cancer at sites other than the lung.

2. RELEVANCE TO PUBLIC HEALTH

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3. HEALTH EFFECTS

3.1 INTRODUCTION

The primary purpose of this chapter is to provide public health officials, physicians, toxicologists, and other interested individuals and groups with an overall perspective on the toxicology of radon. It contains descriptions and evaluations of toxicological studies and epidemiological investigations and provides conclusions, where possible, on the relevance of toxicity and toxicokinetic data to public health.

A glossary and list of acronyms, abbreviations, and symbols can be found at the end of this profile.

Radon (Rn) is an inert noble gas that does not interact chemically with other elements. All of the isotopes of radon are radioactive and evaluation of the adverse health effects due to exposure to radon requires additional consideration of the effects of radiation. Radioactive elements are those that undergo spontaneous transformation (decay) in which energy is released (emitted) either in the form of particles, such as alpha and beta particles, or photons, such as gamma or x-rays. This disintegration, or decay, results in the formation of new elements, some of which may themselves be radioactive, in which case, they will also decay. The process continues until a stable (nonradioactive) state is reached. The isotopes of radon encountered in nature (^{219}Rn, ^{220}Rn, and ^{222}Rn) are part of long decay chains starting with isotopes of uranium (U) or thorium (Th), more precisely ^{235}U, ^{232}Th, and ^{238}U, respectively, and ending with stable lead (Pb). The intermediates between radon and stable lead are termed radon daughters or radon progeny (see Chapter 4, Figures 4-1, 4-2, and 4-3 for radioactive decay schemes of ^{235}U, ^{232}Th, and ^{238}U, respectively). The isotope ^{222}Rn is a direct decay product of radium-226 (^{226}Ra), which is part of the decay series that begins with uranium-238 (^{238}U). Thorium-230 and -234 (^{230}Th and ^{234}Th) are also part of this decay series. Other isotopes of radon, such as ^{219}Rn and ^{220}Rn, are formed in other radioactive decay series. However, ^{219}Rn usually is not considered in the evaluation of radon-induced health effects because it is not abundant in the environment (^{219}Rn is part of the decay chain of ^{235}U, a relatively rare isotope) and has an extremely short half-life (4 seconds). The isotope ^{220}Rn has usually not been considered when evaluating radon-related health effects, although many recent assessments have attempted to include measurements of ^{220}Rn as well as ^{222}Rn. While the average rate of production of ^{220}Rn is about the same as ^{222}Rn, the amount of ^{220}Rn entering the environment is much less than that of ^{222}Rn because ^{220}Rn is a noble gas with a short half-life (56 seconds). As a noble gas, it diffuses slowly from the ground but decays so rapidly into polonium (a particle that bonds with the soil) that most radon does not reach the atmosphere. The soil characteristics that enhance or retard radon migration from the

soil indirectly affect air concentrations of radon and radon progeny. All discussions of radon in the text refer to ^{222}Rn unless otherwise indicated.

The decay rate or activity of radioactive elements has traditionally been specified in curies (Ci). The activity defines the number of radioactive transformations (disintegrations) of a radionuclide over unit time. The curie is the amount of radioactive material in which 37 billion disintegrations (decay events) occur each second ($3.7x10^{10}$ transformations per second). In discussing radon, a smaller unit, the picocurie (pCi), is used, where 1 pCi=$1x10^{-12}$ Ci. In international usage, the S.I. unit (the International System of Units) for activity is the becquerel (Bq), which is the amount of material in which one atom disintegrates each second (1 Bq is approximately 27 pCi). The activity concentration of radon or any radionuclide in air is typically expressed in units of pCi/L or Bq/m^3 of air. One pCi/L is equivalent to 37 Bq/m^3. The activity concentration is typically a description of the concentration of radioactive material in air or water. The product of concentration and exposure time equals exposure; models are used to estimate a radiation dose to tissue from exposure. Since the isotopes continue to decay for some time, and some excretion occurs, the term dose refers specifically to the amount of radiant energy absorbed per mass in a particular tissue or organ and is expressed in rad (or gray).

As radon and its progeny decay, they cumulatively emit alpha and beta particles as well as gamma- and x-rays. The health hazard from radon does not come primarily from radon itself, but rather from its radioactive progeny (see Chapter 4 for more information on the chemical and physical properties of radon). When an atom of radium transforms to radon, the alpha particle it emits slows down by the attraction of nearby electrons until it captures two electrons and becomes a stable atom of helium (He). The transformed radon and subsequent decay product atoms are charged and tend to attach to aerosol particles. Radon progeny are similarly charged, readily aggregate, form clusters, and attach to dust particles in air. The main health problems arise when primarily those radon progeny that are attached to dust particles (termed the attached fraction) are inhaled, deposit in the airway (particularly the tracheobronchial tree), and irradiate nearby cells repetitively with alpha particles as each atom transforms through the decay chain. These alpha particles can deliver a large localized radiation dose. The attached fraction is much higher in homes with smokers relative to those with nonsmokers, and in dusty mines relative to those that are well ventilated. Exposures to radon gas are accompanied by exposure to radon progeny, although the exact mix of radon and progeny are determined by several physical-chemical and environmental factors. In this toxicological profile, unless indicated otherwise, *exposure to radon* refers to exposure to the mixture of radon and progeny.

Because it is not feasible to measure the activities of individual radon progeny in the environment and while they decay inside the body, a unit termed the "Working Level (WL)" is used for the purpose of quantifying the cumulative radiation dose from inhaled radon progeny, which may not be in secular equilibrium. The WL unit is a measure of the amount of alpha radiation emitted from the short-lived progeny of radon. As applied to exposures to ^{222}Rn, this encompasses the decay series, $^{222}Rn(\alpha)\rightarrow$ $^{218}Po(\alpha)\rightarrow$ $^{214}Pb\rightarrow$ $^{214}Bi\rightarrow$$^{214}Po(\alpha)$ $\rightarrow$$^{210}Pb$, and represents any combination of the short-lived progeny of radon. Working Level (WL) means the concentration of short-lived radon progeny in 1 L of air that will release $1.3x10^{5}$ million electron volts (MeV) of alpha energy during decay. One WL is equivalent to the potential alpha energy of $2.08x10^{-5}$ joules in 1 cubic meter of air (J/m^3).

To convert between units of ^{222}Rn concentration (pCi/m^3 or Bq/m^3) and the potential alpha energy that can be released by its progeny as they fully decay (WL or J/m^3), the equilibrium between radon gas and its progeny at the time of exposure must be known or assumed (see Chapter 10 for conversion formula). When radon is in secular equilibrium with its progeny (i.e., when each of the short-lived radon progeny is present at the same activity concentration in air as ^{222}Rn), each pCi of radon in air will give rise to (almost precisely) 0.01WL (EPA 2003). By definition, 1 WL is equal to 100 pCi of radon gas. However, when removal processes other than radioactive decay are operative, such as with room air ventilation or air filtration, the concentration of short-lived progeny will be less than the equilibrium amount. In such cases, an equilibrium factor (F) is applied. The National Research Council Committee on Health Risks of Exposure to Radon (BEIR VI) assumes 40% equilibrium (F=0.4) between radon and radon progeny in the home (NAS 1999a), in which case, 1 pCi/L (37 Bq/m^3) of ^{222}Rn in the air is approximately equivalent to 0.004 WL.

The unit of measurement used to describe cumulative human exposure to radon progeny in mines is the Working Level Month (WLM). It is the product of the average concentration in WL and the exposure time in months. One WLM is defined as exposure at a concentration of 1 WL for a period of 1 working month (WM). A working month is assumed to be 170 hours. The S.I. unit for WLM is J-hour/m^3; 1 WLM=$3.6x10^{-3}$ J-hours/m^3.

Measurements in WLM can be made using special equipment that measures the total alpha emission of short-lived radon progeny. However, measurements in homes are typically made for radon gas and are expressed in Bq/m^3 or pCi/L. To convert from residential exposures expressed in pCi/L, it is considered that 70% of a person's time is spent indoors and that 1 pCi/L of radon in the indoor air is equivalent to

0.004 WL of radon progeny (EPA 2003; NAS 1999a). These conditions result in the following relationship:

1 pCi/L x 0.004 WL/pCi/L x 0.7 x (8,760 hours/WL-year ÷ 170 hours/WL-M) = 0.144 WLM/year

Because 1 pCi/L is equivalent to 37 Bq/m^3, a residential exposure scenario using equivalent assumptions to those described above results in the same cumulative exposure to radon progeny (0.144 WLM/year).

As discussed in detail in Section 3.2.1 (Inhalation Exposure), lung cancer is the toxicity concern following long-term exposure to radon and radon progeny. The high-energy alpha emissions from radon progeny, deposited predominantly in the tracheobronchial tree, and to a lesser extent in the lung, are the major source of toxicity concern. As shown in Figure 4-1, the radiological half-life for radon (^{222}Rn) is 3.8 days. The radioactive decay of radon to ^{218}Po (radiological half-life=3.05 minutes) is accompanied by the release of high-energy (5.5 MeV) alpha particles; decay of ^{218}Po to lead-214 (^{214}Pb; radiological half-life=26.8 minutes) also releases high-energy (6.0 MeV) alpha particles. Subsequent radioactive decay to bismuth-214 (^{214}Bi; radiological half-life=19.7 minutes) and ^{214}Po involve release of beta and gamma radiation, which are of sufficiently low energy and long range as to be considered of little relative toxicity concern to nearby cells. The decay of ^{214}Po via release of high-energy (7.69 MeV) alpha particles occurs so rapidly (radiological half-life=$1.6x10^{-4}$ seconds) that, in radiation dose modeling, these alpha emissions are generally attributed to ^{214}Bi decay (i.e., the rate of decay of ^{214}Bi is essentially equal to the rate of formation of ^{210}Pb due to the essentially instantaneous decay of ^{214}Po from ^{214}Bi). The subsequently-formed radioactive radon progeny (^{210}Pb, ^{210}Bi, and ^{210}Po in respective order of decay) are not considered to make significant contributions to respiratory tract toxicity (relative to the short-lived progeny). This is, in large part, because the radiological half-life associated with the decay of ^{210}Pb is 22.2 years, which is sufficiently long that biological clearance mechanisms limit the radiation dose attributed to it and the other progeny. Therefore, the radon progeny of primary toxicity concern are ^{218}Po and ^{214}Po (due to the rapid decay of these alpha emitters, especially when part of the attached fraction).

3.2 DISCUSSION OF HEALTH EFFECTS OF RADON BY ROUTE OF EXPOSURE

To help public health professionals and others address the needs of persons living or working near hazardous waste sites, the information in this section is organized first by route of exposure (inhalation, oral, and dermal) and then by health effect (death, systemic, immunological, neurological, reproductive,

developmental, genotoxic, and carcinogenic effects). These data are discussed in terms of three exposure periods: acute (14 days or less), intermediate (15–364 days), and chronic (365 days or more).

ATSDR Toxicological Profiles typically include tables and figures for each route and duration in which levels of significant effects (LSEs) are presented. Points in the figures show no-observed-adverse-effect levels (NOAELs) or lowest-observed-adverse-effect levels (LOAELs) and reflect the actual doses (levels of exposure) used in each study for which adequate information is available regarding exposure level and a particular effect. LOAELs are classified into "less serious" or "serious" effects. "Serious" effects are those that evoke failure in a biological system and can lead to morbidity or mortality (e.g., acute respiratory distress or death). "Less serious" effects are those that are not expected to cause significant dysfunction or death, or those whose significance to the organism is not entirely clear.

The December 1990 ATSDR Toxicological Profile for Radon included an LSE table and figure for exposure via the inhalation route in which levels of significant exposure were presented for noncancer effects in radon-exposed animals and cancer effect levels (CELs) were presented for lung cancer in humans exposed in the workplace, with the exception of one study of residential exposure. However, the LSE table and figure in the 1990 version of the Toxicological Profile for Radon were not retained in this update Toxicological Profile for Radon for the following reasons:

- LSEs for noncancer end points in the animal studies occurred at exposure levels that were several orders of magnitude higher than exposure levels expected to be of toxicological consequence in humans and are thus not reliable indicators of expected LSEs for noncancer end points in humans.

- Most occupational and residential studies of cancer end points (mainly lung cancer) include uncertain estimations of historical exposure levels for radon and radon progeny, and occupational studies are limited by confounding exposure to other substances including known human carcinogens.

- Assessment of individual epidemiological studies leads to uncertainty regarding human health effects associated with exposure to radon and radon progeny because individual studies may provide conflicting results.

- Recent emphasis has focused on pooled results from multiple human studies to provide more comprehensive evaluation that increases statistical power and decreases uncertainty, and it is not appropriate to assign LSEs from pooled analyses of individual epidemiological studies.

Presentation of epidemiological data for radon and radon progeny in this updated Toxicological Profile for Radon is focused on results of pooled data from individual studies of occupationally-exposed cohorts

and pooled data from individual studies that assessed residential exposure. Refer to the introductory statement of Section 3.2.1 for additional information regarding presentation of epidemiological data for radon and radon progeny.

A User's Guide has been provided at the end of this profile (see Appendix B).

3.2.1 Inhalation Exposure

Epidemiological studies designed to assess human health risks from exposure to radon mainly consist of: (1) cohort mortality studies of underground miners that investigated possible associations between lung cancer and individual exposure to radon or radon progeny, (2) residential case-control studies that investigated possible associations between lung cancer cases and residential radon levels using estimates of individual exposure for lung cancer cases as well as controls, and (3) ecological studies that investigated possible associations between rates of selected diseases within a geographic population and some measure of average radon levels within the same defined geographic region. It should be noted that there is no known threshold dose for exposure to alpha radiation from sources including radon and radon progeny, and there is evidence of an inverse exposure rate response at low dose rates (i.e., for a given total exposure, the effect might be greater if delivered at a lower rate over a longer time period). The response relative to increased radon progeny exposure was 25 times larger for nonsmokers (HPA 2009) and tended to decrease with time since the exposure ended, attained age since exposure ended, and exposure duration or exposure rate effect. This apparent inverse dose rate effect may not be real since it was predicated on effects observed for the most highly exposed individuals (early miners in highly dusty environments) for which radon progeny were not measured and equilibrium factors had to be assumed, making dose assignments more uncertain (Lubin et al. 1995b). Also, the portion of the estimated radon cancer risk that is due to silica dust is yet to be evaluated in mining studies before 2000 since crystalline silica was not recognized by the International Agency for Research on Cancer (IARC) as a known human carcinogen until 1997 (IARC 1997). Studies since then have found a high correlation between radon and silica regarding lung cancer and concluded that exposure to quartz can be an important confounder (Bergdahl et al. 2010).

Compelling evidence of radon-induced health effects in humans derives from numerous studies of underground miners, particularly uranium miners exposed beginning in the middle part of the twentieth century in the United States and several European countries. Although these cohort mortality studies typically involved rather crude estimates of exposure to high levels of radon in the working environment

and inherent uncertainty due to confounding factors such as smoking status and coexposure to known or suspected human carcinogens (diesel exhaust and arsenic), the results nevertheless consistently demonstrate increased risk of lung cancer with increasing exposure to radon in the working environment. These results are consistent across the various individual studies of mining cohorts and with analyses of pooled data from multiple cohorts. However, the miner studies were completed prior to crystalline silica and diesel exhaust being designated as known and suspected human carcinogens, respectively. The highest exposure groups in those studies tended to receive most of their dose before adequate ventilation was established to reduce mine air dust. An assessment of a cohort of iron ore miners with exposure information for radon, diesel exhaust, and silica found excess lung cancers (relative risk [RR] 5.65; 95% confidence interval [CI] 3.15–10.14) in a group of workers at the Malmberget mine with radon exposure >80 mBq-year/m^3 (Bergdahl et al. 2010). After accounting for silica exposure, the RR was only 3.90 (95% CI 1.21–12.55). The study authors concluded that accounting for silica exposure in epidemiological studies involving exposure to both radon and silica is important to prevent overestimating the cancer risk from radon. This high correlation between radon, inorganic arsenic, and silica was also reported for a cohort of German uranium miners (Taeger et al. 2008, 2009).

Reported associations between radon and lung cancer in the mining cohorts raised concern regarding the potential health effects of radon in homes, where levels are usually lower than those experienced in mining cohorts and do not include confounding by arsenic and silica dust. Numerous residential case-control studies of lung cancer have been performed in the United States and in many other countries, including Canada, China, Finland, Germany, Sweden, and the United Kingdom. Some of these studies reported positive or weakly positive associations between lung cancer risk and residential radon concentrations, and others suggested that radon reduced the cancer risk, whereas no consistent associations were observed in others. None of the residential case-control studies available for the pooling reported a statistically significant negative association (i.e., decreasing cancer risk in association with increasing radon exposure). Limitations of these studies include: (1) uncertainty in estimating long-term radon levels from relatively few prospective and/or retrospective periodic measurements of radon levels in a particular location; (2) uncertainty in assumptions regarding radon levels in homes where measurements were not made, length of residence and history of prior residences; and (3) accuracy of reported data on confounding factors such as smoking history or active smoker in the home, or including different percentages of smokers in the control and exposed groups. The individual residential case-control studies typically employed relatively low numbers of cases and matched controls, which limits the statistical power of an individual study to identify a statistically significant association between radon exposure and an adverse health outcome such as lung cancer. The statistical power is further reduced by

measurement error, and residential mobility. In order to more precisely estimate risk, most of the residential study investigators have pooled data from their studies. The pooled analyses have found statistically significant, positive associations between lung cancer and residential radon levels among smokers, but not among lifelong nonsmokers (Darby et al. 2005).

Several ecological studies have been performed to assess possible relationships between selected cancers and estimated radon levels within particular geographic regions where environmental radon levels appear to be higher than other geographic regions. Typically, estimates of mean radon levels for the geographic regions were significantly elevated, but were based on relatively few actual measurements of radon levels in homes in the region and were not matched to individuals. This is problematic because radon (particularly indoor) levels can vary greatly between residences in a particular geographic region. Additional sources of uncertainty in methodology used to estimate radon levels in ecological studies include use of current exposure to represent past exposure, inherent error in measuring devices, use of indirect measures of indoor concentrations as an index of indoor radon exposure, use of sample measurements rather than total-population data, and estimation of individual exposure from group data (Greenland et al. 1989; Morgenstern 1995; Stidley and Samet 1993). Other factors that can lead to inaccurate results regarding associations between exposure to radon and lung cancer include inadequate control of confounding, model misspecification, and misclassification of factors such as health end points, job classifications, and exposure. Results of available ecological studies assessing possible associations between environmental radon levels and lung cancer incidence are mixed; reports include positive and negative associations, as well as no significant associations. Several ecological studies have indicated positive associations between radon levels and selected types of leukemia. Statistically significant associations between radon levels and leukemia were also reported in a miner cohort study (Řeřicha et al. 2006), but not in residential case-control studies from which outcomes and exposures were more accurately matched to individuals.

The health effects chapter of this toxicological profile for radon focuses, primarily, on health effects observed in studies of occupationally-exposed miners and results of pooled analyses of residential case-control studies. Results of animal studies provide additional support to the compelling evidence of radon-induced lung cancer in the miner cohorts and to the evidence of radon-induced lung tumors from results of pooled analyses of residential case-control studies, especially among cigarette smokers. Since these studies are discussed in various sections of the profile, the general design features, attributes, limitations and major findings of the studies that form the bases for conclusions regarding the epidemiological evidence of health effects of radon exposures in humans are provided here.

Mining cohorts have been followed for several decades or more. Continued follow-up and refined assessments of the most widely-studied mining cohorts have resulted in improved exposure estimates and more complete categorization of individuals according to cause of death, mining history, and smoking status. However, until recently, studies of mining cohorts did not address confounding by silica exposure since crystalline silica was not recognized as a known human carcinogen before most of these studies were published. Assessments also did not necessarily include adjustments for confounding exposures to arsenic and/or diesel exhaust. The bulk of health effects information for the mining cohorts reported in this toxicological profile for radon derives from the most recent analyses of pooled data from 11 mining cohorts (Lubin et al. 1997; NAS 1999a; NIH 1994) using the most recent and comprehensive follow-up results from available studies of individual mining cohorts. Requirements for inclusion of a particular cohort in the analysis of pooled results included: (1) a minimum of 40 lung cancer deaths and (2) estimates of radon progeny exposure in units of WLM for each member of the cohort based on historical measurements of either radon or radon progeny. All 11 studies reported positive associations between lung cancer mortality and radon progeny exposure. For all subjects in each study cohort, person-years were accumulated from the date of entry (based on a minimum time of employment or the occurrence of a medical examination in some studies). A latency period of 5 years was incorporated to represent the expected minimum time necessary for a transformed cell to result in death from lung cancer. Although the accuracy of exposure estimates varied widely among the individual study cohorts, no attempt was made to restrict or limit the role of any particular cohort in the combined analysis. Relative risk for lung cancer was calculated as a function of cumulative WLM after adjustments for cohort, age, other occupational exposures (except silica dust), and ethnicity (NIH 1994). Selected characteristics of the individual cohorts and pooled data are presented in Table 3-1, as well as relative risks of lung cancer mortality for selected categories of cumulative WLM. The results provide evidence for increasing risk of lung cancer mortality with increasing cumulative WLM. Updated analysis of the 11 mining cohorts that contributed to the pooled data of NIH (1994) was particularly focused on relative risk of lung cancer in the miners exposed to relatively low cumulative WLM (Lubin et al. 1997); results demonstrate significant risk of lung cancer mortality at well below 100 WLM (Table 3-2). Excess relative risks (ERRs) for lung cancer mortality (excess risk per WLM) were estimated to be 0.0117/WLM (95% CI 0.002–0.025) for exposures <50 WLM and 0.0080/WLM (95% CI 0.003–0.014) for exposures <100 WLM.

Table 3-1. Selected Characteristics and Exposure Data for Individual Miner Cohort Studies Included in the Analysis of Pooled Data from the Individual Studies, and Lung Cancer Mortality Rates and Relative Risks by Cumulative WLM for Pooled Data[a]

		Follow-up		Non-exposed workers		Exposed workers and mean cumulative WLM		
Study cohort	Mine type	Period	Length (years)	Number	Person-years	Number	Person-years	WLM
China	Tin	1976–1987	10.2	3,494	39,985	13,649	135,357	277.4
Czech Republic	Uranium	1952–1990	25.2	0	4,216	4,284	103,652	198.7
Colorado	Uranium	1950–1987	24.6	0	7,403	3,347	75,032	807.2
Ontario	Uranium	1955–1986	17.8	0	61,017	21,346	319,701	30.8
Newfoundland	Fluorspar	1950–1984	23.3	337	13,713	1,751	35,029	367.3
Sweden	Iron	1951–1991	25.7	0	841	1,294	32,452	80.6
New Mexico	Uranium	1943–1985	17.0	12	12,152	3,457	46,797	110.3
Beaverlodge	Uranium	1950–1980	14.0	1,591	50,345	6,895	68,040	17.2
Port Radium	Uranium	1950–1980	25.2	683	22,222	1,420	30,454	242.8
Radium Hill	Uranium	1948–1987	21.9	1,059	26,301	1,457	25,549	7.6
France	Uranium	1948–1986	24.7	16	4,556	1,769	39,487	68.7
Totals[b]				7,176	242,332	60,570	908,983	
Averages			17.2					161.6

Cumulative WLM	Lung cancer cases	Person-years	Mean WLM	Relative risk[d] (95% CI)
0	107	214,089	0.0	1.00
1–49	367	502,585	14.8	1.03 (0.8–1.4)
50–99	212	118,196	73.0	1.30 (1.0–1.7)
100–199	462	132,207	144.8	1.74 (1.3–2.3)
200–399	511	91,429	280.4	2.24 (1.7–3.0)
400–799	612	65,105	551.7	2.97 (2.2–3.9)
800–1,599	294	27,204	1105.1	4.06 (3.0–5.4)
≥1,600	140	10,336	2408.4	10.2 (7.4–14.0)
Totals	2,705	1,161,150	130.6[c]	

[a]Table entries include 5-year lag interval for radon progeny exposure.
[b]Totals adjusted for 115 workers (including 12 lung cancer cases) who were included in both New Mexico and Colorado cohorts.
[c]Mean WLM among exposed miners is 160.2.
[d]Adjusted for cohort, age, other occupational exposures, and ethnicity.

CI = confidence interval; WLM = working level months

Source: NIH 1994

Table 3-2. Selected Results from Analysis of Pooled Data from 11 Mining Cohorts[a], Based on Deciles of Case Exposures That Were Each Under 100 WLM[b]

Cumulative WLM	Lung cancer cases[c]	Person-years	Mean WLM	Relative risk[d] (95% CI)
0	115	274,161	0.0	1.00
0.1–3.5	56	111,424	2.4	1.37 (1.0–2.0)
3.6–6.9	56	95,727	5.3	1.14 (0.8–1.7)
7.0–15.1	56	72,914	12.4	1.16 (0.8–1.7)
15.2–21.2	57	67,149	17.3	1.45 (1.0–2.2)
21.3–35.4	56	57,890	33.1	1.50 (1.0–2.2)
35.5–43.5	57	42,068	38.6	1.53 (1.0–2.2)
43.6–59.4	56	25,622	53.2	1.69 (1.1–2.5)
59.5–70.3	56	40,220	63.3	1.78 (1.2–2.6)
70.4–86.5	56	28,076	81.1	1.68 (1.1–2.5)
86.6–99.9	56	23,682	91.4	1.86 (1.2–2.8)

[a]The 11 mining cohorts and reports used for the pooled analysis included China (Xuan et al. 1993), Sweden (Radford and Renard 1984), Newfoundland (Morrison et al. 1988), Czech Republic (Ševc et al. 1988; Tomášek et al. 1994b), Colorado (Hornung and Meinhardt 1987; Hornung et al. 1995), Ontario (Kusiak et al. 1993), New Mexico (Samet et al. 1991), Beaverlodge (Howe et al. 1986), Port Radium (Howe et al. 1987), Radium Hill (Woodward et al. 1991), and France (Tirmarche et al. 1993).
[b]Table entries include 5-year lag interval for radon progeny exposure.
[c]Totals adjusted for 115 workers (including 12 lung cancer cases) who were included in both New Mexico and Colorado cohorts.
[d]Adjusted for cohort, age, other occupational exposures, and ethnicity; excess relative risks for lung cancer mortality were 0.0117 per WLM (95% CI: 0.002–0.025) for exposures <50 WLM and 0.0080 per WLM (95% CI: 0.003–0.014) for exposures <100 WLM.

CI = confidence interval; WLM = working level months

Source: Lubin et al. 1997

Assessments of pooled data from major residential case-control studies include a combined analysis of 2 China case-control studies (Lubin et al. 2004), a combined analysis of 7 North American case-control studies (Krewski et al. 2005, 2006), and a combined analysis of 13 European case-control studies (Darby et al. 2005, 2006).

The combined analysis of the residential case-control studies in China included a study that assessed all incident lung cancer cases recorded with the Shenyang Cancer Registry and diagnosed between September 1985 and September 1987 (Blot et al. 1990; Xu et al. 1989) and all incident lung cancer cases occurring in two rural prefectures of Gansu Province between June 1994 and April 1998 (Wang et al. 2002). The combined analysis included 1,050 lung cancer cases and 1,996 controls (Lubin et al. 2004). As shown in Table 3-3, odds ratios (ORs) increased significantly with increasing radon concentration. For subjects residing in the current home for ≥30 years, the OR at 100 Bq/m^3 was 1.32 (95% CI 1.07–1.91).

The individual case-control studies that contributed to the combined analysis of North American case-control studies (Krewski et al. 2005, 2006) were performed in regions of New Jersey, the Canadian Province of Winnipeg, Missouri, Iowa, Connecticut, and Utah-South Idaho. Requirements for inclusion in the combined analysis of North American case-control studies included: (1) ascertainment of at least 200 lung cancer cases (histologically or cytologically confirmed); (2) radon exposure estimates based primarily on long-term α-track detectors located in living areas of homes; and (3) in-person or telephone interviews with subjects or next of kin to obtain data on a variety of demographic, socioeconomic, and smoking-related factors. Of 10,127 total subjects in the 7 North American case-control studies, 765 subjects were excluded from the pooled analysis due to no radon measurements, no residence data within a 5–30-year time exposure window prior to the index date, or insufficient smoking data. The 5–30-year time exposure window presumes that neither radon exposure within 5 years of lung cancer occurrence nor 30 years prior to the index date contributes to lung cancer, although the window is presumed to be generally reflective of a biologically relevant exposure. Thus, the combined analysis included 4,081 lung cancer cases and 5,281 matched controls (Krewski et al. 2006). Selected characteristics of the study subjects and exposure estimates are presented in Table 3-4, along with ORs for lung cancer from pooled data without restriction and ORs resulting from restriction to subjects residing in one or two houses with ≥20 years of the residence time covered by α-track monitors. All analyses of the data were conducted using conditional likelihood regression for matched or stratified data and included covariates for sex, age at index date, number of cigarettes smoked per day, duration of smoking, and an indicator variable for each study. An excess odds ratio (EOR) was 0.10 per 100 Bq/m^3

Table 3-3. ORs for Lung Cancer from Combined Analysis of Two China Residential Case-Control Studies (Using a 5–30-Year Exposure Time Window)

ORs for lung cancer				
Radon concentration		Number of subjects		OR[a]
Bq/m^3	pCi/L	Cases	Controls	(95% CI)
<100	<2.70	164	298	1.00
100–149	2.70–4.01	223	387	1.13 (0.94–1.31)
150–199	4.05–5.38	198	354	1.05 (0.86–1.27)
200–249	5.41–6.73	181	372	1.14 (0.90–1.45)
250–299	6.76–8.08	114	256	1.22 (0.95–1.56)
≥300	≥8.11	148	307	1.29 (0.93–1.80)
Excess OR (β)=0.133 per 100 Bq/m^3 (95% CI 0.01–0.36)[b]				
Excess ORs by years covered by radon detectors and residential mobility within the 5–30-year exposure time window prior to enrollment				
Years in exposure time window		25	20–24	<20
Excess OR		0.319	-0.134	-0.072
Number of homes		1	2	≥3
Excess OR		0.332	-0.071	0.099

[a]ORs adjusted for sex, age, smoking risk, years in exposure time window, and number of homes inhabited in the exposure time window.
[b]Based on linear model: $OR(x)=1+\beta x$, where x is the radon concentration in the exposure time window.

CI = confidence interval; OR = odds ratio

Source: Lubin et al. 2004

(95% CI -0.1–0.28) for the unrestricted dataset, indicating that radon was not associated with residential lung cancer, but the EOR increased to 0.18 per 100 Bq/m^3 (95% CI 0.02–0.43) when restricting to subjects residing in one or two houses with ≥20 years of the residence time covered by α-track monitors. This combined analysis provides evidence of an association between residential radon and lung cancer risk (Table 3-4). Histologically, no effect of radon concentration was found for any specific lung cancer type.

The analysis of pooled data from residential case-control studies in 13 European studies (Darby et al. 2005, 2006) included Austria, the Czech Republic, nationwide Finland, south Finland, France, eastern Germany, western Germany, Italy, Spain, nationwide Sweden, never smokers in Sweden, Stockholm Sweden, and the United Kingdom. The pooled data included 7,148 lung cancer cases and 14,208 controls. Inclusion in the analysis required detailed residential histories for at least 15 years, at least 2 months of measurements of radon gas concentrations that were likely to be representative of levels experienced by the study subjects during their tenure in the residences, and details regarding smoking habits. Each study in the pooled analysis included at least 150 lung cancer cases and 150 control subjects. Results of this analysis provide additional evidence of an association between residential radon and lung cancer risk, but mostly among smokers and recent ex-smokers for which the risk was as much as 25 times higher than for never smokers. The evidence for smokers includes statistically significant relative risks at exposure concentrations ≥400 Bq/m^3 (10.8 pCi/L), an ERR of 0.084 per 100 Bq/m^3 (95% CI 0.03–0.158) for the full range of observed radon concentrations, and ERRs of 0.140 per 100 Bq/m^3 (95% CI 0.004–0.309) for exposure concentrations <200 Bq/m^3 (<5.4 pCi/L), 0.095 per 100 Bq/m^3 (95% CI 0.005–0.206) for exposure concentrations <400 Bq/m^3 (<10.8 pCi/L), and 0.078 per 100 Bq/m^3 (95% CI 0.012–0.164) for exposure concentrations <800 Bq/m^3 (<21.6 pCi/L) (Table 3-5). For lifelong nonsmokers, an ERR of 0.106 per 100 Bq/m^3 (95% CI 0.003–0.280) was observed for the full range of observed radon concentrations.

Although the dose-response coefficients from the mining studies and residential studies are expressed in different units of exposure (i.e., WLM vs. Bq-year/m^3), they can be compared by applying the relationship described above, namely that 1 pCi/L (37 Bq/m^3) of continuous exposure throughout the year (i.e., 37 Bq-year/m^3) is equivalent to 0.144 WLM for that year. Thus, a 25-year exposure at 200 Bq/m^3 (5.4 pCi/L) would be equivalent to a cumulative exposure of 19.5 WLM. Using this conversion factor, an estimated excess relative risk of 0.0117/WLM at occupational exposures <50 WLM (Lubin et al. 1997) would be roughly equivalent to an ERR of 0.114 per 100 Bq/m^3, assuming that the miners were not exposed to silica dust since accounting has not yet been conducted for confounding by this carcinogen.

Table 3-4. Selected Characteristics of Study Subjects, Exposure Estimates, and ORs for Lung Cancer from Combined Analysis of Seven North American Residential Case-Control Studies (Using a 5–30-Year Exposure Time Window)

	Number of subjects[a]		Time-weighted average radon concentration in Bq/m^3		
Region	Lung cancer cases	Controls	Lung cancer cases	Controls	All subjects
New Jersey	480	442	26.5	24.9	25.7
Winnipeg	708	722	137.4	146.9	142.2
Missouri-I	530	1,177	62.2	62.9	62.7
Missouri-II	477	516	55.3	56.1	55.7
Iowa	412	613	136.2	121.3	127.3
Connecticut	963	949	32.2	32.8	32.5
Utah-Idaho	511	862	55.4	58.1	57.1

ORs for lung cancer

Radon concentration		Number of subjects		OR[b]
Bq/m^3	pCi/L	Cases	Controls	(95% CI)
<25	<0.68	994	1,055	1.00
25–49	0.68–1.32	1,169	1,549	1.13 (0.94–1.31)
50–74	1.35–2.00	704	1,087	1.05 (0.86–1.27)
75–99	2.03–2.68	356	507	1.14 (0.90–1.45)
100–149	2.70–4.03	513	602	1.22 (0.95–1.56)
150–199	4.05–5.38	166	229	1.19 (0.86–1.66)
≥200	≥5.45	179	252	1.29 (0.93–1.80)
Excess OR (β)=0.10 per 100 Bq/m^3 (95% CI -0.01–0.28)[c]				

ORs for lung cancer with data restricted to subjects residing in one or two houses in the exposure window with ≥20 years covered by α-track air monitors

Radon concentration		Number of subjects		OR[b]
Bq/m^3	pCi/L	Cases	Controls	(95% CI)
<25	<0.68	503	596	1.00
25–49	0.68–1.32	481	717	1.01 (0.80–1.28)
50–74	1.35–2.00	295	418	1.29 (0.98–1.70)
75–99	2.03–2.68	181	293	1.22 (0.88–1.69)
100–149	2.70–4.03	202	282	1.28 (0.91–1.78)
150–199	4.05–5.38	115	160	1.41 (0.83–2.14)
≥200	≥5.45	133	185	1.29 (0.91–2.06)
Excess OR (β)=0.18 per 100 Bq/m^3 (95% CI 0.02–0.43)[c]				

[a]For the combined analysis of the 7 North American residential case-control studies, 339 lung cancer cases and 426 control subjects were excluded based on lack of smoking, radon, and/or residence data.
[b]ORs stratified by sex and categories of age, duration of smoking, number of cigarettes smoked per day, number of residences, and years with α-track measurements in the exposure time window.
[c]Based on linear model: $OR(x)=1+\beta x$, where x is the radon concentration in the exposure time window.

CI = confidence interval; OR = odds ratio

Source: Krewski et al. 2006

Table 3-5. Relative Risk and Excess Relative Risk of Lung Cancer by Radon Level in Homes 5–34 Years Previously, Estimated from the Pooled Data for 13 European Residential Case-Control Studies

Radon concentration			Number of subjects		
Range (Bq/m^3)	Mean (Bq/m^3)	Mean (pCi/L)	Lung cancer cases	Controls	RR (95% CI)
<25	17	0.46	566	1,474	1.00 (0.87–1.15)
25–49	39	1.05	1,999	3,905	1.06 (0.98–1.15)
50–99	71	1.92	2,618	5,033	1.03 (0.96–1.10)
100–199	136	3.68	1,296	2,247	1.20 (1.08–1.32)
200–399	273	7.38	434	936	1.18 (0.99–1.42)
400–799	542	14.65	169	498	1.43 (1.06–1.92)
≥800	1,204	32.54	66	115	2.02 (1.24–3.31)

Excess relative risk for lung cancer according to selected ranges of radon concentrations

Range of radon concentrations		Lung cancer cases	Controls	ERR per 100 Bq/m^3 (95% CI)
<800 Bq/m^3	21.6 pCi/L	7,082	14,093	0.078 (0.012–0.164)
<400 Bq/m^3	10.8 pCi/L	6,913	13,595	0.095 (0.005–0.206)
<200 Bq/m^3	5.4 pCi/L	6,479	12,659	0.140 (0.004–0.309)
<100 Bq/m^3	2.7 pCi/L	5,183	10,412	0.025 (-0.192–0.306)
All radon concentrations		7,148	14,208	0.084 (0.030–0.158)

CI = confidence interval; ERR = excess relative risk; RR = relative risk

Source: Darby et al. 2006

This value is similar to the estimates for excess relative risk (0.084/Bq/m^3) estimated from the analysis of pooled data from the 13 European case-control studies (Darby et al. 2005, 2006) and EOR (0.18 per 100 Bq/m^3) estimated from the pooled analysis of the North American residential case-control studies restricted to subjects residing in one or two houses with ≥20 years of the residence time covered by α-track monitors (Krewski et al. 2006). Based on this comparison, the studies of mining cohorts and the residential studies appear to converge on similar estimates for the relationship between exposure to radon (and its progeny) and risk of lung cancer mortality. However, since the miners were exposed to silica dust and those studies did not assess confounding by this substance (which was confirmed as a known human carcinogen after those studies were published), attempts to correlate radon risk from residential and mining studies may be premature. This is emphasized in the re-assessed results of Swedish mines in which strong correlation was found between radon and silica, and accounting for silica reduced the RR previously attributed to radon by approximately 30%, from 5.65 to 3.90 (Bergdahl et al. 2010).

Available animal data consist mainly of inhalation studies performed at the University of Rochester (UR) in the 1950s and 1960s using rats, mice, and dogs (AEC 1961, 1964, 1966; Morken 1955, 1973); at the Pacific Northwest Laboratory (PNL, presently Pacific Northwest National Laboratory [PNNL]) between the 1960s and 1980s using rats, dogs, and hamsters (Cross 1988, 1994; Cross et al. 1981a, 1981b, 1984; Dagle et al. 1992; Gilbert et al. 1996; NIEHS 1978; Palmer et al. 1973); and at laboratories in France using rats (Chameaud et al. 1974, 1980, 1982a, 1982b, 1984; Monchaux 2004; Monchaux and Morlier 2002; Monchaux et al. 1999; Morlier et al. 1992, 1994). Most of these studies employed exposure levels that were many orders of magnitude higher than those considered to be relevant to human health. Discussion of animal studies in Section 3.2.1 is limited to studies that employed exposure levels considered relevant to plausible human exposure scenarios (Chameaud et al. 1984; Morlier et al. 1994).

3.2.1.1 Death

Possible associations between exposure to radon and lung cancer mortality among underground miners are discussed in Section 3.2.1.7 (Cancer).

Excess mortality from noncancer diseases reported in some of the mining cohorts include all noncancer respiratory diseases, pneumoconioses, emphysema, interstitial pneumonitis, other (unspecified) chronic obstructive respiratory diseases, and tuberculosis (Lundin et al. 1971; Muller et al. 1985; Roscoe 1997; Roscoe et al. 1989, 1995; Samet et al. 1991; Tirmarche et al. 1993; Waxweiler et al. 1981). However, confounding factors such as exposure to other respiratory toxicants (most notably arsenic and silica dust),

ethnicity, smoking history, and work experience were likely major contributors to mortalities from noncancer respiratory diseases. A statistically significant excess of mortality due to chronic nephritis and renal sclerosis was also reported in the U.S. uranium miner cohort, although it is unclear whether this was related to exposure to radon, uranium ore, or other mining conditions or to nonmining factors (Waxweiler et al. 1981).

No significant association was observed between cumulative exposure to radon progeny and death from cardiovascular diseases in cohorts of German uranium miners (Kreuzer et al. 2010) or Newfoundland fluorspar miners (Villeneueve et al. 2007a).

Limited information is available regarding exposure to radon and death in animals. No significant effects on longevity were observed in male Sprague-Dawley rats exposed to atmospheres of radon and radon progeny for 6 hours/day, 5 days/week during 18 months to obtain a cumulative exposure of 25 WLM (Morlier et al. 1994) or in rats exposed to a cumulative exposure of 20 WLM (1 hour exposures twice weekly for 42 total exposures) or 40 WLM (1-hour exposures twice weekly for 82 total exposures) (Chameaud et al. 1984). It should be noted that these studies employed relatively low dose rates.

3.2.1.2 Systemic Effects

No studies were located regarding gastrointestinal, musculoskeletal, hepatic, dermal, or body weight effects after inhalation exposure to radon and its progeny at exposure levels considered relevant to human health.

Respiratory Effects. Possible associations between exposure to radon and lung cancer are discussed in Section 3.2.1.7. Adverse noncancer respiratory effects have been observed in humans under occupational conditions and in laboratory animals exposed to radon and its progeny. Some studies of miner cohorts identified excess cases of nonmalignant respiratory diseases such as asthma, bronchitis, pneumoconioses, emphysema, interstitial pneumonitis, pulmonary fibrosis, and tuberculosis (Boice et al. 2008; Fox et al. 1981; Lundin et al. 1971; Muller et al. 1985; Roscoe 1997; Roscoe et al. 1989, 1995; Samet et al. 1991; Tirmarche et al. 1993; Waxweiler et al. 1981). However, potential confounding by smoking and respirable dust, especially crystalline silica dust, were likely major contributors to mortalities from noncancer respiratory diseases. Excess mortality associated with exposure to silica dust was reported in California diatomaceous earth miners for which the standard mortality ratio (SMR) was 2.01 (95% CI 1.56–2.55). The mortality rate increased sharply with exposure using a 15-year latency, which is longer

than the 5-year latency used for most miner and residential radon studies (Checkoway et al. 1997). Chronic lung disease was reported to increase with increasing cumulative exposure to radiation and with cigarette smoking (Archer 1980). In addition, nonsmoking uranium miners were also reported to have increased deaths from nonmalignant respiratory disease compared to a nonsmoking U.S. veteran cohort (Roscoe et al. 1989). For non-miners, the rate of chronic obstructive pulmonary disease (COPD) was reported to increase with increasing radon exposure (Turner et al. 2012).

Alterations in respiratory function have been reported in studies of U.S. uranium miners (Archer et al. 1964; Samet et al. 1984a; Trapp et al. 1970). Archer et al. (1964) reported decrements in pulmonary function with increasing cumulative exposure; however, the study also noted that pulmonary disability was affected by age and smoking more than by radiation exposure. Samet at al. (1984a) reported significantly increased prevalence of dyspnea with increasing duration of underground mining. Evaluations of these respiratory end points did not include assessment of the effects of each of the other possible mine pollutants, such as ore dust, silica, or diesel engine exhaust.

No information was located regarding respiratory effects in animals following exposure to radon and its progeny at concentrations considered relevant to human health.

Cardiovascular Effects. No significant association was observed between cumulative exposure to radon progeny and death from cardiovascular diseases in cohorts of German uranium miners (Kreuzer et al. 2010) or Newfoundland fluorspar miners (Villeneueve et al. 2007a). A significant relationship was noted between cumulative radon exposure and prevalence of mortality from cerebrovascular disease (excess relative risk of 0.49 [95% CI 0.07–1.23] per 100 WLM) in a French cohort study of uranium miners between 1946 and 1999 (Nusinovici et al. 2010). However, the study authors cautioned that a lack of data limited the ability to assess possible confounding by cardiovascular risk factors.

No information was located regarding cardiovascular effects in animals following exposure to radon and its progeny at concentrations considered relevant to human health.

Hematological Effects. No studies were located regarding hematological effects after inhalation exposure to radon at concentrations considered relevant to human health.

Renal Effects. Although a statistically significant increase in mortality due to kidney disease, characterized by chronic nephritis and renal sclerosis, was reported among U.S. uranium miners

(Waxweiler et al. 1981) and in Canadian miners at the Eldorado mines (Muller et al. 1985), this finding is not generally considered to be related to radon exposure *per se*.

No information was located regarding renal effects in animals following exposure to radon and its progeny.

Ocular Effects. Abdelkawi et al. (2008) reported significantly increased refractory index, decreased protein concentration, and increased protein molecular weight after 6 weeks of exposure in the lens and cornea of mice exposed to radon at a mean concentration of 55.8 kBq/m^3 (attached fraction of 0.62) for 6 hours/day, 5 days/week for up to 8 weeks. Effective radon lung doses ranged from 20.92 to 83.68 mSv. The study investigators considered the effects on the lens and cornea to have resulted from systemic distribution of inhaled radioactivity. Although the dermal route of exposure was not considered, the permeability of corneal epithelium to atmospheric gases could allow radon at the high concentrations used in the study to diffuse toward and expose both the cornea and lens to alpha radiation.

3.2.1.3 Immunological and Lymphoreticular Effects

No information was located regarding immunological effects after inhalation exposure to radon at concentrations considered relevant to human health.

3.2.1.4 Neurological Effects

No studies were located regarding neurological effects after inhalation exposure to radon at concentrations considered relevant to human health.

3.2.1.5 Reproductive Effects

No maternal or fetal reproductive effects in humans have been attributed to exposure to radon and its progeny. However, a decrease in the secondary sex ratio (males:females) of the children of male underground miners may be related to exposure to radon and its progeny (Dean 1981; Muller et al. 1967; Wiese and Skipper 1986). Ismail and Jaafar (2010) assessed possible relationships between radiation dose to the lungs from radon and radon progeny and rates of infertility within various locations in Iraqi Kurdistan. Radon levels were measured in homes; annual effective lung doses by inhalation of radon and radon progeny were estimated to range from approximately 2 to 6 mSv/yr. The dose to the gonads was not estimated, but would have been lower than that for the lungs and orders of magnitude lower than the

protracted external radiation doses stated to induce temporary sterility (400 mSv/yr) or permanent sterility (2000 mSv/year). The study authors reported an exponential relationship between annual effective lung dose and the rate of male infertility that is not supported by the reported low estimates of radiation dose. The authors also stated that there were increases in blood and prostate cancers (which influence male fertility), but did not provide quantitative data. Overall, the scientific value of this study is questionable.

No information was located regarding reproductive effects in animals following exposure to radon and its progeny at concentrations considered relevant to human health.

3.2.1.6 Developmental Effects

No studies were located regarding developmental effects in humans following inhalation exposure to radon and its progeny.

No information was located regarding developmental effects in animals following exposure to radon and its progeny at concentrations considered relevant to human health.

3.2.1.7 Cancer

Associations between exposure to radon and lung cancer mortality have been examined in studies of underground miners at facilities in the United States (Archer et al. 1973, 1976, 1979; Boice et al. 2008; Checkoway et al. 1985; Gottlieb and Husen 1982; Hornung and Meinhardt 1987; Hornung et al. 1998; Lane et al. 2010; Lubin et al. 1995a, 1995b; Luebeck et al. 1999; Lundin et al. 1971; Moolgavkar et al. 1993; NIH 1994; Roscoe 1997; Roscoe et al. 1989, 1995; Samet et al. 1984b, 1989, 1991, 1994; Schubauer-Berigan et al. 2009; Stayner et al. 1985; Stram et al. 1999; Thomas et al. 1994; Wagoner et al. 1963, 1964; Waxweiler et al. 1981), Australia (Woodward et al. 1991); Brazil (Veiga et al. 2006), Canada (Howe and Stager 1996; Howe et al. 1986, 1987; Kusiak et al. 1993; L'Abbé et al. 1991; Morrison et al. 1985, 1998; Muller et al. 1985), China (Qiao et al. 1989, 1997; Yao et al. 1994), the Czech Republic (Kulich et al. 2011; Ševc et al. 1988, 1993; Tomášek 2002, 2011; Tomášek and Darby 1995; Tomášek and Plaček 1999; Tomášek and Žárská 2004; Tomášek et al. 1993, 1994a, 1994b, 2008), England (Fox et al. 1981; Hodgson and Jones 1990b), France (Amabile et al. 2009; Laurier et al. 2004; Leuraud et al. 2007; Rogel et al. 2002; Tirmarche et al. 1993; Vacquier et al. 2007, 2009), Germany (Brüske-Hohlfeld et al. 2006; Kreuzer et al. 2000, 2010; Schnelzer et al. 2010; Taeger et al. 2006, 2008, 2009; Walsh et al. 2010), Italy (Carta et al. 1994), Norway (Solli et al. 1985), and Sweden (Axelson and Sundell 1978; Bergdahl et al. 2010; Damber and Larsson 1982; Edling and Axelson 1983; Jonsson et al. 2010;

Jorgensen 1984; Radford and Renard 1984; Snihs 1974). The mining cohorts were primarily uranium miners, but included some cohorts mining other metals, hard rock, or coal.

Lubin et al. (1997) provide combined results from eleven of these cohorts; the results demonstrate increased risk of mortality from lung cancer with increasing WLM (see Table 3-2). The combined data included 115 lung cancer deaths among workers without known occupational exposure to radon and 2,674 lung cancer deaths among exposed miners. Some of these miners had been exposed to more than 10,000 WLM; the mean exposure among the pooled miner data was 162 WLM. In order to make more meaningful comparisons between radon exposure among mining cohorts and residential radon exposure, Lubin et al. (1997) assessed mortality from lung cancer among two groups of workers with the lowest exposure levels (<50 and <100 WLM, respectively). Even in these groups of miners with relatively low-level exposure, relative risk of lung cancer mortality exhibited an apparent linear and statistically significant increasing trend with WLM (in decile categories). RRs for the two highest exposure categories (142.3–250.8 and >250.8 Bq/m^3; equivalent to 3.84–6.77 and >6.77 pCi/L, respectively) were 1.28 (95% CI 1.0–1.6) and 1.20 (95% CI 1.0–1.5), respectively. ERRs per WLM were estimated to be 0.0117/WLM (95% CI 0.002–0.025) for exposures <50 WLM and 0.0080/WLM (95% CI 0.003–0.014) for exposures <100 WLM. General patterns of declining excess relative risk per WLM with attained age, time since exposure, and exposure rate were observed in both the unrestricted pooled data and in those restricted to <50 and <100 WLM. Lubin et al. (1997) noted an apparent inadequacy in the fit of the ERR model, but this was not improved using nonlinear or linear threshold models. Lubin et al. (1997) also noted that results for the mining cohorts with relative low-level exposure might not be applicable to residential radon exposure due to uncertainties in estimating miner exposure to radon, radon progeny, and other carcinogens (e.g., silica dust) during the earliest years of mining when ventilation was poor.

Leuraud et al. (2011) assessed the effects of exposure to radon and radon decay products and smoking status on the risk of lung cancer in a combined analysis of 1,046 lung cancer cases and 2,492 controls with detailed radon exposure data and smoking status selected from three major minor cohorts in the Czech Republic (Tomášek et al. 2003), France (Laurier et al. 2004), and Germany (Kreuzer et al. 2010). The combined analysis resulted in an ERR/WLM of 0.010 (95% CI 0.006–0.018) unadjusted for smoking and an ERR/WLM of 0.008 (95% CI 0.004–0.014) after adjustment for smoking, which was based on four categories: never smoker, ex-smoker for ≥10 years, ex-smoker for <10 years, and current smoker. The results of Leuraud et al. (2011) suggest a sub-multiplicative interaction between radon exposure and smoking.

The results of the miner studies consistently demonstrate significant positive associations between lung cancer and exposure to radon. However, most miner studies were performed prior to the identification of other substances as known human carcinogens (silica dust and arsenic; NTP 2011) or probable human carcinogens (diesel exhaust particulates; Attfield et al. 2012; NTP 2011) in the mining air. Accounting for these carcinogens would likely reduce the calculated impact of radon on lung cancer mortality in the mining cohorts. For example, Xuan et al. (1993) estimated a 75% reduction in the lung cancer risk to a cohort of Chinese tin miners after adjusting for arsenic exposure. Bergdahl et al. (2010) reported decreased lung cancer risk from radon after adjusting for silica exposure within the highest exposure group from a cohort of Swedish iron ore miners. Statistically significant excess lung cancer mortality has been associated with average cumulative exposures to radon progeny as low as 36–39 WLM in Czech and French cohorts of uranium miners (Ševc et al. 1988; Vacquier et al. 2007); exposure levels were higher among many of the other uranium miner cohorts. Vacquier et al. (2009) reported an ERR per 100 WLM of 0.58 ($p<0.01$) for lung cancer within a cohort of 5,086 French uranium miners (4,133 with positive radon exposure; mean cumulative exposure of 36.6 WLM) and 159 lung cancer cases during 30 years of follow up and noted that higher risk persisted when the effects of hard labor and period of exposure were taken into account. An inverse exposure rate effect (i.e., lower exposure rates for long periods are more hazardous than equivalent cumulative exposure received at higher exposure rates over a shorter time) was evident at relatively high exposure levels (WL) (Hornung et al. 1998; Lubin et al. 1995a, 1997; Luebeck et al. 1999; Moolgavkar et al. 1993; NIH 1994); however, this effect appeared to be attenuated or absent at relatively low exposure levels (Lubin et al. 1995a; NIH 1994; Tomášek et al. 2008). The apparent inverse exposure rate effect could have been associated with using no-threshold models, a restriction that was not required in the European residential assessment (HPA 2009).

Among smoking and nonsmoking uranium miners, the most frequently reported type of lung cancer was small cell lung carcinoma (SCLC) in the early phase of follow-up (Archer et al. 1974; Auerbach et al. 1978; Butler et al. 1986; Gottlieb and Husen 1982; Saccomanno et al. 1971, 1988; Samet 1989). Archer et al. (1974) also noted relatively high rates of epidermoid and adenocarcinomas, while large-cell undifferentiated and other morphological types of lung cancer were seen less frequently. A report on the German uranium mining cohort identified squamous cell carcinoma as the predominant lung tumor cell type, followed by adenocarcinoma and SCLC (Kreuzer et al. 2000). Jonsson et al. (2010) reported lung cancer risk in a cohort of 5,449 male iron ore miners in Sweden; the follow-up period spanned the years 1958–2000. A total of 3,597 of the miners had been exposed to radon; the average cumulative radon exposure was 65 WLM over an average of 14.6 years of employment. For all lung cancers, the ERR per kBq-year/m^3 was 0.046 (95% CI 0.015–0.077), which equals an ERR/WLM of 0.022WLM (95% CI

0.007–0.038). For small cell cancer (55 cases), squamous cell cancer (51 cases), and adenocarcinoma (12 cases), ERRs per kBq-year/m^3 were 0.072 (95% CI -0.003–0.147), 0.049 (95% CI -0.003–0.102), and 0.000 (95% CI 0.017–0.017), respectively. After adjusting for cumulative quartz (silica) together with attained age and calendar period, the ERR for all lung cancers was 0.031 per kBq-year/m^3 (95% CI 0.009–0.070), which equals an ERR of 0.015 per WLM (95% CI 0.04–0.034).

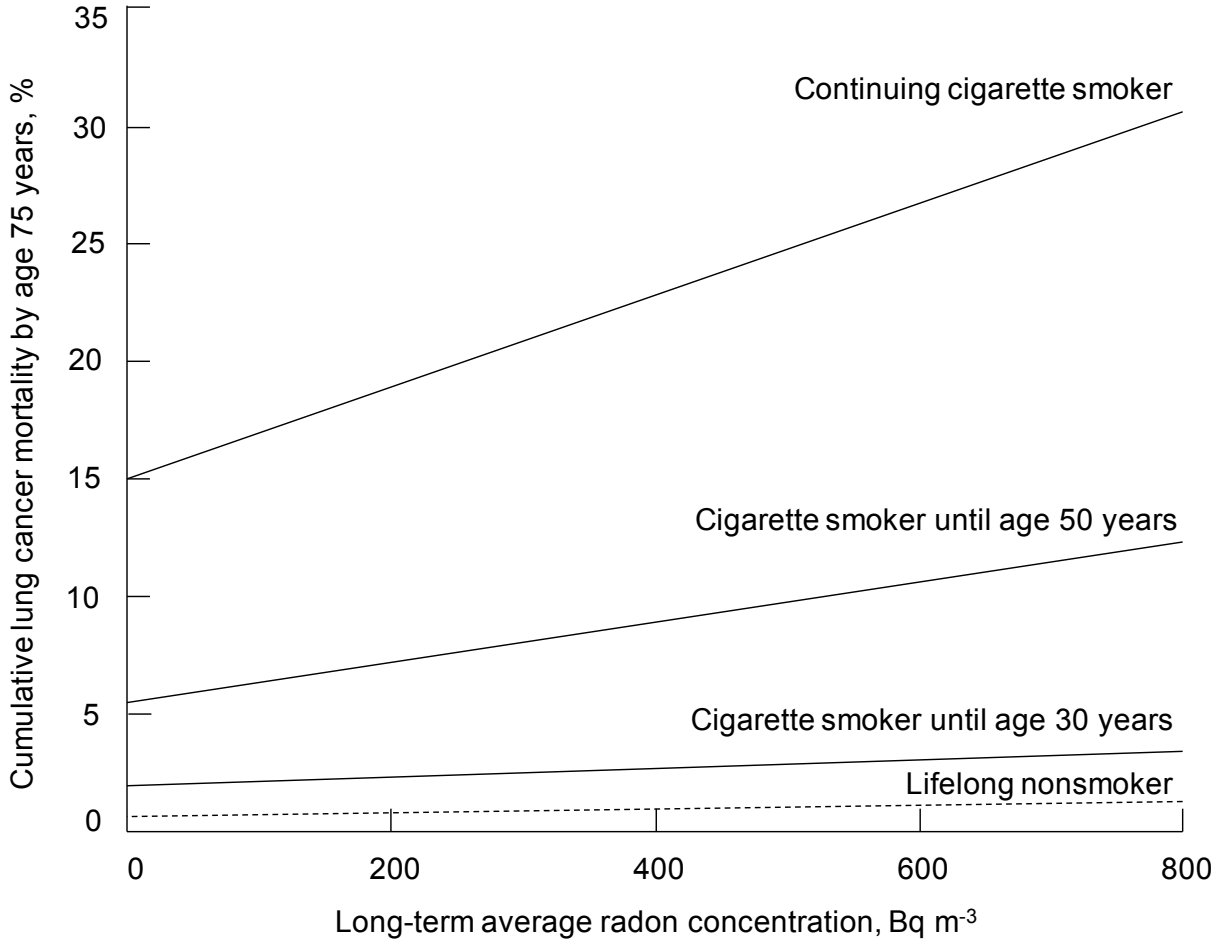
In a subcohort of 516 white nonsmoking uranium miners (drawn from a larger cohort of U.S. uranium miners), mean exposure was reported as 720 WLM. For this cohort, the mortality risk for lung cancer was found to be 12-fold greater than that of nonsmoking, nonmining U.S. veterans; the SMR was 12.7 (95% CI 8.0–20.1) for lung cancer in nonsmoking mining cohort. No lung cancer deaths were found in nonsmoking miners (Colorado Plateau cohort) who had exposure <465 WLM (Roscoe et al. 1989); continued follow-up of this cohort (1960–2005) revealed SMRs of 2.9 (95% CI 1.8–4.4) for never smokers with cumulative exposure to radon progeny in the range of 400–1,000 WLM and 6.3 (95% CI 4.6–8.5) for never smokers with cumulative exposure to radon progeny ≥1,000 WLM (Schubauer-Berigan et al. (2009). These results for nonsmokers follow a dose rate rather than an inverse dose rate response curve.

Some studies of mining cohorts included assessments of mortality from cancers other than lung cancer. Kreuzer et al. (2010) reported a slight, but statistically significant excess of cancers of the extrathoracic airways and trachea (ERR/WLM = 0.062%; 95%CI 0.002–0.121%) within a cohort of 58,987 male uranium miners at the Wismut mine in Germany with follow-up from 1946 to 2003. Řeřicha et al. (2006) reported significant positive associations between cumulative radon exposures and incidences of leukemia (RR=1.75; 95% CI 1.10–2.78) and incidences of chronic lymphocytic leukemia (CLL) (RR=1.98; 95% CI 1.10–3.59) in a cohort of Czech uranium miners at 110 WLM. In apparent contrast, this same group did not find this relationship to hold in a longer-term follow-up of the same population (Kulich et al. 2011). Möhner et al. (2006, 2010) observed no significant associations between leukemia risk (from acute myeloid leukemia [AML], CLL, or all types) and exposure to radon progeny (from <50 to >1,500 WLM) among 377 leukemia cases and 980 individually matched controls from a cohort of 360,000 uranium miners at the Wismut mine in the former East Germany that supported the Soviet nuclear weapons program. However, the leukemia risk became significant (OR 2.64, 95% CI 1.60–2.35) in the highest dose category when doses were lagged 20 years (Möhner et al. 2010), the same period used by Pelucchi et al. (2006) for the silica dust study, but much longer than 5 years used in other studies in this section. This indicates that the 5-year lag period might be too short. Results of a few other studies indicate statistically significant excessive mortalities from laryngeal, liver, kidney, stomach, and/or gall bladder cancers

(Kreuzer et al. 2004, 2008; Tirmarche et al. 1992; Tomášek et al. 1993; Vacquier et al. 2007); however, the excess mortalities from these cancers did not appear to be related to cumulative exposure to radon and were not supported by results from other studies of mining cohorts (Kreuzer et al. 2010; Kulich et al. 2011; Laurier et al. 2004; Möhner et al. 2008).

Numerous residential case-control studies of lung cancer have been performed in the United States and other countries, including Brazil, Canada, China, Croatia, the Czech Republic, Finland, France, Germany, Israel, Italy, Japan, Romania, Spain, Sweden, and the United Kingdom. Some of these studies reported positive or weakly positive associations between lung cancer risk and residential radon concentrations, whereas no significant associations were observed in others. As discussed earlier, recent assessment of available residential case-control studies includes analyses of pooled data from 2 China case-control studies (Lubin et al. 2004), a combined analysis of 7 North American case-control studies (Krewski et al. 2005, 2006), a combined analysis of 13 European case-control studies (Darby et al. 2005, 2006), and a comparative assessment of the three combined analyses (HPA 2009). Pooling resulted in much larger numbers of lung cancer cases and controls than were achieved in individual case-control studies. The results of these analyses of pooled data provide evidence of increased risk for lung cancer with increasing residential levels of radon (Tables 3-3, 3-4, and 3-5) for cigarette smokers, including a statistically significant relative risk of lung cancer at mean radon concentrations ≥542 Bq/m^3 (14.65 pCi/L) reported by Darby et al. (2006) (Table 3-5). The HPA (2009) assessment identified flaws that resulted in the China and North American studies overestimating the radon cancer risk. According the HPA (2009), the European study properly assessed radon risk by using more accurate dosimetry and including more homes, and the resulting radon risk estimate paralleled that of the whole China and North American database. However, the China and North American studies selected only a portion of the database, limiting inclusion to those living in one or two homes with more complete dosimetry, but the manner in which homes were selected would have introduced socioeconomic bias, which in addition to lower dosimetry approach, caused the China and North American studies to overestimate the radon risk. Nevertheless, all three combined analyses support the conclusion that residential radon is carcinogenic. HPA (2009) estimated that the cumulative (absolute) radon-induced lung cancer risk to age 75 for long-term exposure to radon at 0, 100, 200, 400, and 800 Bq/m^3 (0, 2.7, 5.41, 10.81, and 21.62 pCi/L) is 15, 17, 19, 23, and 30%, respectively, for lifetime smokers, and 0.4, 0.5, 0.5, 0.7, and 0.9%, respectively, for lifetime nonsmokers. Overall, the risk for the lifetime nonsmokers was 25 times lower than for the lifetime smokers (Darby et al. 2006; HPA 2009). Figure 3-1 shows the cumulative absolute risk of death from lung cancer by age 75 years relative to long-term average in-home radon concentration for

Figure 3-1. Cumulative Absolute Risk of Death from Lung Cancer by Age 75 Years Versus Long-Term Average Radon Concentration at Home for Continuing Smokers, Ex-Smokers, and Lifelong Nonsmokers in the United Kingdom



Source: adapted from HPA 2009

continuing smokers, ex-smokers, and lifelong nonsmokers in the United Kingdom, as reported by Darby et al. (2006) and HPA (2009).

Assessment of the results of residential case-control studies and comparisons between the presently-available pooled results of the China case-control studies (Lubin et al. 2004), North American case-control studies (Krewski et al. 2005, 2006), and European case-control studies (Darby et al. 2005, 2006) must take into account the effects of exposure measurement error and methodological differences in final analyses. Estimates based on measured radon concentrations will likely underestimate the true risks associated with residential radon, due to misclassification of exposure from detector measurement error, spatial radon variations within a home, temporal radon variation, missing data from previously occupied homes that currently are inaccessible, failure to link radon concentrations with subject mobility, and measuring radon gas concentration as a surrogate for radon progeny exposure (Field et al. 1996, 2002). Generally, if exposure misclassification does not differ systematically between cases and controls, the observed results tend to be biased toward the null (for example, the true effect is actually underestimated). In fact, Field et al. (2002) demonstrated that empirical models with improved retrospective radon exposure estimates were more likely to detect an association between prolonged residential radon exposure and lung cancer. Direct comparisons between the pooled results of the China case-control studies (Lubin et al. 2004), North American case-control studies (Krewski et al. 2005, 2006), and those of the European case-control studies (Darby et al. 2005, 2006) are problematic because only the pooled results of the European case-control studies included regression calibration in an attempt to adjust for some of the measurement error.

Turner et al. (2011) recently reported the results of a large prospective study that found positive associations between ecological indicators of residential radon and lung cancer. The study included a cohort of 811,961 individuals from nearly 1.2 million participants recruited in 1982 for the American Cancer Society Cancer Prevention Study-II. The cohort encompasses 2,754 U.S. counties and 3,493 observed lung cancer deaths as of 1988. Ecological estimates of residential radon concentrations were obtained from the Lawrence Berkeley National Laboratory and were intended to represent the average annual radon concentrations in the main living areas of homes by primary county of residence. The study authors reported a significant positive trend between categories of radon concentrations and lung cancer mortality ($p=0.02$), a 15% (95% CI 1–31) increase in risk of lung cancer mortality per 100 Bq/m^3 (2.7 pCi/L) increase in radon, and a 34% (95% CI 7–68) increase in risk of lung cancer mortality among residents with estimated radon concentrations above the EPA guideline value of 148 Bq/m^3 (4 pCi/L).

Information regarding radon-induced lung cancer in animals exposed to radon and its progeny at concentrations considered relevant to human health includes significantly increased incidences of lung tumors in rats repeatedly exposed to radon and its progeny at cumulative exposures as low as 20–50 WLM (Chameaud et al. 1984; Morlier et al. 1994). These results are consistent with the demonstrated associations between lung cancer risk and exposure to radon and radon progeny in occupationally-exposed miners and residentially-exposed individuals.

3.2.2 Oral Exposure

No studies were located regarding the following health effects, other than cancer, in humans or animals after oral exposure to radon or its progeny:

3.2.2.1 Death

3.2.2.2 Systemic Effects

3.2.2.3 Immunological and Lymphoreticular Effects

3.2.2.4 Neurological Effects

3.2.2.5 Reproductive Effects

3.2.2.6 Developmental Effects

3.2.2.7 Cancer

Information regarding cancer in humans after exposure to radon and its progeny in water is limited to ecological studies. As noted earlier, ecological studies are limited by several factors that may include bias in estimated indoor radon levels, inadequate control of confounding, model misspecification, and misclassification. Radon levels were measured in 2,000 public and private wells in 14 counties in Maine (Hess et al. 1983). The county averages were compared to cancer rate by county to determine any degree of correlation. Significant correlation was reported for all lung cancer and all cancers combined, when both sexes were combined, and for lung tumors in females. Confounding factors (e.g., smoking) were not considered in this analysis. In addition, exposure from radon in these water supplies could have been by the inhalation route as well as the oral route. Results of some ecological studies suggest positive associations between radon levels in ground water sources and incidences of cancers, including lung cancer (Hess et al. 1983), all cancers combined (Mose et al. 1990), and childhood cancer (leukemias and all cancers combined) (Collman et al. 1990). In another study, Collman et al. (1988) found no consistent associations between radon concentrations in ground water and cancer mortality. More recent case-cohort

studies in Finland found no significant associations between mean concentrations of radon in well water and cases of stomach cancer (Auvinen et al. 2005) or bladder or kidney cancer (Kurttio et al. 2006).

No studies were located regarding cancer in animals after oral exposure to radon and its progeny.

3.2.3 Dermal Exposure

3.2.3.1 Death

3.2.3.2 Systemic Effects

No studies were located regarding respiratory, cardiovascular, gastrointestinal, musculoskeletal, hepatic, renal, endocrine, dermal, body weight, or metabolic effects in humans or animals following exposure to radon and radon progeny.

Ocular Effects. Abdelkawi et al. (2008) reported increased refractory index, increased molecular weight, and decreased concentration of soluble proteins in the cornea and lens of mice exposed to radon at a mean concentration of 55.8 kBq/m^3 for 6 hours/day, 5 days/week for up to 8 weeks. Effective radon lung doses ranged from 20.92 to 83.68 mSv for combined dermal contact and inhaled radioactivity. Corneal effects were observed after 2 weeks, followed by lenticular effects (after 6 weeks). The study authors suggested that the corneal effects resulted from direct radon exposure and plating out of radon progeny on the cornea; thus, effects on both the cornea and lens might be the result of combined external and internal exposures.

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

3.2.3.3 Immunological and Lymphoreticular Effects

3.2.3.4 Neurological Effects

3.2.3.5 Reproductive Effects

3.2.3.6 Developmental Effects

3.2.3.7 Cancer

A statistically significant increase in the incidence of basal cell skin cancers (103.8 observed vs. 13.0 expected) was observed in uranium miners in the Czech Republic who were exposed to radon and

radon progeny for >10 years (Ševcová et al. 1978). The study authors used the permissible concentration of radon progeny in the workplace air (41,000 MeV/L; approximately equal to 31.9 pCi/L) at the time of the study to calculate a skin contamination of 2.3±0.7 kBq/m^2 (6.22 pCi/cm^2), based on total alpha activity per unit area from the radon progeny, for an experimental group of the miners. Assuming 1,700 working hours per year and using a quality factor of 10 for alpha radiation, the study authors calculated a mean dose equivalent to the basal layer of the epidermis of 60 rem/year. The standard quality factor (now termed radiation weighting factor) for alpha particles is 20, which would yield an equivalent dose of 120 rem/year. Additionally, the study authors noted that during earlier times, concentrations of radon progeny in the uranium mines were up to 10 times higher than the permissible concentration in the late 1970s. Exposure to other agents (such as arsenic, a known dermal carcinogen (see Agency for Toxic Substances and Disease Registry [2007a])) in the uranium mining environment, as well as minor traumas of the skin, may also have contributed to the observed incidence of skin cancer. Increased incidences of skin cancer have not been reported in other uranium miner cohorts or for workers in other types of mining, such as metal or coal mines; these end points were not examined in most of these studies.

Eatough and coworkers performed a series of studies designed to estimate the average dose of alpha radiation from radon and radon progeny to the skin under normal environmental exposure conditions in which airborne particles containing radon and radon progeny make dermal contact (Eatough 1997; Eatough and Henshaw 1992; Eatough et al. 1999). In the study of Eatough et al. (1999), results of personnel monitoring of airborne radon progeny ^{218}Po and ^{214}Po in which individuals were immersed under normal environmental conditions in the United Kingdom indicated that at the average radon concentration of 20 Bq/m^3 (0.54 pCi/L) to continuously exposed skin would result in 3,500–28,000 decays/cm^2/year from ^{218}Po and 7,000–21,000 decays/cm^2/year from ^{214}Po. The results of Eatough and coworkers indicate a potential for radon and radon progeny to elicit skin cancer under normal environmental conditions. Few of the alpha particles from those decays would actually reach and expose the dermis since fewer than half would be released toward the body (reducing the values by more than 50%) and most of their energy would transfer to the nonliving epidermis, leaving little to expose the underlying dermis.

No studies were located regarding cancer in animals after dermal exposure to radon and its progeny.

3.3 GENOTOXICITY

Abundant information is available regarding the genotoxicity of ionizing radiation (refer to the Toxicological Profile for Ionizing Radiation for a detailed discussion of the genotoxic effects of various forms of ionizing radiation). The genotoxicity of alpha radiation from radon and its progeny has been investigated in underground miners, in individuals residing in homes with measured radon levels, in laboratory animals *in vivo*, and in a variety of *in vitro* test systems. Tables 3-6 and 3-7 present the results of *in vivo* and *in vitro* genotoxicity assessments, respectively.

Increases in chromosomal aberrations have been reported in peripheral blood lymphocytes of underground miners exposed to relatively high levels of radon and radon progeny (Bilban and Jakopin 2005; Brandom et al. 1978; Smerhovsky et al. 2001, 2002). Significantly increased frequency of micronuclei was also noted in peripheral blood lymphocytes of lead-zinc miners in the Czech Republic (Bilban and Jakopin 2005). Significantly increased frequency of mutations of glycophorin A was reported in the blood from a cohort of Radium Hill uranium miners in Australia (Shanahan et al. 1996). The mutation rate tended to increase with increasing radon exposure, with the exception of the most highly exposed group (>10 WLM); there was no clear relation between HPRT mutation rates and previous occupational exposure to radon.

Several studies investigated possible associations between residential exposure to radon and radon progeny and genotoxic end points. Significantly increased frequency of chromosomal aberrations was noted in peripheral blood lymphocytes of a small group of individuals in Germany who resided in homes where radon concentrations were 4–60 times higher than the national average of 50 Bq/m^2 (Bauchinger et al. 1994). The prevalence of DNA damage in peripheral blood lymphocytes was significantly associated with increased residential radon levels at airborne levels exceeding 200 Bq/m^3; no correlation was seen in comparisons of DNA damage to levels of radon in the drinking water for these same individuals, at levels drinking water ranging from 10 to 2,410 Bq/L (Hellman et al. 1999). Results of one small study of 20 individuals indicated a positive association between HPRT mutations in peripheral blood lymphocytes and measured radon levels (Bridges et al. 1991). However, a subsequent assessment by the same investigators using a larger number of exposed subjects (n=66) found no significant positive or negative association between HPRT mutation rates and indoor radon levels (Cole et al. 1996). Radon did not induce increased HPRT mutation rates in another study of a small group (n=11) of residentially-exposed subjects (Albering et al. 1992). No significant increase in the frequency of chromosomal aberrations was

Table 3-6. Genotoxicity of Radon and Radon Progeny *In Vivo*

Species (test system)	End point	Results	Reference
Mammalian systems:			
Human (peripheral blood lymphocytes)	Chromosomal aberrations	+	Bauchinger et al. 1994; Bilban and Jakopin 2005; Brandom et al. 1978; Hellman et al. 1999; Pohl-Rüling and Fischer 1979, 1982; Pohl-Rüling et al. 1976; Smerhovsky et al. 2001, 2002; Stenstrand et al. 1979
Human (peripheral blood lymphocytes)	Chromosomal aberrations	–	Maes et al. 1996
Human (peripheral blood lymphocytes)	Micronuclei	+	Bilban and Jakopin 2005
Human (peripheral blood lymphocytes)	Gene mutations (HPRT)	–	Shanahan et al. 1996
Human (peripheral blood lymphocytes)	Gene mutations (HPRT)	–	Cole et al. 1996
Human (peripheral blood lymphocytes)	Gene mutations (HPRT)	–	Albering et al. 1992
Human (whole blood)	Gene mutations (glycophorin A)	+	Shanahan et al. 1996
Human (lymphocytes)	DNA repair	+	Tuschl et al. 1980
Rat (tracheal epithelial cells)	Chromosomal aberrations	+	Brooks et al. 1992
Rabbit (somatic cells)	Chromosomal aberrations	–	Leonard et al. 1981
Mouse (bone marrow)	Chromosomal aberrations	+	Abo-Elmagd et al. 2008
Rat (alveolar macrophages)	Micronuclei	+	Taya et al. 1994
Rat (lung fibroblasts)	Micronuclei	+	Brooks et al. 1994; Khan et al. 1994, 1995
Syrian hamster (lung fibroblasts)	Micronuclei	+	Khan et al. 1995
Chinese hamster (lung fibroblasts)	Micronuclei	+	Khan et al. 1995
Mouse (red blood cells)	Micronuclei	+	Abo-Elmagd et al. 2008
Rat (bone marrow)	Sister chromatid exchanges	+	Poncy et al. 1980

– = negative result; + = positive result

Table 3-7. Genotoxicity of Radon and Radon Progeny *In Vitro*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
Mammalian cells:				
Human (blood lymphocytes)	Chromosomal aberrations	No data	+	Wolff et al. 1991
Human (blood lymphocytes)	Chromosomal aberrations	No data	+	Hamza and Mohankumar 2009
Human (fibroblasts)	Chromosomal aberrations	No data	+	Loucas and Geard 1994
Chinese hamster (ovary AA8 cells)	Chromosomal aberrations	No data	+	Schwartz et al. 1990
Chinese hamster (ovary EM9 cells)	Chromosomal aberrations	No data	+	Schwartz et al. 1990
Chinese hamster (ovary K-1 cells)	Chromosomal aberrations	No data	+	Shadley et al. 1991
Chinese hamster (ovary xrs-5 cells)	Chromosomal aberrations	No data	–	Shadley et al. 1991
Chinese hamster (ovary K-1 cells)	Gene mutations	No data	+	Shadley et al. 1991
Chinese hamster (ovary xrs-5 cells)	Gene mutations	No data	+	Shadley et al. 1991
Chinese hamster (ovary AA8 cells)	Gene mutations	No data	+	Schwartz et al. 1990
Chinese hamster (ovary EM9 cells)	Gene mutations	No data	+	Schwartz et al. 1990
Chinese hamster (ovary C18 cells)	Gene mutations	No data	+	Jostes et al. 1994
Mouse (L5178Y cells)	Gene mutations	No data	+	Evans et al. 1993a, 1993b

— = negative result; + = positive result

found in another small group (n=22) of subjects with residential exposure to radon at concentrations in the range of 50–800 Bq/m^3 (Maes et al. 1996).

Increases in chromosomal aberrations were reported among spa-house personnel and in area residents in Badgastein, Austria, who were chronically exposed to radon and radon decay products present in the environment (Pohl-Rüling and Fischer 1979, 1982; Pohl-Rüling et al. 1976). A study by Tuschl et al. (1980) indicated a stimulating effect of repeated low-dose *in vitro* ultraviolet or beta irradiation on DNA repair in lymphocytes of persons occupationally exposed to radon (3,000 pCi/L of air [$1.1x10^5$ Bq/m^3]). The study authors suggested that this "stimulating" effect of either type of radiation might be attributable to induction of de novo synthesis of repair enzymes. They noted that an error-free repair pathway for DNA involving de novo synthesis of proteins had been reported in *Escherichia coli*, and that miners exposed to radon in Badgastein (a community with elevated levels of background radiation) had fewer chromosomal aberrations than the public despite being exposed to more radiation.

An increase in chromosomal aberrations in lymphocytes was observed in 18 Finnish people of different ages chronically exposed to radon in household water at concentrations of $2.9x10^4$–$1.2x10^6$ pCi radon/L of water ($1.1x10^3$–$4.4x10^4$ Bq/L) compared with people who did not have a history of exposure to high radon levels (Stenstrand et al. 1979). This study also indicated that the frequencies of chromosomal aberrations and multiple chromosomal breaks were more common in older people than in younger people exposed to radon. Although the radon was in household water, it is probable that much of this radon volatilized and was available to be inhaled. Therefore, this route of exposure includes both oral and inhalation routes.

Available *in vivo* animal data generally support the human data. Significantly increased frequency of micronuclei was observed in lung fibroblasts of Wistar rats, Syrian hamsters, and Chinese hamsters that inhaled radon and radon progeny; cumulative exposures were 115–323 WLM for the rats, 126–278 WLM for the Syrian hamsters, and 496 WLM for the Chinese hamsters (Khan et al. 1994, 1995). The Chinese hamsters appeared to be 3 times more sensitive than rats. Significantly increased frequency of chromosomal aberrations was noted in tracheal epithelial cells of F-344/N rats that had inhaled radon and radon progeny at cumulative exposures of 900 or 1,000 WLM (Brooks et al. 1992). Abo-Elmagd et al. (2008) exposed Swiss albino mice to airborne radon from a pitchblende powder source for 5–25 weeks at concentrations resulting in accumulated radon doses in the range of 13.01–65.05 WLM and reported exposure-related increased structural chromosomal aberrations and decreased mitotic index in bone marrow cells and increased micronuclei in red blood cells. Brooks and coworkers (Brooks et al. 1994)

reported significantly increased frequency of micronuclei in lung fibroblasts of Wistar rats exposed to radon at levels resulting in cumulative exposures ranging from 115 to 320 WLM. Significantly increased frequency of alveolar macrophages with micronuclei was observed in rats exposed to radon and its progeny at levels designed to give cumulative exposures ranging from 120 to 990 WLM (Taya et al. 1994). Evidence of chromosomal aberrations was equivocal in two rabbit studies. Rabbits exposed to high natural background levels of radon (12 WLM) for over 28 months displayed an increased frequency of chromosomal aberrations (Leonard et al. 1981). However, when a similar study was conducted under controlled conditions (10.66 WLM), chromosomal aberrations were not found. According to the authors, the increased chromosomal aberrations in somatic cells of rabbits exposed to natural radiation were mainly due to the gamma radiation from sources other than radon. Exposure of Sprague-Dawley male rats to radon at cumulative doses as low as 100 WLM resulted in an increase in sister chromatid exchanges (SCEs) in bone marrow by 600 days postexposure (Poncy et al. 1980). At 750 days postexposure, the number of SCEs reached 3.21 per cell. The SCEs in the 500 and 3,000 WLM groups reached constant values of 3.61 and 4.13 SCEs per cell. In the high-dose group (6,000 WLM), SCEs continued to increase from 100 to 200 days after exposure, reaching a mean value of 3.5 SCE per cell. In controls, SCEs were constant with age (2.4 per cell).

The genotoxicity of radon and radon progeny has been assessed in a variety of mammalian cells *in vitro*. Chromosomal aberrations were reported in human blood lymphocytes (Hamza and Mohankumar 2009; Wolff et al. 1991) and human fibroblasts (Loucas and Geard 1994). Hamza and Mohankumar (2009) noted increasing frequency of chromosomal aberrations with increasing radon dose (range 0–0.127 Gy and dose rate (range 5.4×10^{-8}–7.08×10^{-4} Gy/min) for 3-hour exposures. Exposure of Chinese hamster ovary (CHO) cells to the radon daughter, bismuth-212 (^{212}Bi) caused chromosomal aberrations and gene mutations (Schwartz et al. 1990; Shadley et al. 1991). Gene mutations were induced by irradiation of CHO cells with radiation from radon (Jostes et al. 1994). Another study employed an isotope of helium (^{4}He) to simulate alpha particles from radon progeny and found exposure-induced gene mutations (Jin et al. 1995). Gene mutations were also induced in mouse L5178Y lymphoblasts exposed to alpha radiation from radon (Evans et al. 1993a, 1993b).

3.4 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 and is expressed in rad (grays). Estimation of this radiation dose to lung tissue or specific cells in the lung from a given exposure to radon and radon progeny is

accomplished by modeling the sequence of events involved in the inhalation, deposition, clearance, and decay of radon progeny within the lung. While based on the current understanding of lung morphometry and experimental toxicokinetics data on radon and radon progeny, 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 ICRP (1982), NEA/OECD (1983), NCRP (1984a), Bair (1985), James (1987), EPA (1988), and NAS (1988).

The focus of this section is on describing the empirical basis for our understanding of the toxicokinetics of radon. Physiologically-based models of radon toxicokinetics used in radon radiation dosimetry are described in Section 3.4.5. A complete discussion of toxicokinetics of radon as it relates to the development of adverse health effects in exposed populations (e.g., respiratory tract cancer) must consider not only the physical trapping of the attached fraction of radon progeny in the respiratory tract, but also the toxicokinetics of radon progeny, both of which contribute to the internal radiation dose that occurs in association with exposures to radon. While radioactive decay of the short-lived radon progeny, contribute most of the radiation dose to the respiratory tract following exposures to radon, they are sufficiently long-lived, relative to rates of toxicokinetics processes that govern transport and distribution, to exhibit radionuclide-specific toxicokinetics. Rather than providing a detailed review of the toxicokinetics of each element in the uranium and thorium decay chains leading to the production of radon and radon progeny elements (uranium, thorium, radium, astatine, polonium, bismuth, lead, and thallium) in this profile, the reader is referred to relevant literature on the toxicokinetics of the most widely-studied of these elements, including uranium (Agency for Toxic Substances and Disease Registry 2011; ICRP 1995a, 1995b); thorium (Agency for Toxic Substances and Disease Registry 1990b; ICRP 1995a, 1995b); radium (Agency for Toxic Substances and Disease Registry 1990a; ICRP 1992, 1995b); polonium (ICRP 1992, 1995b; NCRP 1980), lead (Agency for Toxic Substances and Disease Registry 2007b; ICRP 1992, 1995b), and thallium (Agency for Toxic Substances and Disease Registry 1992). The longer-term fate of radon progeny in the body will be reflected in the toxicokinetics of longer-lived progeny, which include ^{210}Pb (radioactive half-life of approximately 22.2 years) and ^{206}Pb (stable end product of the ^{222}Rn decay chain). The reader is referred to the Toxicological Profile for Lead (Agency for Toxic Substances and Disease Registry 2007b) for a discussion of the toxicokinetics of lead. A further complication in relating radon toxicokinetics to adverse health effects associated with exposure to radon is that radon progeny are present with radon in the environment and are inhaled or ingested along with radon. Progeny formed in the environment contribute substantially to radiation dose associated with environments that contain radon gas (Kendall and Smith 2002).

3.4.1 Absorption

3.4.1.1 Inhalation Exposure

Inhalation exposures to radon deliver the gas and its progeny (e.g., ^{214}Bi, ^{214}Pb, ^{210}Pb, ^{218}Po, and ^{210}Po; some attached to atmospheric particles and the rest unattached) into the respiratory tract (Marsh and Birchall 2000). Longer-lived radon progeny (e.g., ^{210}Pb and ^{210}Po) contribute little to the radiation dose to lung tissue because they have a greater likelihood of being physically cleared from the lung by mucociliary or cellular transport mechanisms before they can decay and deliver a significant radiation dose.

Progeny aerosol formation involves distinct physical-chemical processes (Butterweck et al. 2002; El-Hussein et al. 1998; Ishikawa et al. 2003b): (1) immediately after formation, progeny react with gases and vapors and form clusters, referred to as *unattached* particles, having diameters of approximately 0.5–3 nm or (2) unattached particles form complexes with other aerosols or particles in air to form *attached* particles, which can undergo hygroscopic growth to achieve diameters ranging from approximately 50 to 1,500 nm. The magnitude of the unattached fraction in inhaled air depends on the concentration and size distribution of aerosols in the ambient environment, and will vary with the exposure conditions (e.g., indoor, outdoor) and activities of the individual (e.g., sleeping, activities that release particulates into the air) (Marsh and Birchall 2000). The sizes and size distributions of attached particles in smoker homes and mines can be approximately the same, while the particle sizes are smaller in nonsmoker residences (HPA 2009). The unattached fraction for typical indoor environments has been estimated to be 5–20% (Porstendörfer 1994, 2001), while EPA assumes 50%. Smoking and other aerosol-generating activities (e.g., vacuum cleaning, cooking, fireplace and circulating fan usage) will increase the attached fraction, which correspondingly increases the dose (Sun 2008).

Deposition and the subsequent absorption of inhaled radon and radioactive decay progeny are influenced by physiological factors as well as chemical and physical characteristics of the radionuclides, carrier aerosols, and atmospheric particles. Radon is a nonreactive noble gas, and deposition and absorption will be determined by Brownian motion, its solubility in lung fluids, its permeability at the lung:circulating blood interface, and blood flow to the lungs. The blood:air partition coefficient for radon has been estimated to be approximately 0.4 (Nussbaum and Hursh 1957; Sharma et al. 1997); therefore, at steady-state, the blood concentration of radon will be approximately 0.4 times the concentration of radon in lung air. Assuming rapid (i.e., near-instantaneous) partitioning of radon between air and blood, the absorption clearance of radon gas from air in the lung will be governed by the blood flow to the lung (i.e., absorption

rate will be flow-limited). At a blood flow to the lung of 5.3 L/minute in an adult, and lung air volume of 2.82 L, the $t_{1/2}$ for absorption of radon from lung to blood would be approximately 0.4 min (rate constant=113 $hours^{-1}$) (Peterman and Perkins 1988). A similar value was estimated for the $t_{1/2}$ for clearance of radon gas from the lung air to external air ($t_{1/2}$=0.4 minute; rate constant=115 $hours^{-1}$) (Peterman and Perkins 1988). Rapid clearance of radon gas from the lung by absorption and exhalation will result in steady-state concentrations of radon in blood within 2–3 minutes of initiating exposure to radon gas. Clearance of radon from the blood following removal from exposure will be governed by blood flow rates to major tissue depots for radon (see Section 3.4.2).

Exposures to radon in air occur along with exposures to aerosols of radon progeny, which will deposit on the lung epithelia. The amounts and location of deposition of radon progeny will be determined by factors that influence convection, diffusion, sedimentation, and interception of particles in the airways. These factors include air flow velocities, which are affected by breathing rate and tidal volume; airway geometry; and aerosol particle size (Cohen 1996; James et al. 1994; Kinsara et al. 1995; Marsh and Birchall 2000; Yu et al. 2006). Radon progeny consist of a mixed distribution of unattached and attached particles. Assuming activity median aerodynamic diameters (AMAD) of approximately 1–3 nm for the unattached fraction and 100–200 nm for attached particles (Butterweck et al. 2002; Ishikawa et al. 2003b), deposition fractions of inhaled radon progeny can be estimated from models of particle deposition in the human respiratory tract (ICRP 1994b). The deposition fraction (i.e., percent of total number of inhaled particles that deposit) for unattached particles is predicted to be approximately 97–99%, with most of the deposition (70–80%) occurring in the extrathoracic region of the respiratory tract. The deposition fraction for attached particles is predicted to be approximately 20–40% with most of the deposition occurring in the alveolar region. Deposition will occur more predominantly in the nasal airways when breathing occurs through the nose. These predictions are based on the ICRP (1994b) human respiratory tract model assuming recommended values for deposition fractions for adult members of the general public exposed to homogeneous aerosols, and will vary with different assumptions for breathing rate and ratio of nose-to-mouth breathing (ICRP 2001). Predictions that deposition will be higher for the unattached fraction compared to the attached fraction and higher for nose-breathing exposures are in reasonable agreement with experiments conducted in humans exposed to heterogeneous distributions of aerosols of radon progeny (Booker et al. 1969; George and Breslin 1967, 1969; Holleman et al. 1969; Hursh and Mercer 1970; Hursh et al. 1969a; Ishikawa et al. 2003b; Pillai et al. 1994; Swift and Strong 1996) and with experiments conducted using casts of the human respiratory tract (Chamberlain and Dyson 1956; Cohen 1996; Kinsara et al. 1995; Martin and Jacobi 1972). The deposition fraction in subjects who inhaled (nose-only) 0.5–0.6-nm particles of ^{218}Po was estimated to be

approximately 94–99% (Swift and Strong 1996). Near complete deposition (>99%) was observed in an adult subject who inhaled (mouth-only) unattached particles of ^{212}Pb formed from decay of ^{220}Rn in a low ambient aerosol environment, whereas the deposition fraction was 34–60% when the exposure was to aerosols formed in room air and having a particle size range of 50–500 nm, more typical of attached particles (Booker et al. 1969). Deposition fractions for radon progeny have been measured during exposures to aerosols in underground uranium mines (George and Breslin 1969; Holleman et al. 1969). Deposition fractions increased with increasing tidal volume, and decreased with increasing aerosol aerodynamic diameter, from 50–70% for diameters <10 nm to 30–40% for diameters >70 nm. Hursh and Mercer (1970) estimated thoracic deposition (i.e., total of bronchi, bronchioles, and alveolar region) based on external gamma counting of the chest area of ^{212}Pb produced from decay of ^{220}Rn and inhaled (mouth-only) as aerosols having AMADs of 20–25 or 200–230 nm. The deposition fractions in adult subjects were approximately 50–62% for the smaller particles and 27–38% for the larger particles. When adult subjects inhaled (mouth-only) natural ^{212}Pb aerosols generated from ^{220}Rn decay in room air, the measured deposition fractions ranged from 14–45% (Hursh et al. 1969a). Pillai et al. (1994) made chest gamma measurements on four subjects who were exposed to ^{212}Pb aerosols for 10–60 minutes in a thorium hydroxide storage facility. The particle size of the ^{212}Pb aerosol was approximately 90 nm. Deposition fraction was estimated to have been 55–76%.

Particles containing radon progeny that deposit in the respiratory tract are subject to three general clearance processes: (1) mucociliary transport to the gastrointestinal tract for progeny deposited in the ciliated airways (i.e., trachea, bronchi, and bronchioles); (2) phagocytosis by lung macrophages and cellular transport to lymph nodes (e.g., lung, tracheobronchial, mediastinal); or (3) absorption and transfer by blood and/or lymph to other tissues. The above processes apply to all forms of deposited radon progeny, although the relative contributions of each pathway and rates associated with each pathway may vary with the physical characteristics (e.g., particle size), chemical form (degree of water solubility), and radiological characteristics (e.g., specific activity).

Absorption half-times ($t_{1/2}$) have been estimated for radon decay progeny in adults who inhaled aerosols of lead and bismuth isotopes generated from decay of ^{220}Rn or ^{222}Rn. Values for ^{212}Pb and ^{212}Bi in an aerosol having an activity median particle diameter of approximately 160 nm (range 50–500 nm), a value typical of attached radon progeny particles, were estimated to be approximately 10 and 13 hours, respectively (Marsh and Birchall 1999). The latter estimates were based on an analysis of data from human inhalation exposures to ^{212}Pb and ^{212}Bi progeny of ^{220}Rn (Booker et al. 1969; Hursh and Mercer 1970; Hursh et al. 1969a; Jacobi 1964; Pillai et al. 1994). However, absorption of unattached radon

progeny may be faster than that of attached progeny. Butterweck et al. (2002) exposed nose- or mouth-breathing human subjects to ^{222}Rn-derived aerosols that had diameters of approximately 0.3–3 nm, typical of unattached progeny particles. Absorption half-times were estimated to be approximately 68 minutes (range 56–86) for ^{218}Po/^{214}Pb and 18 minutes (range 17–21) for ^{214}Bi. Binding of unattached radon progeny in the respiratory tract may result in slower absorption kinetics. Butterweck et al. (2002) proposed that a 10-hour $t_{1/2}$ would apply to the unattached fraction after binding in the respiratory tract, and that the unbound fraction may have an absorption $t_{1/2}$<10 minutes. This behavior would be consistent with dissolution of deposited particles being the rate-limiting step in absorption and smaller particles dissolving faster than larger particles.

3.4.1.2 Oral Exposure

Exposure to radon by the oral route can occur as a result of radon gas dissolving in water. At equilibrium, the concentration of radon dissolved in water will be approximately 0.25 of that in air (i.e., Henry's law constant=4.08 at 20 °C) (NAS 1999b). Radioactive decay of radon in water produces radon progeny; therefore, ingestion of water containing dissolved radon will also result in ingestion of radon progeny. Absorption of radon is thought to occur primarily in the stomach and small intestine, although some absorption may also occur in the large intestine (Ishikawa et al. 2003a; Khursheed 2000; NAS 1999b). Radon is relatively nonreactive and its absorption from the stomach will be determined largely by rates of diffusion of radon from stomach contents to vascularized mucosa; its solubility in the stomach tissues and blood; blood flow to the stomach; and rates of transfer of stomach contents into the intestine (Ishikawa et al. 2003a; NAS 1999b). Diffusion of radon from stomach contents to stomach tissues may be rate-limiting in absorption (NAS 1999b). However, assuming rapid (i.e., near-instantaneous) partitioning of radon from vascularized mucosa to blood, the absorption clearance of radon from stomach mucosa will be governed by the blood flow rate to the stomach (i.e., absorption rate will be flow-limited). At a stomach blood flow of 1% of cardiac output (1% of 6.5 L/minute in an adult), and stomach wall volume of approximately 0.15 L (NAS 1999b), the $t_{1/2}$ for absorption of radon from the stomach wall to blood would be approximately 1.6 minutes (rate constant=0.43 minute^{-1}). An absorption $t_{1/2}$ of 1–2 minutes is consistent with observations of peak blood radon concentrations and peak radon concentrations in exhaled air within 5 minutes following ingestion of radon in water by adults (Brown and Hess 1992; Hursh et al. 1965; Sharma et al. 1997).

Kinetics of absorption of radon progeny are more complex, reflecting different mechanisms (e.g., membrane cation transport proteins and channels) and sites of absorption for radon and progeny.

Absorption of radon progeny following oral exposure is thought to occur largely in the small intestine (Agency for Toxic Substances and Disease Registry 2007b; ICRP 1994c). As a result, absorption of ingested progeny, and progeny formed from radon after ingestion, will be influenced by rates of transfer of stomach contents into the small intestine, as well as rates of absorption of progeny from the small intestine. Ishikawa et al. (2003a) used external gamma counting to measure the kinetics of elimination of ^{214}Pb and ^{214}Bi from the stomach following ingestion of water containing radon. Elimination kinetics from the stomach exhibited multiple components, with a fast phase (40–50% of ingested activity) having a $t_{1/2}$ value of approximately 10 minutes and two slower phases having $t_{1/2}$ values of 150 and 240 minutes. The presence of food in the stomach delays stomach emptying and may alter the absorption kinetics of radon and progeny (Brown and Hess 1992; Hursh et al. 1965; Suomela and Kahlos 1972). ICRP (1995c, 2001) recommends values of 0.05 and 0.1 as gastrointestinal absorption fractions for bismuth and polonium, respectively. The absorption fraction for ingested inorganic lead varies with age; from 40 to 50% in infants and children to approximately 8–15% in adults (Agency for Toxic Substances and Disease Registry 2007b; Leggett 1993; O'Flaherty 1993).

3.4.1.3 Dermal Exposure

Data regarding the absorption of radon following dermal exposure are very limited. Dermal absorption of radon has been measured in subjects after bathing in a radon-water spa (Furuno 1979; Pohl 1965) or after application of a radon-containing ointment to the intact skin (Lange and Evans 1947). After bathing for 5–15 minutes, radon concentrations in expired air reached approximately 0.9% of that in the water and ranged from 17.9 to 49.1 pCi/L of air (662–1,817 Bq/m^3) compared to pre-bath levels of <1 pCi/L of air (37 Bq/m^3). Radon concentrations in the water were reported by the authors as 5,800 pCi (215 Bq)/kg. However, the relative contributions of the dermal and inhalation routes of absorption cannot be determined in these studies (Furuno 1979). Radon concentrations in blood reached 0.85–1% of the radon concentration in the bath water, which was 1.8×10^5 pCi (4.9×10^6 Bq)/L of water after 30–40 minutes of bathing while breathing compressed air (Pohl 1965). Approximately 4.5% of the radon applied in ointment to intact skin was measured in expired air within 24 hours following application (Lange and Evans 1947).

Peterman and Perkins (1988) proposed a model for simulating the absorption of radon, based on a model largely parameterized to simulate absorption of xenon gas through the skin. Although parameter values for radon were not reported and skin penetration of radon was not modeled, the general structure is potentially relevant to estimating radon absorption rates. In the Peterman and Perkins (1988) model, the

rate-limiting step in dermal absorption was considered to be the diffusion of xenon through the skin to the subcutaneous fat. Transfer from subcutaneous fat to blood was assumed to be flow-limited and determined by blood flow to subcutaneous fat. Peterman and Perkins (1988) estimated the dermal diffusion rate of xenon to be approximately 0.18 $hour^{-1}$. This rate would be equivalent to a $t_{1/2}$ value of approximately 4 hours and is substantially slower than the $t_{1/2}$ for absorption from lung ($t_{1/2}$=0.4 minutes; rate constant=115 $hours^{-1}$) (Peterman and Perkins 1988). The corresponding $t_{1/2}$ value for absorption from subcutaneous fat was approximately 38 minutes (rate=0.018 $minute^{-1}$), assuming a blood flow of 0.16 L/minute and a tissue volume of 8.2 L.

3.4.2 Distribution

3.4.2.1 Inhalation Exposure

Based on studies conducted in animals, the distribution of absorbed radon appears to reflect its solubility in water and fat. Nussbaum and Hursh (1957) exposed rats to radon gas in an enclosed exposure chamber (whole body) for periods of 30 minutes to 48 hours and measured tissue radon levels at the conclusion of the exposure. The highest radon concentrations were observed in fat. Tissue:air concentration ratios were as follows (mean±standard error [SE]): omental fat 4.83±0.07, venous blood 0.405±0.016, brain 0.309±0.008, liver 0.306±0.004, kidney 0.285±0.012, heart 0.221±0.013, testis 0.184±0.007, and skeletal muscle 0.154±0.005. Tissue:air ratios for soft tissues reported by Nussbaum and Hursh (1957) are close to those expected for a Henry's law constant of 4 (i.e., water:air=0.25) and a lipid:air partition coefficient of 6 (Nussbaum and Hursh 1957). For example, assuming fat and water contents of soft tissue of 5 and 70%, respectively, in the rat (Davies and Morris 1993), the tissue:air ratio for soft tissue would be approximately 0.36 if solubility in water and fat were the only determinants of tissue radon levels. The corresponding fat:air ratio would be 5.85 for a lipid content of adipose tissue of 80% and water content of 15%. The tissue:air ratios reported in Nussbaum and Hursh (1957) are the bases of tissue:blood partition coefficients that have been used in various biokinetics models (e.g., Khursheed 2000; NAS 1999b; Peterman and Perkins 1988; Sharma et al. 1997).

Nussbaum and Hursh (1957) also reported information on the kinetics of uptake of inhaled radon in tissues. In all tissues studied, except fat, steady-state levels of radon were achieved within 1 hour of initiating a continuous inhalation exposure. Uptake into omental fat was slower and exhibited fast and slow components having $t_{1/2}$ values of 21 and 138 minutes, respectively. The slower uptake kinetics of fat may reflect, in part, the relatively slower blood perfusion of adipose tissue (per unit mass of tissue)

compared to other soft tissues. Similarly, relatively slow perfusion of fat should contribute a slower component to total body elimination kinetics following cessation of exposure to radon (see Section 3.4.3).

Information about the distribution of absorbed radon progeny, bismuth, lead, and polonium can be found in reviews of these subjects (Agency for Toxic Substances and Disease Registry 2007b; ICRP 1980, 1994c, 1995c). A relatively large fraction of inhaled ^{212}Pb (inhaled as natural ^{212}Pb aerosols generated from ^{220}Rn decay in room air) distributes to red blood cells (Booker et al. 1969; Hursh et al. 1969a). Red cell ^{212}Pb burdens, expressed as percent of the lead initially deposited in the respiratory tract, increased from approximately 5% within 1–2 hours following exposure to approximately 50% at times >24 hours following exposure (Hursh et al. 1969a). Long-lived (^{210}Pb) and stable progeny (^{206}Pb, ^{207}Pb, and ^{208}Pb), can be expected to deposit and be retained in bone, where approximately 90% of the total lead body burden resides (Agency for Toxic Substances and Disease Registry 2007b). Following chronic exposure in humans, ^{210}Pb has been found in bone (Black et al. 1968; Blanchard et al. 1969; Cohen et al. 1973; Fry et al. 1983) and teeth (Clemente et al. 1982, 1984). ICRP (1980, 2001) recommends, for the purpose of modeling bismuth-derived radiation doses, that 40% of absorbed bismuth distributes to kidneys and 30% to other tissues; the remaining 30% is assumed to be excreted rapidly and does not contribute to distribution beyond the central compartment. Retention in kidneys and other tissues are assumed to be the same (elimination $t_{1/2}$ values of 0.6 and 5 days for fast and slow phases); therefore, approximately 40% of the body burden of bismuth would be in the kidneys. ICRP (1994c, 2001) recommends the following values for percentages of absorbed polonium distributed to tissues: 30% liver, 10% kidney, 10% red marrow, 5% spleen, and 45% other tissues. Retention in all tissues is assumed to be the same (elimination $t_{1/2}$=50 days); therefore, the latter percent distributions will reflect the distribution of the body burden of polonium (e.g., 30% in liver).

3.4.2.2 Oral Exposure

Measurements of the tissue distribution of radon or progeny following ingestion of radon have not been reported. However, as discussed in Section 3.4.2.1, the distribution of absorbed radon appears to reflect its solubility in water and fat; therefore, steady-state distribution following absorption from the gastrointestinal tract would be determined by tissue:blood partition coefficients and the rate of approach to steady state would be determined by tissue blood flows. Based on tissue:air ratios reported by Nussbaum and Hursh (1957) during inhalation exposures of rats (see Section 3.4.2.1 for further discussion), the following tissue:blood ratios (i.e., tissue:blood=tissue:air/blood:air) can be estimated for

radon in the rat: omental fat 12, brain 0.76, liver 0.76, kidney 0.70, heart 0.55, testes 0.45, and skeletal muscle 0.38. Therefore, the highest concentrations of radon would be predicted for adipose tissues.

Distribution of absorbed radon progeny would be expected to be similar to the distribution following inhalation exposures, although, first-pass delivery to the liver from the gastrointestinal tract may influence the tissue distribution. As discussed in Section 3.4.2.1, the largest fractions of the body burdens for radon progeny would be expected to be found in bone for lead, kidney for bismuth, and liver for polonium (Agency for Toxic Substances and Disease Registry 2007b; ICRP 1980, 1994c, 2001).

3.4.2.3 Dermal Exposure

No studies were located regarding distribution in humans or laboratory animals after dermal exposure to radon or its progeny. However, as discussed in Sections 3.4.2.1 and 3.4.2.2, the distribution of absorbed radon appears to reflect its solubility in water and fat; therefore, steady-state distribution following absorption from the skin would be determined by tissue:blood partition coefficients and the rate of approach to steady state would be determined by tissue blood flows.

3.4.3 Metabolism

Radon is an inert noble gas that does not interact chemically with cellular macromolecules. Radon does not undergo metabolism in biological systems.

3.4.4 Elimination and Excretion

3.4.4.1 Inhalation Exposure

Measurements of exhaled radon following ingestion of radon dissolved in water indicate that absorbed radon is rapidly excreted in exhaled air (see Section 3.4.4.2). Inhaled ^{212}Pb is excreted in urine and feces. Hursh et al. (1969a) estimated that, following inhalation of natural ^{212}Pb aerosols generated from ^{220}Rn decay in room air, 3% of the amount initially deposited in the respiratory tract was excreted in urine per day and approximately 3%/day was excreted in feces. Longer-term kinetics of excretion of ^{210}Pb following chronic exposures to radon progeny may be contributed from slow release of ^{210}Pb accumulated in bone (Black et al. 1968). Additional information on the elimination of inhaled radon progeny can be found in reviews of the biokinetics of bismuth, lead, and polonium (Agency for Toxic Substances and Disease Registry 2007b; ICRP 1980, 1994c, 2001). ICRP (1995c, 2001) recommends the following values for the purpose of modeling bismuth-derived radiation doses: a urine:fecal excretion ratio of 1:1

and elimination $t_{1/2}$ values of 0.6 (60% of issue burden) and 5 days (40% of tissue burden) for fast and slow phases, respectively. ICRP (1995c, 2001) recommends the following values for elimination of polonium from tissues into urine and feces: a urine:fecal excretion ratio of 1:2 and an elimination $t_{1/2}$ value of 50 days.

3.4.4.2 Oral Exposure

Measurements of exhaled radon following ingestion of radon dissolved in water indicate that exhaled air is the dominant route of excretion of ingested radon (Brown and Hess 1992; Gosink et al. 1990; Hursh et al. 1965). Biological elimination kinetics of absorbed radon in exhaled air exhibit multiple phases, with the first half-time ranging from 15 to 80 minutes (Brown and Hess 1992; Gosink et al. 1990; Hursh et al. 1965). Hursh et al. (1965) estimated the following $t_{1/2}$ values for fast, moderate and slow phases of biological elimination: approximately 13 minutes (61% of body burden), 19 minutes (34%), and 207 minutes (5%), respectively; 95% of the dose was eliminated within 100 minutes. The slow phase of elimination is consistent with observations made in rats of relatively slow accumulation of radon in adipose tissue during continuous inhalation exposures to radon (Nussbaum and Hursh 1957). The latter $t_{1/2}$ values were estimated for subjects who ingested radon in water during fasting. In a subject who ingested radon in water with a meal, moderate and slow phases of elimination appeared to be delayed, with approximate $t_{1/2}$ values of 12 minutes (39% of body burden), 60 minutes (51%), and 300 minutes (10%), respectively. Slowing of elimination when radon is ingested with a meal or with lipid has been observed in several studies and may be related to a delay in stomach emptying that alters the absorption kinetics of radon and progeny (Brown and Hess 1992; Hursh et al. 1965; Meyer 1937; Suomela and Kahlos 1972; Vaternahm 1922).

Suomela and Kahlos (1972) estimated radon elimination kinetics in adults who ingested radon in water by monitoring external gamma-radiation from ^{214}Bi (i.e., assuming ^{214}Bi:^{222}Rn disequilibrium ratios ranging from 0.4 to 1). Biological elimination $t_{1/2}$ values ranged from 30 to 50 minutes; these are consistent with estimates based on exhaled radon as described above. Out of 10 subjects, ^{214}Bi was detected in urine in two subjects (0.4 and 1.8% of ingested ^{214}Bi dose; duration of urine collection was not reported). Additional information on the elimination of ingested radon progeny can be found in reviews of the biokinetics of bismuth, lead, and polonium (Agency for Toxic Substances and Disease Registry 2007b; ICRP 1980, 1994c, 2001). In general, the rates and routes of elimination of each progeny absorbed from the gastrointestinal and respiratory tracts are likely to be similar. Information on elimination of inhaled radon progeny is discussed in Section 3.4.4.1.

3.4.4.3 Dermal Exposure

Information on the excretion of radon and its progeny following dermal exposure is very limited. Within 24 hours, 4.5% of the radon, which was applied as a salve to intact human skin, was eliminated by exhalation, while 10% was exhaled after application of the radon to an open wound (Lange and Evans 1947). Bathers breathing compressed air while immersed in radon-containing water had exhaled approximately one-third of radon measured in blood immediately after bathing (Pohl 1965). By 6–8 minutes after bathing, these persons were exhaling one-half of the amounts exhaled immediately after bathing. The author stated that the remaining radon which distributed to fatty tissue was excreted more slowly.

3.4.4.4 Other Routes of Exposure

Experiments in animals have reported the retention of radon after exposure by the intraperitoneal and intravenous routes. Following intravenous administration, 1.6–5.0% of the administered activity was retained in the animals after 120 minutes (Hollcroft and Lorenz 1949). Retention was greatest at 120 minutes following intraperitoneal administration, but by 240 minutes, it was nearly the same for both routes of administration. These authors also reported that the amount of radon retained in tissues was greater in obese mice than in normal mice, especially after intraperitoneal administration (Hollcroft and Lorenz 1949). Radon retention has also been studied in dogs following intravenous administration of ^{226}Ra. The amount of radon in bone was found to increase with increasing time after injection (Mays et al. 1975).

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

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

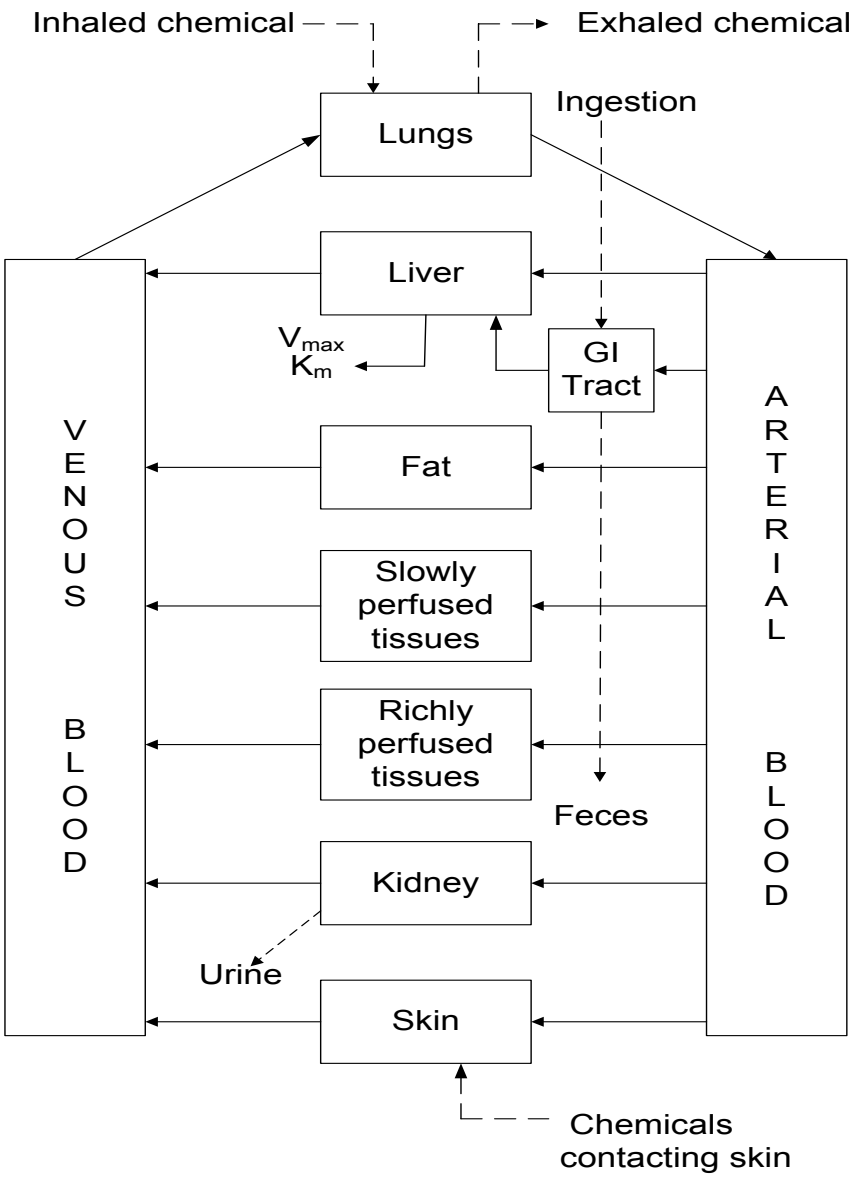
PBPK/PD models refine our understanding of complex quantitative dose behaviors by helping to delineate and characterize the relationships between: (1) the external/exposure concentration and target tissue dose of the toxic moiety, and (2) the target tissue dose and observed responses (Andersen and Krishnan 1994; Andersen et al. 1987). These models are biologically and mechanistically based and can be used to extrapolate the pharmacokinetic behavior of chemical substances from high to low dose, from route to route, between species, and between subpopulations within a species. The biological basis of PBPK models results in more meaningful extrapolations than those generated with the more conventional use of uncertainty factors.

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

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

PBPK models improve the pharmacokinetic extrapolations used in risk assessments that identify the maximal (i.e., the safe) levels for human exposure to chemical substances (Andersen and Krishnan 1994). PBPK models provide a scientifically sound means to predict the target tissue dose of chemicals in humans who are exposed to environmental levels (for example, levels that might occur at hazardous waste sites) based on the results of studies where doses were higher or were administered in different species. Figure 3-2 shows a conceptualized representation of a PBPK model.

Figure 3-2. Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a Hypothetical Chemical Substance



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

Source: adapted from Krishnan and Andersen 1994

PBPK models for radon are discussed in this section in terms of their use in risk assessment, tissue dosimetry, and dose, route, and species extrapolations. For radionuclides, the PBPK model depicted in Figure 3-2 is replaced with a set of physiologically based biokinetic (PBBK) models for inhalation, ingestion, and submersion. These were developed to accomplish virtually the same end as the PBPK models above, while integrating additional parameters (for radioactive decay, particle and photon transport, and compound-specific factors). Goals are to facilitate interpreting chest monitoring and bioassay data, assessing risk, and calculating radiation doses to a variety of tissues throughout the body. The standard for these models has been set by the ICRP, and their models receive international support and acceptance. ICRP periodically considers newer science in a type of weight of evidence approach toward improving the state of knowledge and reducing uncertainties associated with applying the model to any given radionuclide. ICRP publications also allow for the use of situation- and individual-specific data to reduce the overall uncertainty in the results. Even though there may be conflicting data for some parameters, such as absorption factors, one can use conservative values and still reach conclusions on whether the dose is below recommended limits. One of the strengths of the ICRP model is that it permits the use of experimentally determined material-specific absorption parameter values rather than requiring the use of those provided for default types. If the material of interest does not include absorption parameter values that correspond to those in the model (e.g., Type F, M, or S), the difference can have a profound effect on the assessment of intake and dose from bioassay measurements. This has been discussed in National Radiological Protection Board (NRPB) published reports on uranium (NRPB 2002).

The ICRP (1994b, 1996a) developed a Human Respiratory Tract Model for Radiological Protection, which contains respiratory tract deposition and clearance compartmental models for inhalation exposure that may be applied to particulate aerosols and gases. The National Council on Radiation Protection and Measurements (NCRP) has also developed a respiratory tract model for inhaled radionuclides (NCRP 1997). At this time, the NCRP recommends the use of the ICRP model for calculating exposures for radiation workers and the general public. Readers interested in this topic are referred to NCRP Report No. 125; Deposition, Retention and Dosimetry of Inhaled Radioactive Substances (NCRP 1997).

Models to estimate radiation doses from inhalation exposures to radon account for the deposition and clearance of radon gas as well as aerosols of radon progeny (Yu et al. 2006). Several radiation dose models for inhaled and/or ingested radon gas and progeny in humans have been reported (Birchall and James 1994; Crawford-Brown 1989; El-Hussein et al. 1998; Harley and Robbins 1994; Ishikawa et al. 2003a, 2003b; James et al. 2004; Khursheed 2000; Marsh and Birchall 2000; NAS 1999b; Peterman and Perkins 1988; Porstendörfer, 2001; Sharma et al. 1997). Some of these are extensions or modifications of

the ICRP (1994b) model that simulates deposition, clearance, and absorption of inhaled gaseous and particulate radionuclides in the human respiratory tract. An example of the latter is the Radon Dose Evaluation Program (RADEP), which has been used extensively in risk assessment of exposures to radon and radon progeny (Birchall and James 1994; Marsh and Birchall 2000). Two other extensions of the ICRP (1994b) model that have been widely applied to radon radiation risk assessment are those of Porstendörfer (2001) and James et al. (2004), which implement different approaches to the simulation of attached and unattached particles (e.g., fractional distributions in inhaled air and hygroscopic growth) and/or effective radiation dose calculations (e.g., tissue weighting factors for radon progeny in respiratory tract tissues). The structure of the biokinetics portion of the generic ICRP human respiratory tract model is described below, along with modifications that have been reported for applications to radon (e.g., RADEP). Systemic distribution and excretion of radon progeny are simulated with models specific for the progeny radionuclides. Descriptions of ICRP models for bismuth, lead, and polonium are reported elsewhere (Agency for Toxic Substances and Disease Registry 2007b; ICRP 1979, 1994c, 1995c; Leggett 1993).

Most physiologically based models of radon biokinetics simulate radon transfers between tissues and blood as flow-limited processes in which clearance is determined by tissue blood flow and tissue concentrations are defined by tissue:blood partition coefficients (Crawford-Brown 1989; Harley and Robbins 1994; Khursheed 2000; NAS 1999b; Peterman and Perkins 1988; Sharma et al. 1997). The model proposed by Peterman and Perkins (1988) was actually developed to simulate noble gases (e.g., xenon); however, it has been applied to radon biokinetics (Peterman and Perkins 1988; Sharma et al. 1997). A unique feature of the model is that it included parameters for simulating absorption of xenon gas through the skin, although parameter values for radon were not reported and skin penetration of radon was not modeled (see Section 3.4.1.3 for discussion of possible implications of this model for dermal absorption of radon). The NAS (1999b) and Khursheed (2000) models are described below as examples of flow-limited models that simulate absorption, distribution, and excretion of inhaled or ingested radon gas. Both were developed to be used in conjunction with ICRP models of progeny to simulate radiation doses from inhalation or ingestion of radon gas in drinking water.

Human Respiratory Tract Model for Radiological Protection (ICRP 1994b)

Deposition. The ICRP (1994b) has developed a deposition model for behavior of aerosols and vapors in the respiratory tract. It was developed to estimate the fractions of radioactivity in breathing air that are deposited in each anatomical region of the respiratory tract. ICRP (1994b) provides information used in

calculating effective doses of radiation to organs and tissues throughout the body based on a unit intake of radioactive material. The model applies to three levels of particle solubility, a wide range of particle sizes (approximately 0.0005–100 μm in diameter), and parameter values that can be adjusted for various segments of the population (e.g., sex, age, and level of physical exertion). This model also allows one to evaluate the bounds of uncertainty in deposition estimates. Uncertainties arise from natural biological variability among individuals and the need to interpret some experimental evidence that remains inconclusive. The model has been used for estimating radiation doses from inhalation of radon gas and aerosols of radon progeny; however, it was developed to be applied to a wide variety of radionuclides and their chemical and physical forms.

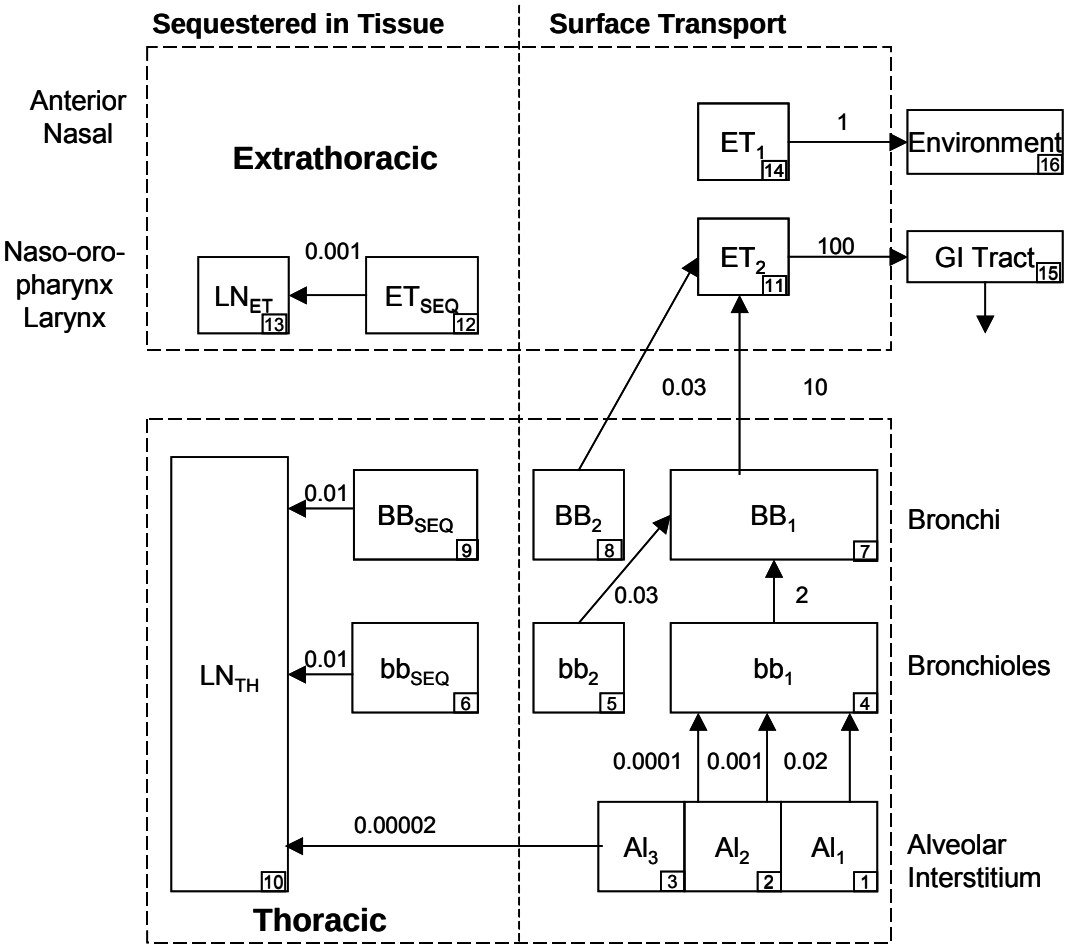
The ICRP deposition model estimates the fraction of inhaled material initially retained in each compartment (see Figure 3-3). The model was developed with five compartments: (1) the anterior nasal passages (ET_1); (2) all other extrathoracic airways (ET_2) (posterior nasal passages, the naso- and oropharynx,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

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

Deposition of inhaled gases and vapors is modeled as a partitioning process that depends on the physiological parameters noted above as well as the solubility and reactivity of a compound in the respiratory tract (see Figure 3-4). The ICRP (1994b) model defines three categories of solubility and reactivity: SR-0, SR-1, and SR-2:

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

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



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

Source: ICRP 1994b

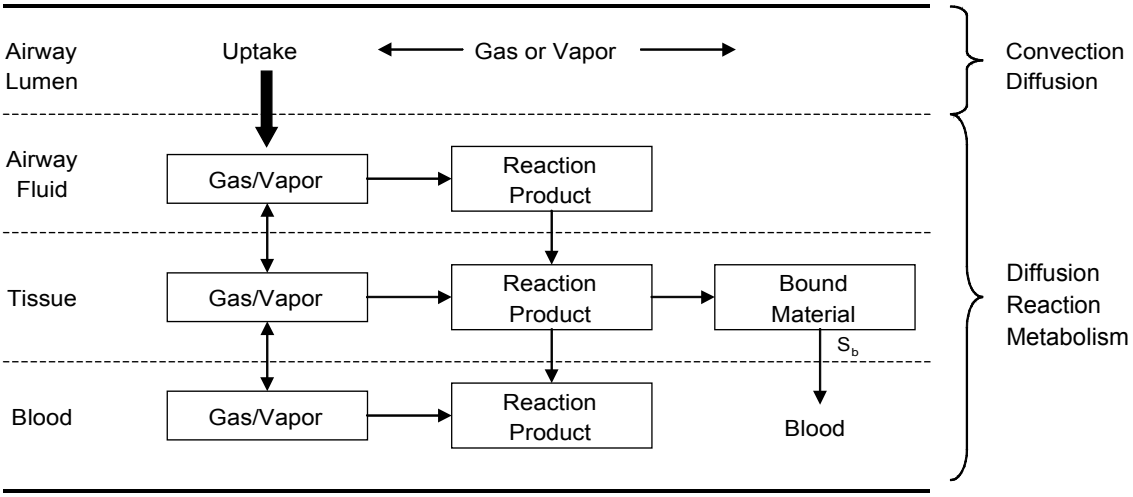
Table 3-8. Reference Respiratory Values for a General Caucasian Population at Different Levels of Activity

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

B = ventilation rate; f_R = respiration frequency; NA = not applicable; V_T = tidal volume

Source: See Annex B (ICRP 1994b) for data from which these reference values were derived.

Figure 3-4. Reaction of Gases or Vapors at Various Levels of the Gas-Blood Interface



Source: ICRP 1994b

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

- Type SR-2 compounds include soluble and reactive gases and vapors which are completely retained in the extrathoracic regions of the respiratory tract. SR-2 compounds include sulfur dioxide (SO_2) and hydrogen fluoride (HF).

Radon gas is categorized by ICRP (1994b) as SR-1, because, even though it has a low reactivity, it is sufficiently soluble to be taken up in the alveolar region where it can be absorbed into blood. ICRP (1994b) recommended default values for regional distribution of inhaled gases (except for those having low solubility) as follows: 10% ET_1, 20% ET_2, 10% BB, 20% bb, and 40% AI. Radon progeny, such as ^{218}Po, ^{214}Pb, and ^{214}Bi are sufficiently reactive to attach to aerosols in the respiratory tract (and external air) and deposit in the respiratory tract according to factors that determine particulate deposition (e.g., sedimentation, inertial impaction, diffusion, and interception). Radon progeny are represented in the ICRP (1994b) model and in extensions of the model (e.g., RADEP) as a mixed distribution of unattached particles (i.e., products of the initial reactions between progeny with gases and vapors) and attached particles (i.e., products of hygroscopic growth of complexes between unattached particles and aerosols in air). AMADs for the two fractions are typically represented in the ICRP model as 1 nm for unattached particles and 200 nm for attached particles (Butterweck et al. 2002; Ishikawa et al. 2003b), although the use of more complex mixed distributions for attached particles has also been used (Marsh and Birchall 2000; Porstendörfer 1994, 2001).

The magnitude of the unattached fraction in inhaled air depends on the concentration and size distribution of aerosols in the ambient environment, and will vary with the exposure conditions (e.g., indoor, outdoor) and activities of the individual (e.g., sleeping, activities that release particulates into the air such as smoking) (Marsh and Birchall 2000). The unattached fraction for typical indoor environments has been estimated to be 5–20% (Porstendörfer 1994, 2001). NRC (1991) recommended a default value of 3% for modeling exposures in homes where smoking occurs and 5% for exposures during cooking or vacuum cleaning activities. The Commission of European Communities recommended a default value of 8% (Monchaux et al. 1999).

Respiratory Tract Clearance. This portion of the model identifies the principal clearance pathways within the respiratory tract. The model was developed to predict the retention of various radioactive materials. The compartmental model represents particle deposition and time-dependent particle transport in the respiratory tract (see Figure 3-3) with reference values presented in Table 3-9. This table provides

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

Part A

Clearance rates for insoluble particles				
Pathway	From	To	Rate (d^{-1})	Half-life[a]
$m_{1,4}$	AI_1	bb_1	0.02	35 days
$m_{2,4}$	AI_2	bb_1	0.001	700 days
$m_{3,4}$	AI_3	bb_1	$1x10^{-4}$	7,000 days
$m_{3,10}$	AI_3	LN_{TH}	$2x10^{-5}$	No data
$m_{4,7}$	bb_1	BB_1	2	8 hours
$m_{5,7}$	bb_2	BB_1	0.03	23 days
$m_{6,10}$	bb_{seq}	LN_{TH}	0.01	70 days
$m_{7,11}$	BB_1	ET_2	10	100 minutes
$m_{8,11}$	BB_2	ET_2	0.03	23 days
$m_{9,10}$	BB_{seq}	LN_{TH}	0.01	70 days
$m_{11,15}$	ET_2	GI tract	100	10 minutes
$m_{12,13}$	ET_{seq}	LN_{ET}	0.001	700 days
$m_{14,16}$	ET_1	Environment	1	17 hours

See next page for Part B

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

Part B

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

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

$$f_s = 0.5 \text{ for } d_{ae} \le 2.5\sqrt{\rho/\chi}\ \mu m \text{ and}$$

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

where

f_s = fraction subject to slow clearance
d_{ae} = aerodynamic particle diameter/(μm)
ρ = particle density (g/cm^3)
χ = particle shape factor

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

Source: ICRP 1994b

clearance rates, expressed as a fraction per day and also as half-time (Part A), and deposition fractions (Part B) for each compartment for insoluble particles. ICRP (1994b) also developed modifying factors for some of the parameters, such as age, smoking, and disease status. Parameters of the clearance model are based on human evidence for the most part, although particle retention in airway walls is based on experimental data from animal experiments.

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

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

Ciliary action removes deposited particles from both the bronchi and bronchioles. Though it is generally thought that mucociliary action rapidly transports most particles deposited here toward the pharynx, a fraction of these particles is cleared more slowly. Evidence for this is found in human studies. For humans, retention of particles deposited in the lungs (BB and bb) is apparently biphasic. The “slow” action of the cilia may remove as much as half of the bronchi- and bronchiole-deposited particles. In human bronchi and bronchiole regions, mucus moves more slowly when it is closer to the alveoli. For the faster compartment, it has been estimated that it takes about 2 days for particles to travel from the bronchioles to the bronchi and 10 days from the bronchi to the pharynx. The second (slower) compartment is assumed to have approximately equal fractions deposited between BB_2 and bb_2, with both fractions having clearance half-times estimated at 20 days. Particle size is a primary determinant of the

fraction deposited in this slow thoracic compartment. A small fraction of particles deposited in the BB and bb regions is retained in the airway wall for even longer periods (BB_{seq} and bb_{seq}).

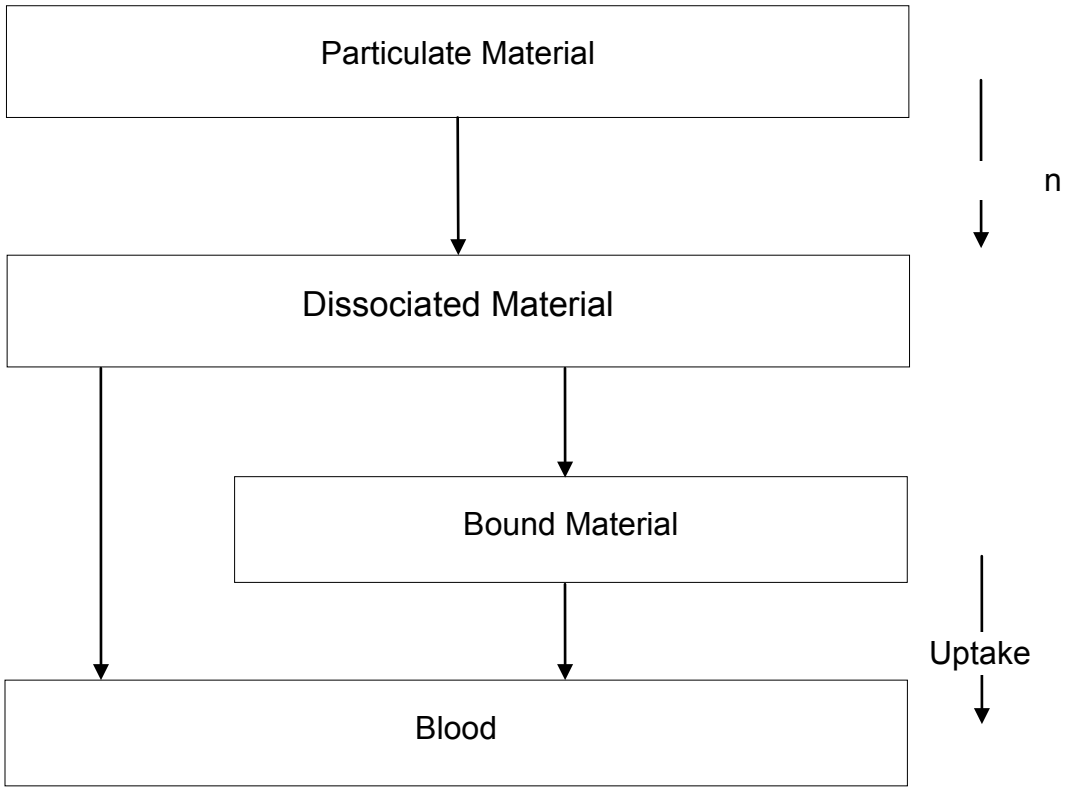
If particles reach and become deposited in the alveoli, they tend to become imbedded in the fluid on the alveolar surface or move into the lymph nodes. Coughing is the one mechanism by which particles are physically resuspended and removed from the AI region. For modeling purposes, the AI region is divided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

In the alveolar-interstitial region, human lung clearance has been measured. The ICRP model uses 2 half-times to represent clearance: about 30% of the particles have a 30-day half-time, and the remaining 70% are assigned a half-time of several hundred days. Over time, AI particle transport falls, and some compounds have been found in lungs 10–50 years after exposure.

Absorption into Blood. The ICRP model assumes that absorption into blood occurs at equivalent rates in all parts of the respiratory tract, except in the anterior nasal passages (ET_1), where no absorption occurs. It is essentially a 2-stage process, as shown in Figure 3-5. First, there is a dissociation (dissolution) of particles; then the dissolved molecules or ions diffuse across capillary walls and are taken up by the blood. Immediately following dissolution, rapid absorption is observed. For some elements, rapid absorption does not occur because of binding to respiratory-tract components. In the absence of specific data for specific compounds, the model uses the following default absorption rate values for those specific compounds that are classified as Types F (fast), M (medium), S (slow), and V (instantaneous):

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

Figure 3-5. The Human Respiratory Tract Model: Absorption into Blood

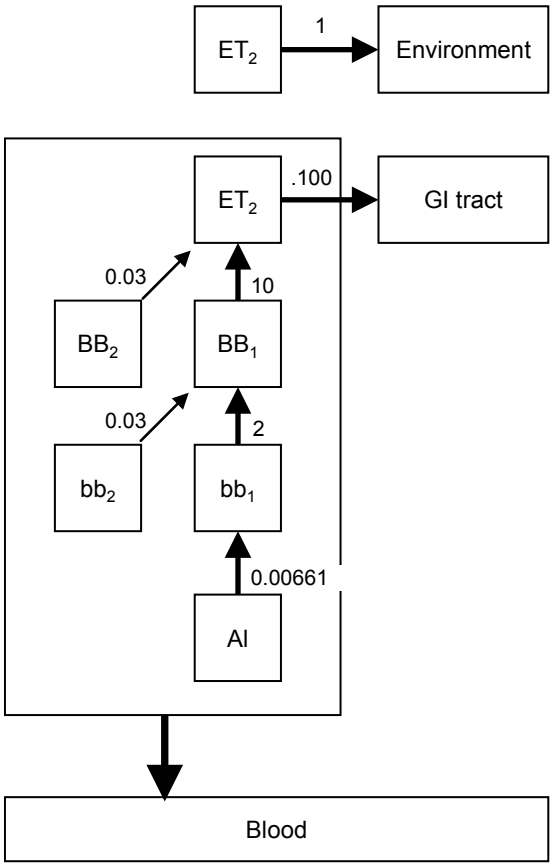


Source: ICRP 1994b

ICRP (1994b) assigned gases and vapors to Type F, unless alternative values for absorption rates are available. However, alternatives to this assumption have been explored, including instantaneous partitioning of radon gas into dissolved blood (Butterweck et al. 2002). Radiation doses from exposures to radon have been estimated assuming radon and its progeny behave as Type F or Type M (Kendall and Smith 2002). The difference between the two categories is important for estimating tissue specific radiation dose coefficients (e.g., Sv/Bq inhaled) because of the relatively fast decay of radon ($t_{1/2}$=3.8 days) and its short-lived progeny (e.g., ^{218}Po, $t_{1/2}$=3.05 minutes; ^{214}Pb, $t_{1/2}$=26.8 minutes; ^{214}Bi, $t_{1/2}$=19.7 minutes). Type F materials (absorption $t_{1/2}$=10 minutes) will have a smaller proportion of progeny formed in the respiratory tract (i.e., prior to clearance) and, as a result, will deliver a smaller internal radiation dose and smaller dose to the respiratory tract relative to systemic tissues. Type M materials (absorption $t_{1/2}$=100 days for 90% of deposited material, $t_{1/2}$=10 minutes for 10%) will have a larger portion of progeny formed in the respiratory tract, which will deliver a larger internal radiation dose and larger dose to the respiratory tract relative to systemic tissues (Kendall and Smith 2002). Absorption $t_{1/2}$ values for ^{212}Pb and ^{212}Bi, in an aerosol having an activity median particle diameter of approximately 160 nm (range 50–500 nm), a value typical of attached radon progeny particles, were estimated to be approximately 10 and 13 hours, respectively (Marsh and Birchall 1999). Use of a $t_{1/2}$ value of 10 hours for radon progeny in the ICRP (1994b) model results in predicted radiation dose coefficients that are similar in magnitude to the Type M assumption (Kendall and Smith 2002). However, absorption of unattached radon progeny may be faster than that of attached particles. Absorption half-times for aerosols having approximately 0.3–3 nm in diameter, typical of unattached progeny particles, were estimated to be approximately 68 minutes (range 56–86) for ^{218}Po and ^{214}Pb and 18 minutes (range 17–21) for ^{214}Bi (Butterweck et al. 2002). Butterweck et al. (2002) proposed that binding of unattached radon progeny in the respiratory tract may result in slower absorption kinetics. They proposed that a 10-hour $t_{1/2}$ would apply to the unattached fraction after binding in the respiratory tract and that the unbound fraction may have an absorption $t_{1/2}$<10 minutes (see Section 3.4.1.1 for further discussion of absorption estimates).

The Radon Dose Evaluation Program (RADEP) implements a simplified version of the ICRP (1994b) model and is designed to simulate radon and radon progeny radiation dosimetry (Marsh and Birchall 2000; Figure 3-6): (1) the alveolar interstitial compartment is represented as a single compartment that has a particle transport rate of 0.00661 d^{-1} to the fast bronchiolar compartment, bb_1; (2) sequestered compartments, ET_{seq}, BB_{seq}, and bb_{seq} are not considered; (3) radon progeny are assumed to not bind to the respiratory tract; and (4) hygroscopic growth of unattached particles is simulated.

Figure 3-6. Simplified Version of the Human Respiratory Tract Model (HRTM)



Source: Marsh and Birchall 2000

Validation of the Model. ICRP (1994b) and RADEP have been evaluated with data on deposition and clearance of inhaled particulate aerosol and gases in humans and absorption of radon progeny (ICRP 1994b; Ishikawa et al. 2003b; Marsh and Birchall 1999). Sensitivity and uncertainty analyses of model predictions have been reported (Marsh and Birchall 2000; Yu et al. 2006).

Risk Assessment. The model has been used to establish the radiation dose (Sv) per unit of inhaled radon (Bq) for ages 3 months to 70 years (Kendall and Smith 2002).

Target Tissues. The model is designed to calculate radiation dose coefficients (Sv/Bq) corresponding to specific inhalation exposures to radionuclides. Dose coefficients for radon and progeny have been estimated for all major organs, including the bone surfaces, bone marrow, and liver, and other tissues (Kendall and Smith 2002).

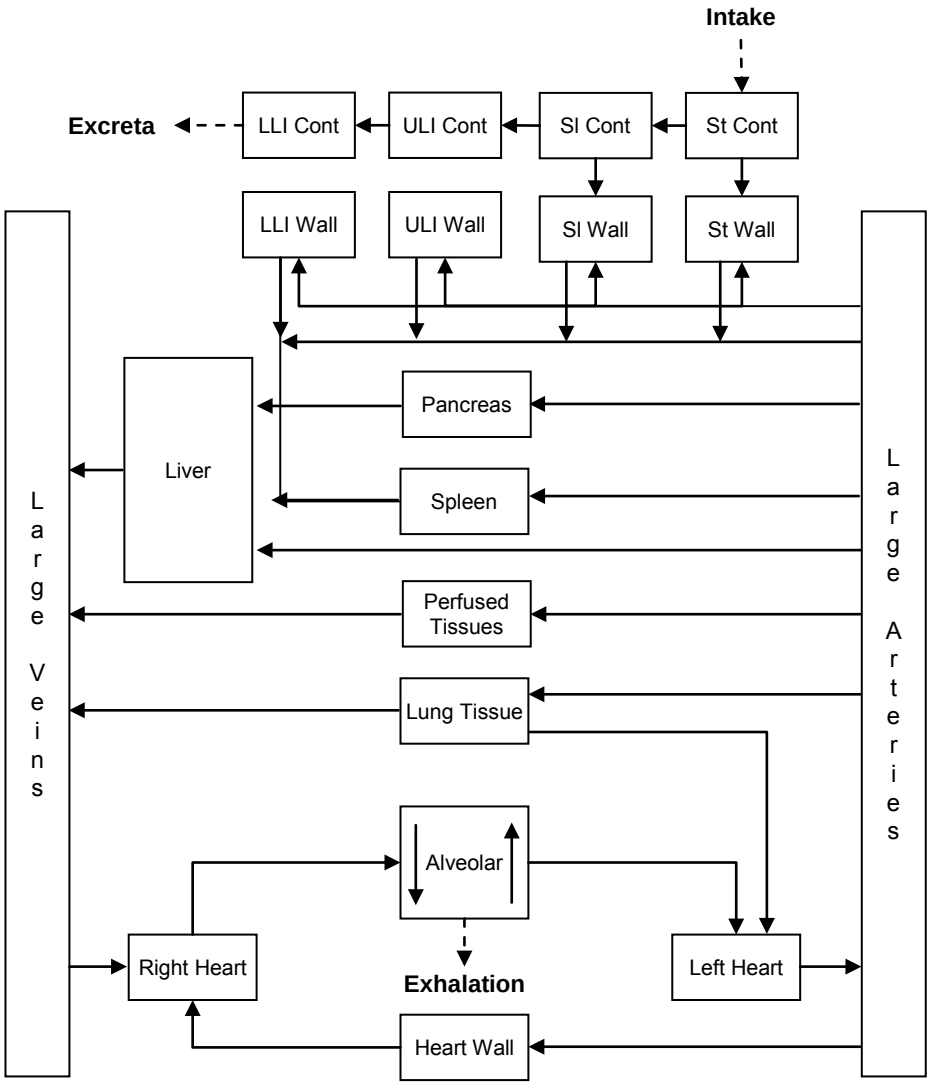
Species Extrapolation. The model is based on both human and animal data. However, it is intended for applications to human dosimetry. Applications to other species would require consideration of species-specific adjustments in modal parameters.

Interroute Extrapolation. The ICRP model is designed to simulate kinetics of inhaled radionuclides. (Note: ICRP/NCRP models are for normal lungs, not those of smokers.)

National Research Council Radon PBPK Model (NAS 1999b)

NAS (1999b) developed a PBPK model for simulating absorption and distribution of ingested or inhaled radioactive materials, including radon gas (Figure 3-7). NAS noted that statistically significant excesses of mortality from leukemia; esophagus, stomach, colon, liver, lung, breast, ovary, and urinary tract cancers; and multiple myeloma had been associated with atomic bomb survivors, but other epidemiological studies were used to establish risk models for thyroid and breast (based mainly on medical exposure data), bone (from radium exposures), and liver (from thoratrast) cancers, along with laboratory animal study data. The NAS cancer risk estimates were based on calculations with specific cancer site risk projection models using the computational method described in Federal Guidance Report No. 13 (EPA 1999a). The model simulates absorption of inhaled radon and distribution to tissues as flow-limited processes (i.e., tissue clearance equivalent to tissue blood flow) with parameters for tissue volumes, blood flow, and blood:tissue partition coefficients. Absorption of radon gas from the stomach and small intestine is simulated as diffusion-limited transfer from the lumen to the wall (i.e., vascularized

Figure 3-7. Schematic Diagram of the NAS (1999b) PBPK Model Developed to Describe the Fate of Radon within Systemic Tissues



Source: NAS 1999b

submucosa), and flow-limited exchange between blood and wall. A separate model is described in NAS (1999b) for estimating wall diffusion rate constants, which predicts a time-integrated radon concentration in the stomach wall of approximately 30% of that of the lumen. Parameter values for adults are presented in Table 3-10. Values for blood flows were derived from Leggett and Williams (1991, 1995); volumes and densities from ICRP (1990); and tissue:blood partition coefficients from Nussbaum and Hursh (1957). Parameter values for infants, children, and adolescents are also presented in NAS (1999b).

Validation of the Model. The NRC model has been evaluated with data on deposition and clearance of inhaled particulate aerosols and gases in humans and absorption of radon progeny (Correia et al. 1988; Crawford-Brown 1989; Harley and Robbins 1994; Harley et al. 1994; Hursh et al. 1965; NAS 1999b).

Risk Assessment. The model has been used to establish the radiation dose (Sv) per unit of inhaled or ingested radon (Bq) for ages 3 months to 70 years (NAS 1999b).

Target Tissues. The model is designed to calculate radiation dose coefficients (Sv/Bq) corresponding to inhalation or ingestion exposures to radon. Dose coefficients for radon and progeny have been estimated for all major organs, including the bone surfaces, bone marrow, and liver, and other tissues (NAS 1999b).

Species Extrapolation. The model is based on both human and animal data. However, it is intended for applications to human dosimetry. Applications to other species would require consideration of species-specific adjustments in modal parameters.

Interroute Extrapolation. The model is designed to simulate kinetics of inhaled or ingested radon. Extrapolation to other routes of external exposure would require modifications of the model to simulate absorption from those routes.

Khursheed (2000) Model

Khursheed (2000) developed a PBPK model for simulating absorption and distribution of ingested or inhaled radon gas (Figure 3-8). The model is similar in structure to the NRC (NAS 1999b) model, with the addition of a tissue compartment representing breast. The model has not had widespread use in risk assessment, relative to that of ICRP (1994b), RADEP, or the NRC (NAS 1999b) models. Absorption of inhaled and ingested radon, and distribution to tissues, are simulated as flow-limited processes (i.e., tissue clearance equivalent to tissue blood flow) with parameters for tissue volumes, blood flow, and

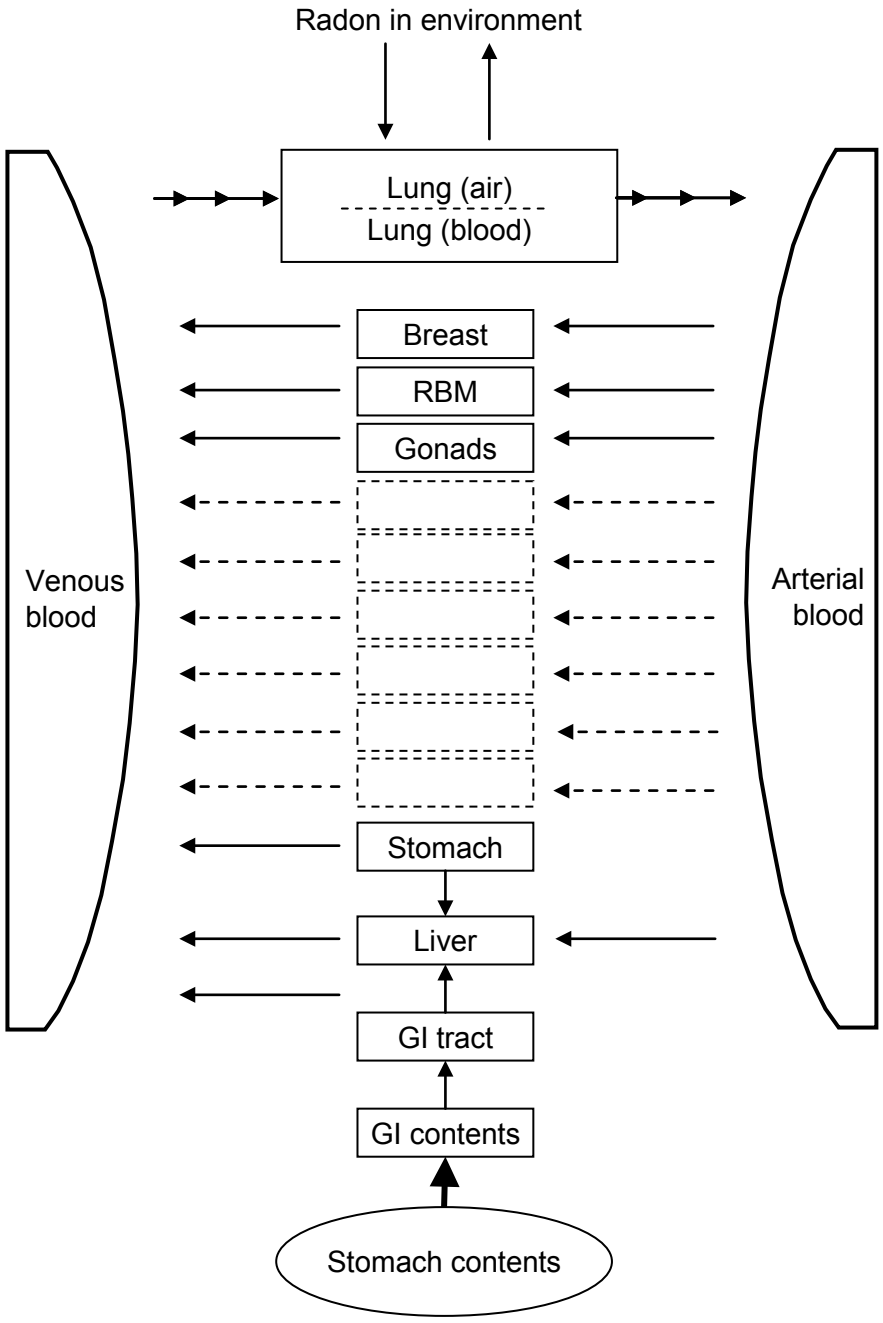
Table 3-10. Parameters in the NAS (1999b) PBPK Model[a]

Compartment	Flow (percent cardiac output)	Tissue mass (kg)	Tissue density	Tissue:blood partition coefficient
Stomach wall	1.0	0.15	1.05	0.7
Small intestine wall	10.0	0.64	1.04	0.7
Upper large intestine wall	2.0	0.21	1.04	0.7
Lower large intestine wall	2.0	0.16	1.04	0.7
Pancreas	1.0	0.10	1.05	0.4
Spleen	3.0	0.18	1.05	0.7
Adrenals	0.3	0.014	1.02	0.7
Brain	12.0	1.4	1.03	0.7
Heart wall	4.0	0.33	1.03	0.5
Liver	6.5	1.8	1.04	0.7
Lung tissue	2.5	0.47	1.05	0.7
Kidneys	19.0	0.31	1.05	0.66
Muscle	17.0	28.0	1.04	0.36
Red marrow	3.0	1.5	1.03	8.2
Yellow marrow	3.0	1.5	0.98	8.2
Trabecular bone	0.9	1.0	1.92	0.36
Cortical bone	0.6	4.0	1.99	0.36
Adipose tissue	5.0	12.5	0.92	11.2
Skin	5.0	2.6	1.05	0.36
Thyroid	1.5	0.02	1.05	0.7
Testes	0.05	0.035	1.04	0.43
Other	3.2	3.2	1.04	0.7

[a]Values shown for physiological parameters (flows, masses, densities) are for adults.

Source: NAS 1999b

Figure 3-8. Khursheed (2000) PBPK Model for Inhalation and Ingestion of Radon Gas



Source: Khursheed 2000

blood:tissue partition coefficients (Table 3-11). Values for blood flows were derived from Leggett and Williams (1991, 1995); and tissue volumes were derived from ICRP (1990). Tissue:blood partition coefficients were derived from Nussbaum and Hursh (1957); however, a single value (0.36) was adopted for all soft tissues, with a higher value used for the gastrointestinal tract and stomach to account for higher fat content of these tissues. Values for partition coefficients for breast and red marrow assumed 30 and 40% fat content, respectively. Although age-dependence of radon biokinetics is discussed in Khursheed (2000), age-specific parameter values for the model are not reported.

Validation of the Model. The model has been evaluated with data on whole body retention kinetics of radon following ingestion of radon in water (Hursh et al. 1965; Khursheed 2000).

Risk Assessment. The model has been used to predict tissue-specific annual radiation doses associated with continuous inhalation exposures to 20 Bq/m^3 of radon, or following ingestion of 1 Bq of radon (Khursheed 2000).

Target Tissues. The model is designed to calculate radiation dose coefficients (Sv/Bq) corresponding to inhalation or ingestion exposures to radon. Dose coefficients for radon and progeny have been estimated for major organs, including the bone surfaces, bone marrow, and liver, and other tissues (Khursheed 2000).

Species Extrapolation. The model is based on both human and animal data (e.g., partition coefficients). However, it is intended for applications to human dosimetry. Applications to other species would require consideration of species-specific adjustments in modal parameters.

Interroute Extrapolation. The model is designed to simulate kinetics of inhaled or ingested radon. Extrapolation to other routes of external exposure would require modifications of the model to simulate absorption from those routes.

3.5 MECHANISMS OF ACTION

3.5.1 Pharmacokinetic Mechanisms

As discussed in Section 3.4 (Toxicokinetics), the radionuclide radon-222 (^{222}Rn; radioactive half-life of 3.82 days) is an inert noble gas found in air and some deep well water sources. Radon occurs in air and water along with its short-lived radioactive progeny (i.e., ^{214}Bi, ^{214}Pb, ^{218}Po). Deposition and absorption

Table 3-11. Parameters in Khursheed (2000) PBPK Model for Radon Gas

Tissue	Tissue:blood partition coefficient	Tissue blood flow (L/minute)	Tissue volume (L)
Lung (blood)		6.5	0.52
Lung (air)	2.33		2.82
Breast	3.07	0.015	0.35
Red bone marrow	4.70	0.195	1.46
Gonads	0.360	0.00325	0.033
Brain	0.411	0.78	1.25
Kidneys	0.33	1.23	0.295
Muscle	0.36	1.11	26.5
Other	0.36	1.05	25.1
Adipose	11.2	0.325	16.4
Bone	0.21	0.13	2.27
Liver	0.36	1.66	1.7
Gastrointestinal (upper intestines)	0.411	1.17	0.95
Stomach wall	0.411	0.065	0.14
Arterial blood		6.5	0.556
Venous blood		6.5	1.19

Source: Khursheed 2000

of inhaled or ingested radon gas will be determined largely by its solubility in tissues and blood flow to the lungs or gastrointestinal tract (i.e., absorption rate will be flow-limited). Distribution of radon and its clearance from the blood following exposure will be governed by its solubility in water and fat and blood flow rates to major tissue depots for radon (i.e., fatty tissues). Absorbed radon is quickly eliminated from the blood by diffusion across the lung, followed by exhalation. Radon can be absorbed through the skin, as demonstrated by its appearance in the blood following dermal exposure; however, underlying mechanisms have not been elucidated.

The pharmacokinetics of inhaled radon progeny will be determined by physiological and physico-chemical characteristics (i.e., relative proportions of particular radon progeny and particle size (unattached particles with diameters of 0.5–3 nm to attached particles with diameters of 50–1,500 nm). The relative proportions vary with exposure conditions (i.e., indoor, outdoor), activities of the individual (e.g., sleeping, activities that release particulates into the air), smoking, and other aerosol-generating activities (i.e., vacuum cleaning, cooking, fireplace and circulating fan usage). Amounts and location of deposition of radon progeny will be determined by factors that influence convection, diffusion, sedimentation, and interception of particles in the airways. Absorption of ingested radon progeny, and progeny formed from radon after ingestion, will be influenced by rates of transfer of stomach contents into the small intestine, as well as rates of absorption of progeny from the small intestine. Specific mechanisms involved in absorption of radon progeny from the small intestine have not been completely elucidated; however, based on our understanding of lead absorption, it is likely that the mechanisms include those common to other divalent cations (e.g., membrane cation transporters and channels). Information regarding the distribution and elimination of radon progeny (bismuth, lead, and polonium) can be found in reviews of these subjects (Agency for Toxic Substances and Disease Registry 2007b; ICRP 1980, 1994c, 1995c). The largest fractions of the body burdens for radon progeny would be expected to be found in bone for lead, kidney for bismuth, and liver for polonium (Agency for Toxic Substances and Disease Registry 2007b; ICRP 1980, 1994c, 2001).

3.5.2 Mechanisms of Toxicity

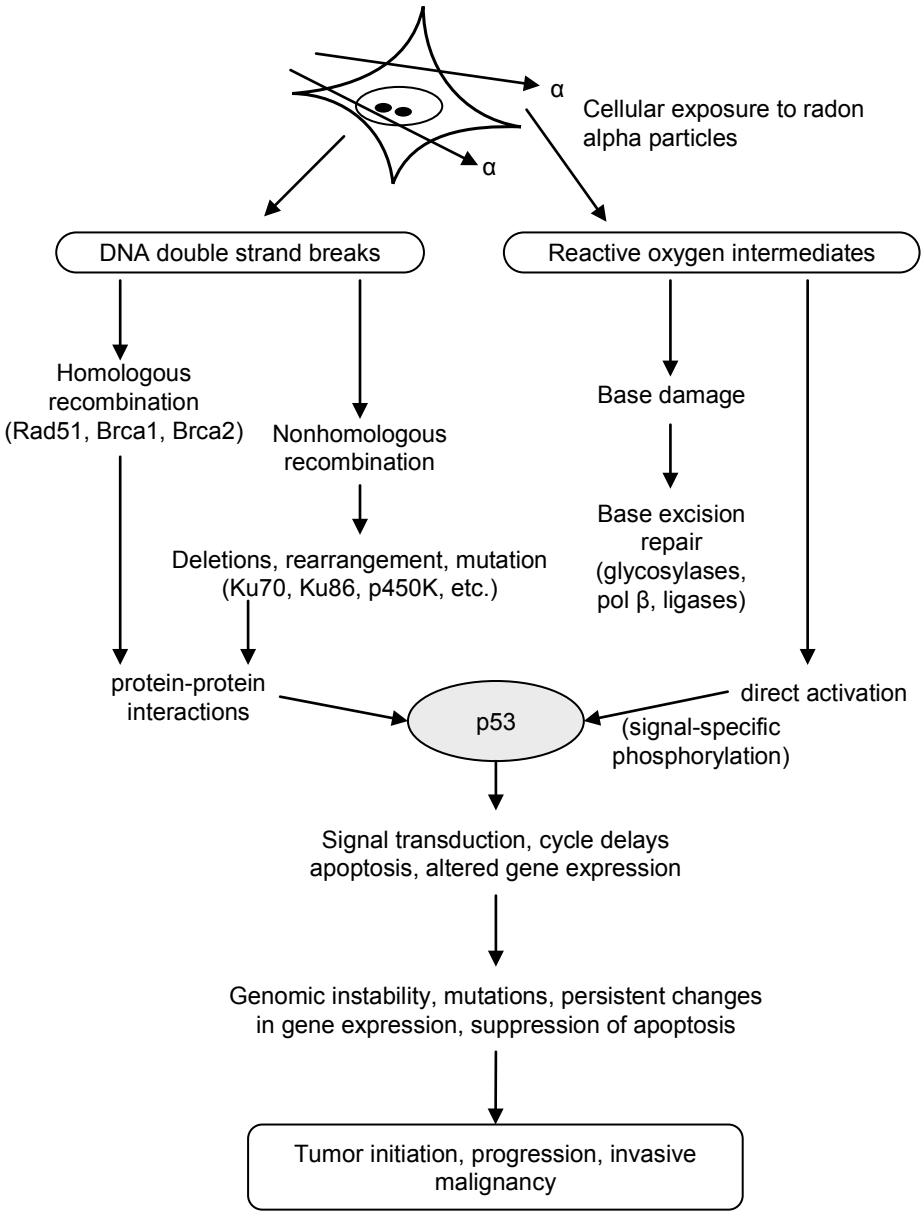
Extensive efforts have been made to elucidate mechanisms responsible for ionizing radiation-induced adverse effects. The Toxicological Profile for Ionizing Radiation (Agency for Toxic Substances and Disease Registry 1999b) includes an in-depth discussion of mechanisms of biological effects of ionizing radiation in general. Summaries of available information regarding underlying mechanisms of radon-induced lung cancer include Evans (1991, 1992) and, more recently, Jostes (1996) and NAS (1999a,

1999b). The intent of this Toxicological Profile for Radon is to provide a brief overview of the present state of the science regarding mechanisms that may play roles in radon-induced lung cancer. The information in this section is summarized predominantly from Chapter 6 (Molecular and Cellular Mechanisms of Radon-Induced Carcinogenesis) of the Risk Assessment of Radon in Drinking Water produced for the National Academy of Sciences (NAS 1999b). The reader is referred to this source for more detailed information on mechanisms of radon-induced lung cancer.

Toxicity of radon derives primarily from the biological effects of alpha radiation released during the radiological decay of radon progeny, particularly ^{218}Po and ^{214}Bi (attributed to essentially instantaneous decay of ^{214}Po to ^{210}Pb following its formation via beta and gamma decay of ^{214}Bi). The sequence of events leading from irradiation of living cells involves ionization that causes cellular damage that includes DNA breakage, accurate or inaccurate repair, apoptosis, gene mutations, chromosomal change, and genetic instability (Kronenberg 1994; Ward 1988, 1990). Figure 3-9 depicts a general conceptual model of the biology leading from alpha irradiation of cells by radon and radon progeny to tumor development (NAS 1999b). The process includes a series of events by which radiation-induced molecular changes affect the normal functions of regulatory genes, leading to genomic instability, loss of normal cell and tissue homeostasis, and development of malignancy.

One pathway leading to tumor formation begins with the induction of DNA damage to irradiated cells (Figure 3-9). The average track of alpha particles through a spherical cell nucleus can cross many individual strands of DNA, depositing energy in ion clusters and producing corresponding numbers of double-strand breaks, known as multiply locally damaged sites (MLDSs) (Ward 1990). Double-strand breaks are the most prominent form of DNA damage to cells irradiated by radon alpha particles. Such double-strand breaks can be repaired by homologous or nonhomologous (illegitimate) rejoining. In homologous repair, pairing proteins such as rad51 and associated modulatory proteins, pair a DNA terminus with the intact DNA homolog. A major signaling protein (p53) that regulates cell-cycle control, apoptosis, and the transcription of many downstream genes may interact with rad51 and suppress rad51-dependent DNA pairing. However, homologous repair of DNA is likely to be highly accurate because sequence information from the intact chromatid is used to repair the broken DNA. The nonhomologous recombination pathway involves end-to-end rejoining of broken DNA ends by supporting proteins including Ku70, Ku86, p450 kinase, and DNA ligase IV. The end result of DNA breakage and rejoining via this pathway may include some degree of deletion, insertion, or rearrangement of genetic material, which can persist over many cell generations.

Figure 3-9. Conceptual Model of the Biology Leading From Alpha Irradiation of Cells by Radon and Radon Progeny to Tumor Development



Source: NAS 1999b

Ionizing radiation that does not directly damage DNA can produce reactive oxygen intermediates that directly affect the stability of p53, resulting in downstream effects on cell regulation and activate cellular systems sensitive to the cellular redox states. Reactive oxygen intermediates can also produce oxidative damage to individual bases in DNA and point mutations by mispairing during DNA replication. Such damage can be repaired by the base-excision repair system which involves glycosylases, polymerase β, and ligases.

The p53 protein plays a critical role in regulating responses that are elicited in damaged cells, particularly responses involving cell-cycle arrest and apoptosis. The p53 protein also interacts with other regulatory and repair proteins. In the presence of cellular damage via direct DNA damage or via reactive oxygen intermediates, the lifetime of p53 increases, which can result in cell cycle delays and apoptosis. Surviving cells may contain gene deletions, rearrangements, amplifications, and persistent genomic instability. Resultant mutations in oncogenes, loss of function in tumor suppressors, and loss of heterozygosity can lead to tumor initiation, progression, and invasive malignancy.

The cells most likely involved in a carcinogenic response to ionizing radiation such as alpha irradiation of the lung by inhaled radon and radon progeny are the cells that incur genetic damage or altered genomic stability, not cells that receive lethal damage. At relatively low exposure levels, most irradiated cells would be expected to survive. The strong synergism between radon exposure and cigarette smoking may be the result of initial radon exposure that produces damaged, yet viable, cells that are further affected by carcinogens in cigarette smoke (Brenner and Ward 1992; Moolgavkar et al. 1993).

Both tobacco smoke and ionizing radiation are known to induce oxidative stress via reactive oxygen species (ROS). Under the assumption that glutathione-*S*-transferase M1 (*GSTM1*) null homozygotes would exhibit decreased ability to neutralize ROS, Bonner et al. (2006) used a case-only design to assess the *GSTM1* genotype of lung cancer cases for whom long-term α-track radon detectors had been used to measure residential radon concentrations. Second-hand smoke levels were also estimated. Radon concentrations in excess of 121 Bq/m^3 (3.27 pCi/L) were significantly associated with *GSTM1* null homozygotes compared to *GSTM1* carriers; an odds ratio for second-hand smoke and *GSTM1* interaction among never smokers was elevated as well. The results provide suggestive evidence that radon and second-hand smoke might promote carcinogenic responses via a common pathway.

A recent study reported a lack of expression of the p16Ink4a protein (Ink4a is a tumor suppressor gene) in 50% of radon-induced lung tumors of rats, suggesting that deregulation of p16Ink4a may play a role in lung tumors induced by radon and radon progeny (Bastide et al. 2009).

3.5.3 Animal-to-Human Extrapolations

Epidemiological studies clearly identify lung cancer as the health effect of greatest concern, both from occupational and residential exposure to radon and its progeny. Results of studies assessing the health effects of exposure to radon in a variety of animal species indicate that rats and dogs are relatively sensitive to radon-induced lung tumor development, whereas hamsters and mice did not develop tumors, even at cumulative exposures >10,000 WLM. This species difference may represent a real difference in sensitivity to radon; however, other factors may also have contributed to the lack of tumors in mice and hamsters, including decreased longevity in some exposed groups (i.e., animals die before tumors could develop) and termination of exposure or observations prior to the development of lung tumors. The lack of demonstrated exposure-related lung cancer in the hamsters may reflect species-specific resistance to alpha radiation-induced lung tumors since similar negative results were observed in hamsters exposed to plutonium, another alpha-emitting radionuclide (Sanders 1977). Based on a wide range of species differences in susceptibility to radon-induced lung cancer and insufficient information regarding mechanisms of interspecies differences in susceptibility, animal-to-human extrapolations for purposes of risk assessment do not appear useful at this time, nor are they needed given the wealth of epidemiological data.

3.6 TOXICITIES MEDIATED THROUGH THE NEUROENDOCRINE AXIS

Recently, attention has focused on the potential hazardous effects of certain chemicals on the endocrine system because of the ability of these chemicals to mimic or block endogenous hormones. Chemicals with this type of activity are most commonly referred to as endocrine disruptors. However, appropriate terminology to describe such effects remains controversial. The terminology endocrine disruptors, initially used by Thomas and Colborn (1992), was also used in 1996 when Congress mandated the EPA to develop a screening program for "...certain substances [which] may have an effect produced by a naturally occurring estrogen, or other such endocrine effect[s]...". To meet this mandate, EPA convened a panel called the Endocrine Disruptors Screening and Testing Advisory Committee (EDSTAC), and in 1998, the EDSTAC completed its deliberations and made recommendations to EPA concerning endocrine disruptors. In 1999, the National Academy of Sciences released a report that referred to these same types of chemicals as hormonally active agents. The terminology endocrine modulators has also been used to

convey the fact that effects caused by such chemicals may not necessarily be adverse. Many scientists agree that chemicals with the ability to disrupt or modulate the endocrine system are a potential threat to the health of humans, aquatic animals, and wildlife. However, others think that endocrine-active chemicals do not pose a significant health risk, particularly in view of the fact that hormone mimics exist in the natural environment. Examples of natural hormone mimics are the isoflavinoid phytoestrogens (Adlercreutz 1995; Livingston 1978; Mayr et al. 1992). These chemicals are derived from plants and are similar in structure and action to endogenous estrogen. Although the public health significance and descriptive terminology of substances capable of affecting the endocrine system remains controversial, scientists agree that these chemicals may affect the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body responsible for maintaining homeostasis, reproduction, development, and/or behavior (EPA 1997). Stated differently, such compounds may cause toxicities that are mediated through the neuroendocrine axis. As a result, these chemicals may play a role in altering, for example, metabolic, sexual, immune, and neurobehavioral function. Such chemicals are also thought to be involved in inducing breast, testicular, and prostate cancers, as well as endometriosis (Berger 1994; Giwercman et al. 1993; Hoel et al. 1992).

Radon itself is a noble gas and would not have hormonally active properties. In addition, no studies were located regarding endocrine disruption in humans and/or animals after exposure radon progeny.

No *in vitro* studies were located regarding endocrine disruption associated with radon progeny.

3.7 CHILDREN'S SUSCEPTIBILITY

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

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

Children sometimes differ from adults in their susceptibility to hazardous substances, but whether there is a difference depends on the substance (Guzelian et al. 1992; NRC 1993). Children may be more or less susceptible than adults to health effects, and the relationship may change with developmental age (Guzelian et al. 1992; NRC 1993). Vulnerability often depends on developmental stage. There are critical periods of structural and functional development during both prenatal and postnatal life, and a particular structure or function will be most sensitive to disruption during its critical period(s). Damage may not be evident until a later stage of development. There are often differences in pharmacokinetics and metabolism between children and adults. For example, absorption may be different in neonates because of the immaturity of their gastrointestinal tract and their larger skin surface area in proportion to body weight (Morselli et al. 1980; NRC 1993); the gastrointestinal absorption of lead is greatest in infants and young children (Ziegler et al. 1978). The infant also has an immature blood-brain barrier (Adinolfi 1985; Johanson 1980) and probably an immature blood-testis barrier (Setchell and Waites 1975). There may also be differences in excretion, particularly in newborns who all have a low glomerular filtration rate and have not developed efficient tubular secretion and resorption capacities (Altman and Dittmer 1974; NRC 1993; West et al. 1948). Children and adults may differ in their capacity to repair damage from substance insults. Children also have a longer remaining lifetime in which to express damage from substances; this potential is particularly relevant to cancer.

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

Available information from children employed as miners in China does not provide evidence of increased susceptibility to the effects of exposure to radon (Lubin et al. 1990; NIH 1994). However, a child in a smoking household will receive a higher radiation dose from radon (and is therefore more susceptible) than one in a nonsmoking household based on exposures to the same concentration of radon because cigarette smoke increases the attached fraction (HPA 2009), which in turn increases the radiation dose. Age-related differences in susceptibility to the effects of exposure to radon and radon progeny have not been demonstrated. Differences in lung morphometry and breathing rates in children could result in higher estimated radiation doses relative to adults (NCRP 1984a; Samet et al. 1989).

3.8 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).

Normally, a biomarker of exposure is defined as a xenobiotic substance or its metabolite(s) or the product of an interaction between a xenobiotic agent and some target molecule(s) or cell(s) that is measured within a compartment of an organism (NAS/NRC 1989). This does not apply to radon or its progeny since they are naturally present in individuals, and xenobiotics are not. The preferred biomarkers of exposure to radon and radon progeny are the substances themselves in readily obtainable body fluid(s), or excreta. However, several factors can confound the use and interpretation of biomarkers of exposure. The body burden of a substance may be the result of exposures from more than one source. Depending on the properties of the substance (e.g., biologic half-life) and environmental conditions (e.g., duration and route of exposure), radon and all of its progeny may have left the body by the time samples can be taken. It may be difficult to identify individuals exposed to hazardous substances that are commonly found in body tissues and fluids (e.g., essential mineral nutrients such as copper, zinc, and selenium). Biomarkers of exposure to radon and radon progeny are discussed in Section 3.9.1.

Biomarkers of effect are defined as any measurable biochemical, physiologic, or other alteration within an organism that, depending on magnitude, can be recognized as an established or potential health impairment or disease (NAS/NRC 1989). This definition encompasses biochemical or cellular signals of tissue dysfunction (e.g., increased liver enzyme activity or pathologic changes in female genital epithelial cells), as well as physiologic signs of dysfunction such as increased blood pressure or decreased lung capacity. Note that these markers are not often substance specific. They also may not be directly adverse, but can indicate potential health impairment (e.g., DNA adducts). Biomarkers of effects caused by radon and radon progeny are discussed in Section 3.9.2.

A biomarker of susceptibility is an indicator of an inherent or acquired limitation of an organism's ability to respond to the challenge of exposure to a specific substance. It can be an intrinsic genetic or other characteristic or a preexisting disease that results in an increase in absorbed dose, a decrease in the biologically effective dose, or a target tissue response. If biomarkers of susceptibility exist, they are discussed in Section 3.11, Populations That Are Unusually Susceptible.

3.8.1 Biomarkers Used to Identify or Quantify Exposure to Radon and Radon Progeny

Biomarkers of exposure to radon and its progeny include the presence of radon progeny in several human tissues and fluids, including bone, teeth, blood, hair, and whiskers; these progeny can be quantified by methods which are both specific and reliable (Blanchard et al. 1969; Clemente et al. 1984; Gotchy and Schiager 1969). Although the presence of radon progeny in these tissues and fluids indicates exposure to radon and radon progeny, particularly as a consequence of absorption of inhaled radon and radon progeny and ingestion of food or water containing radon-producing radionuclides such as uranium and thorium, exposure to uranium or radium may also result in the presence of these decay products. The isotope ^{210}Po may also be found in tissues after exposure to cigarette smoke. Levels of ^{210}Pb in teeth have been associated with levels of radon in the environment in an area with high natural background levels of radon and its progeny (Clemente et al. 1984). Black et al. (1968) reported a correlation between radiation exposure and ^{210}Pb levels in bone from uranium miners. However, cumulative exposure to these individuals was estimated. Biomarkers of exposure to radon or its progeny may be present after any exposure duration (e.g., acute, intermediate, chronic). Because of the relatively short half-lives of most radon progeny, with respect to a human lifetime, the time at which the biological sample is taken related to time of exposure may be important. However, for the longer-lived progeny the time factor is less critical.

Models are available which estimate exposure to radon and its progeny, ^{210}Pb and ^{210}Po, in bone, teeth, and blood (Blanchard et al. 1969; Clemente et al. 1982, 1984; Eisenbud et al. 1969; Gotchy and Schiager 1969; Weissbuch et al. 1980). However, these models make numerous assumptions, and uncertainties inherent in all models are involved in these estimates. Therefore, at present, these estimated levels of biomarkers of exposure are not useful for quantifying exposure to radon and its progeny.

3.8.2 Biomarkers Used to Characterize Effects Caused by Radon and Radon Progeny

The principal target organ identified in both human and animal studies following exposure to radon and its progeny is the lung. Alterations in sputum cytology have been evaluated as an early indicator of radiation damage to lung tissue. The frequency of abnormalities in sputum cytology, which may indicate potential lung cancer development, increased with increasing cumulative exposures to radon and its progeny (Band et al. 1980; Saccomanno et al. 1974). Abnormal sputum cytology can be used in diagnosis of lung cancer (Rivera et al. 2003). Abnormal sputum cytology may be observed following radon exposure, as well as exposure to other carcinogens such as cigarette smoke; it is not recommended as a screening tool for radon exposure. In addition, even though increases in the frequency of abnormal

sputum cytology parameters can be measured, they may not provide reliable information regarding predicted health effects in exposed individuals.

Associations between chromosomal aberrations and environmental levels of radon have been reported (Pohl-Rüling and Fischer 1983; Pohl-Rüling et al. 1976, 1987). Signs of genotoxicity in underground miners exposed to radon and other potentially genotoxic substances include increased frequencies of chromosomal aberrations and micronuclei in lymphocytes (Bilban and Jakopin 2005; Brandom et al. 1978; Smerhovsky et al. 2001, 2002) and increased frequency of mutations of glycophorin A in blood (Shanahan et al. 1996). However, these genotoxic effects cannot be exclusively attributed to exposure to radon and its progeny.

3.9 INTERACTIONS WITH OTHER CHEMICALS

Interactions of radon, cigarette smoke, arsenic, crystalline silica dust, and diesel exhaust particulates and the possible effects on radon-induced toxicity is an actively-researched complex issue. Cigarette smoke appears to interact with radon and its progeny to potentiate their effects. In general, epidemiological studies have reported synergistic, multiplicative, or additive effects of cigarette smoke in lung cancer induction among miners exposed to radon and its progeny (see NAS 1999a for an in-depth discussion of interactions between smoking and exposure to radon).

Some studies of occupational exposure to radon and radon progeny provide information to indicate that lung cancer was more prevalent among exposed workers who smoked compared to nonsmoking workers. For example, studies by Lundin et al. (1969, 1971) reported 10 times more lung cancer among U.S. uranium miners who smoked. Modeling results of Thomas et al. (1994), using data on lung cancer mortality in a Colorado Plateau uranium mining cohort, indicated a multiplicative synergistic relationship between lung cancer mortality and exposure to radon among smokers. Modeling results of data from another mining cohort in China (Yao et al. 1994) suggested that the synergistic effect of radon exposure and smoking was greater than additive and less than multiplicative; furthermore, the risk of lung cancer was higher if smoking and exposure to radon progeny occurred together rather than if smoking was initiated following the cessation of occupational exposure to radon progeny. Leuraud et al. (2011) assessed the effects of exposure to radon and radon decay products and smoking status on the risk of lung cancer in a combined analysis of 1,046 lung cancer cases and 2,492 controls with detailed radon exposure data and smoking status selected from three major miner cohorts in the Czech Republic (Tomášek et al. 2003), France (Laurier et al. 2004), and Germany (Kreuzer et al. 2010). The combined analysis resulted

in a significant excess risk of lung cancer with and without adjustment for smoking; the study authors indicated that the results of the combined analysis suggest a sub-multiplicative interaction between radon exposure and smoking. Analysis of pooled results from 13 European residential case-control studies resulted in findings that the absolute risk of death from lung cancer at age 75 years at usual residential radon concentrations of 0, 100, and 400 Bq/m^3 (0, 2.7, and 10.8 pCi/L) would be 25 times greater for cigarette smokers than lifelong nonsmokers (Darby et al. 2005, 2006). It should be noted that these studies were typically limited by lack of adjustment for concomitant exposure to other known or probable human carcinogens such as arsenic, crystalline silica dust, and diesel exhaust particulates.

Interactions between radon and arsenic were evaluated in a cohort of Chinese tin miners (Xuan et al. 1993). A 75% reduction in the lung cancer risk was indicated after adjusting for arsenic exposure. In another study (Bergdahl et al. 2010), decreased lung cancer risk from radon exposure was indicated after adjusting for silica exposure within the highest exposure group of a cohort of Swedish iron ore miners. In a multistate study of 12,315 non-metal underground and surface workers exposed to diesel exhaust particulates at facilities in Missouri, New Mexico, Ohio, and Wyoming (Attfield et al. 2012), an SMR of 1.26 (95% CI 1.09–1.44) was calculated for mortality from lung cancer among the workers compared to state-based mortality rates.

Some animal studies support the theory that cigarette smoke potentiates the effects of radon and its progeny alone or in conjunction with uranium ore dust. A study by Chameaud et al. (1982b) reported an increase in the incidence of lung cancer, as well as a decrease in the cancer latency period in rats exposed to radon and then to cigarette smoke, compared to rats exposed to radon and its progeny alone. This study did not include untreated controls. Alterations in normal blood parameters, including carboxyhemoglobin levels and leukocyte counts, were observed in dogs exposed to cigarette smoke followed by exposure to radon progeny plus uranium ore dust, compared to animals exposed to only radon progeny plus uranium ore (Filipy et al. 1974). In contrast, some studies suggest an antagonistic interaction between smoking and radon progeny-induced lung cancer. Dogs exposed daily to cigarette smoke followed immediately by exposure to radon and its progeny and uranium ore dust exhibited a decrease in the incidence of lung tumors, compared to dogs exposed to radon and its progeny plus uranium ore dust (Cross et al. 1982b). Cross (1988) reported that this was possibly due to a thickening of the mucus layer as a result of smoking and, to a lesser extent, a stimulatory effect of cigarette smoke on mucociliary clearance, although no empirical evidence was collected during the experiment to test these possibilities.

In rats, administration of chemicals present in cigarette smoke after exposure to radon and its progeny resulted in a decrease in the lung cancer latency period when compared to the time-to-tumor induction in animals treated with radon alone. This effect was seen with 5,6-benzoflavon (Queval et al. 1979) and cerium hydroxide (Chameaud et al. 1974).

Other airborne irritants, as well as ore dust and diesel exhaust, may act synergistically with radon and its progeny to increase the incidence of adverse health effects. Epidemiological and other studies report the presence of other airborne irritants in mining environments, including arsenic, hexavalent chromium, nickel, cobalt (Ševc et al. 1984), serpentine (Radford and Renard 1984), silica dust (Maciejewska 2008), iron ore dust (Damber and Larsson 1982; Edling and Axelson 1983; Radford and Renard 1984), and diesel exhaust (Damber and Larsson 1982; Ševc et al. 1984).

Cross and colleagues at Pacific Northwest Laboratory have conducted extensive experiments involving exposure of dogs, mice, rats, and hamsters to radon and its progeny in conjunction with uranium ore dust and/or diesel exhaust (Cross 1988; Cross et al. 1981a, 1982b, 1984; NIEHS 1978; Palmer et al. 1973). Studies in hamsters, mice, and rats have shown that exposure to uranium ore dust and/or diesel exhaust increases the pulmonary effects of radon. Radon and combinations of uranium ore dust and/or diesel exhaust produced greater incidences of pulmonary emphysema and fibrosis in hamsters than radon and its progeny alone (Cross 1988). Exposure to uranium ore dust or diesel exhaust alone caused significant bronchial hyperplasia, but not as great an effect as combining either of these with radon and its progeny. The incidence of severe lesions of the upper respiratory tract (nasal passages and trachea) of mice and rats was increased following exposure to radon and uranium ore dust, compared to animals exposed to radon and its progeny alone (Palmer et al. 1973). An increased incidence of thoracic cancer (40%) was observed in rats treated with asbestos (mineral dust) after inhalation of radon and its progeny, compared with animals exposed to radon alone (Bignon et al. 1983). However, these tumors may have been due to asbestos rather than to an interaction between agents. This experiment did not include a group exposed only to mineral dusts. In a study of tin miners in China, radon was found to account for only around 25% of the age-adjusted ERR/WLM once arsenic was accounted for as a confounder (Xuan et al. 1993). Inhalation exposure to radon and its progeny in conjunction with silicon dioxide increased the incidence of nodular fibrosis of the lungs in rats (Kushneva 1959).

3.10 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

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

Smokers who are exposed to elevated levels of radon and radon progeny are at much higher risk of lung cancer than nonsmokers (Darby et al. 2005, 2006). Nonsmoking children in smoking households are more susceptible than nonsmoking children in nonsmoking households since smoke increases the attached fraction and therefore the radiation dose (HPA 2009). People who have chronic respiratory disease, such as asthma, emphysema, or fibrosis often have reduced expiration efficiency and increased residual volume (i.e., greater than normal amounts of air left in the lungs after normal expiration) (Guyton 1977). Radon progeny can remain in the lungs for long periods of time, increasing the risk of damage to the lung tissue. Persons who have existing lung lesions may be more susceptible to the tumor-causing effects of radon progeny (Morken 1973). In an assessment of lung cancer cases pooled from three residential case-control studies, radon concentrations >121 Bq/m^3 (3.3 pCi/L) were associated with more than a 3-fold interaction odds ratio among glutathione-*S*-transferase M1 (GSTM1) null homozygotes compared to GSTM1 carriers (Bonner et al. 2006). In the study, it was hypothesized that GSTM1 null homozygotes would have decreased ability to neutralize reactive oxygen species induced by ionizing radiation and tobacco smoke. Thus, GSTM1 null homozygotes may exhibit increased susceptibility to the respiratory effects of radon progeny.

3.11 METHODS FOR REDUCING TOXIC EFFECTS

As discussed in detail in Section 3.2.1 (Inhalation Exposure), lung cancer is the primary toxicity concern following long-term exposure to radon and radon progeny. The high-energy alpha emissions from radon progeny deposited in the airways are the source of toxicity concern. The sequence of events leading from irradiation of living cells is generally believed to involve ionization that causes cellular damage including DNA breakage, accurate or inaccurate repair, apoptosis, gene mutations, chromosomal change, and genetic instability. Cigarette smoke appears to interact with radon and its progeny to potentiate their effects.

There are no known methods for reducing the toxic effects of radon once exposure has occurred. Inhaled radon, as a noble gas, is rapidly absorbed from the lung and readily excreted in exhaled air. Inhaled radon progeny that are attached to dust particles and tobacco products may lodge in the lung. Most radon progeny decay via alpha or beta emission with half-lives so short that conventional methods for reducing toxicity would be ineffective. Although selected radon progeny (e.g., ^{210}Po) have longer half lives, conventional medical interventions such as pulmonary lavage carry significant risk and are not recommended. Methods for reducing the potential exposure to radon (and therefore its toxic effects) consist of periodically testing for radon in indoor air and reducing radon concentrations to below the EPA recommended action level of 4 pCi/L, using active soil depressurization (ASD) in existing homes and radon-reducing features in new home construction. If ASD does not reduce levels sufficiently, reversing the fan direction to pressurize the subslab can be used to determine the more effective method (Kearney and Mason 2011). Measures to prevent high radon levels in new home construction are expected to be effective at reducing radon-related lung cancer deaths, while remediating old homes with high radon levels may be more expensive and less effective. An additional method to reduce toxic effects of radon is to stop smoking (EPA 2009a; Mendez et al. 1998, 2011) since the presence of smoke particles increases the radiation dose from radon progeny. Port-of-entry mitigation methods for reducing radon levels in drinking water are recommended over mitigation at the tap since the latter is not effective for radon (EPA 2009a; 2012a).

3.11.1 Reducing Peak Absorption Following Exposure

There are no methods for reducing peak absorption of radon gas following exposure and radon progeny decay via alpha or beta emission so rapidly that efforts to remove inhaled radon progeny would be ineffective.

3.11.2 Reducing Body Burden

There are no known methods for reducing the body burden of absorbed radon and radon progeny.

3.11.3 Interfering with the Mechanism of Action for Toxic Effects

There is an increasing amount of information regarding the possible efficacy of dietary micronutrients at reducing lung cancer risk in smokers. Alavanja (2002) published a review of tobacco smoke- and radon-induced damage and potential preventive interventions. Since smoking multiplies the risk of lung cancer

from radon exposure, stopping smoking could significantly reduce the risk of radon induced lung cancer; however, reducing exposure to radon is a first consideration. It was noted that available data indicate that micronutrients associated with a reduction in lung cancer risk among smokers might also reduce the risk in nonsmokers, possibly via antioxidant properties. Thus, diets high in fruits and vegetables might be of benefit in neutralizing reactive oxygen species produced by cigarette smoke and radon. However, the American College of Chest Physicians does not recommend the use of supplements for the prevention of lung cancer as they have not been shown to be helpful, and beta-carotene has been associated with increases in lung cancer (Alberts 2007).

3.12 ADEQUACY OF THE DATABASE

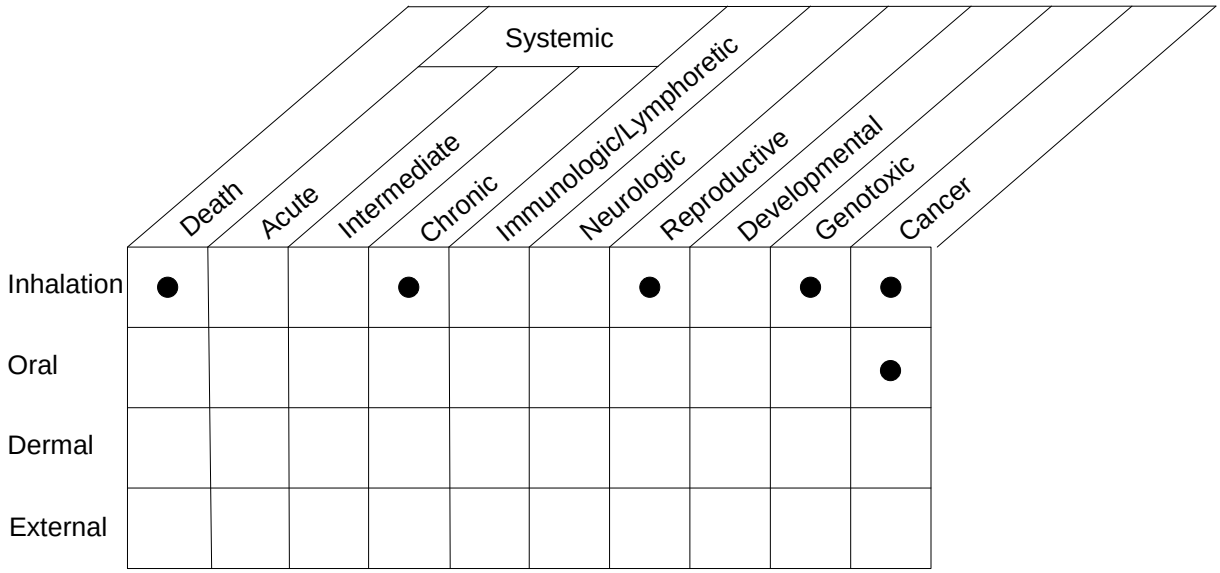
Section 104(I)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of radon is available. Where adequate information is not available,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

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

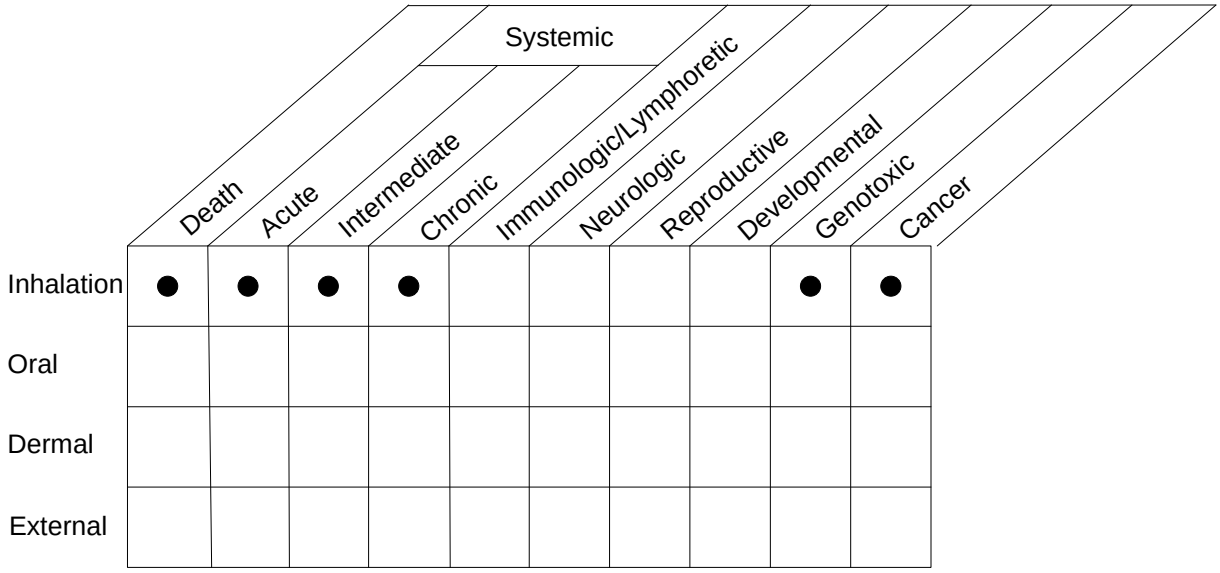
3.12.1 Existing Information on Health Effects of Radon

The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to radon are summarized in Figure 3-10. The purpose of this figure is to illustrate the existing information concerning the health effects of radon. Each dot in the figure indicates that one or more studies provide information associated with that particular effect. The dot does not necessarily imply anything about the quality of the study or studies, nor should missing information in this figure be interpreted as a “data need”. A data need, as defined in ATSDR’s *Decision Guide for Identifying Substance-Specific Data Needs Related to Toxicological Profiles* (Agency for Toxic Substances and Disease Registry 1989), is substance-specific information necessary to conduct comprehensive public health assessments.

Figure 3-10. Existing Information on Health Effects of Radon



Human



Animal

● Existing Studies

Generally, ATSDR defines a data gap more broadly as any substance-specific information missing from the scientific literature.

Figure 3-10 graphically describes whether a particular health effect end point has been studied for a specific route and duration of exposure. Most of the information on health effects in humans caused by exposure to radon and radon progeny was obtained from epidemiological studies of uranium and other hard rock miners. These studies of chronic occupational exposure to radon via inhalation provide information on cancer and lethality, and limited insight into reproductive and genetic effects. Limited information is also available regarding cancer following dermal exposure to radon and its progeny. No information on the health effects of radon and its progeny in humans was available following acute or intermediate exposure by any route. No information on the health effects of radon and its progeny in animals following acute, intermediate, or chronic oral or dermal exposure was located. The only information available from animal studies was by the inhalation route of exposure, which provides data on systemic and genetic effects, as well as cancer.

3.12.2 Identification of Data Needs

Acute-Duration Exposure. No data were located regarding adverse health effects in humans following acute exposure to radon and its progeny by any route. Single dose studies are available for laboratory animals that have been exposed by the inhalation and parenteral routes. No information is available on acute oral exposure in laboratory animals. Information is available on lethality following acute inhalation exposure to high doses. However, this study did not provide information on target organs, sensitive tissues, or cause of death. No information is available on effects in humans or animals following relatively low-level acute exposure to radon and its progeny. However, the greatest health concern for radon and its progeny is lung cancer, which results from long-term exposure, not acute-duration exposure. Studies designed to assess the potential for adverse health effects in humans following acute-duration exposure to radon and its progeny do not appear necessary at this time.

Intermediate-Duration Exposure. No data were located regarding adverse health effects associated with intermediate-duration exposure of humans to radon and its progeny by any exposure route. Epidemiological miner-based studies, in general, have focused on cohorts exposed to radon and its progeny for durations >1 year. Animal studies demonstrate that intermediate exposure to high levels of radon and its progeny can cause chronic respiratory toxicity and lung cancers and indicate that similar effects might occur following intermediate-duration exposure in humans. The relationship between the

nature and severity of the respiratory toxicity and the amount of radon exposure is not clearly defined; nor is there any information regarding systemic toxicity following intermediate-duration exposure. Additional research on the dose-duration-response relationship between radon exposure and the type and permanence of resulting toxicity would provide pertinent information. If populations exposed to radon and its progeny for intermediate durations can be identified, such populations could be assessed for potential adverse health outcomes.

Chronic-Duration Exposure and Cancer. Knowledge of the adverse health effects in occupationally-exposed humans following chronic-duration exposure to radon and its progeny is historically based on studies in adult male underground miners. These studies describe predominantly respiratory end points, such as pneumoconiosis, emphysema, interstitial pneumonitis, pulmonary fibrosis, tuberculosis, and cancer. Interactions of radon and known or probable human carcinogens in occupational and residential exposure scenarios need to be evaluated for the earlier study groups as well as more recent and current exposed populations. One study of a cohort of uranium miners in the Czech Republic included a finding of significant positive associations between cumulative radon exposures and incidences of chronic lymphocytic leukemia and all leukemias combined (Řeřicha et al. 2006). Additional studies of occupationally- and residentially-exposed individuals are needed to more completely assess the potential for radon-induced leukemias. To a large extent, other health effects have not been studied; additional studies assessing health effects other than cancer do not appear necessary.

Numerous residential case-control studies are available for which possible associations between lung cancer and residential radon levels have been assessed. Collectively, these studies provide evidence of radon-induced lung cancer from long-term residential exposure. Continued assessment of residential radon exposure should include improved methods such as glass-based retrospective radon detectors (Field et al. 1999b; Steck et al. 2002; Sun 2008) and validation of such methods to more accurately estimate exposure scenarios. In addition, extensive data regarding radon exposure in non-residential and residential buildings that use radon-emitting building materials (e.g., natural stone counter tops, floors, and heat sinks) are needed.

Although radon dissolved in drinking water is a source of human exposure, few studies have reported on the potential health implications associated with ingested radon and radon progeny. However, additional studies do not appear necessary at this time.

Genotoxicity. The genotoxicity of alpha radiation from radon and radon progeny has been investigated in underground miners, in individuals residing in homes with measured radon levels, in laboratory animals *in vivo*, and in a variety of *in vitro* test systems. Increases in chromosomal abnormalities have been reported in peripheral blood lymphocytes of underground miners and occupants of residences where relatively high levels of radon were measured. Results of numerous *in vivo* and *in vitro* studies support the findings of radiation-induced chromosomal abnormalities associated with exposure to radon and radon progeny. Additional studies do not appear necessary at this time.

Reproductive Toxicity. Results of a few epidemiological studies indicated that exposure to radon and its progeny during uranium mining may be associated with alterations in the secondary sex ratio among offspring (Dean 1981; Muller et al. 1967; Wiese and Skipper 1986). More recent assessments of mining cohorts did not focus on reproductive end points. Limited animal data are available regarding potential reproductive effects following exposure to radon and radon progeny. Available toxicokinetic data do not implicate reproductive tissues as particularly vulnerable tissues of concern following exposure to radon and radon progeny.

Developmental Toxicity. Available information regarding the potential for radiation-induced developmental effects following exposure to radon and radon progeny is limited to negative findings in rats following inhalation exposure to 12 WLM of radon and radon progeny (absorbed onto ore dust) for 18 hours/day at a rate of 124 WLM/day on gestation days 6–19 (Sikov et al. 1992). Additional animal studies could be designed to support or refute the results of Sikov et al. (1992).

Immunotoxicity. No information was located regarding potential radon-induced effects on the immune system of humans or in animals exposed to radon and its progeny at concentrations considered relevant to human health.

Neurotoxicity. Cells and tissues in the nervous system may be less radiosensitive, due to a lack of cell turnover or cellular regeneration, than faster regenerating cells of the gastrointestinal tract or pulmonary epithelium. Consequently, neuronal impairment as a result of radon alpha emissions is not expected. Therefore, studies that specifically or directly measure either pathological or functional damage to the nervous system following exposure to radon do not appear to be necessary at this time.

Epidemiological and Human Dosimetry Studies. Knowledge of the adverse health effects in occupationally-exposed humans following chronic-duration exposure to radon and its progeny is based on

studies in primarily adult male underground miners. These studies describe predominantly respiratory end points, such as pneumoconiosis, emphysema, interstitial pneumonitis, pulmonary fibrosis, tuberculosis, and cancer. However, lung cancer is the only respiratory effect that has been clearly associated with exposure to radon and radon progeny. One study of a cohort of uranium miners in the Czech Republic included a finding of significant positive associations between cumulative radon exposures and incidences of chronic lymphocytic leukemia and all leukemias combined (Řeřicha et al. 2006). Additional studies of occupationally- and residentially-exposed individuals could be of benefit in assessing the potential for radon-induced leukemias; however, such studies would need to include large numbers of subjects given the low incidences of leukemias observed in available studies of radon. To a large extent, other health effects have not been either reported or studied; additional studies assessing health effects other than respiratory and cancer end points do not appear necessary.

Numerous residential case-control studies are available for which possible associations between lung cancer and residential radon levels have been assessed. Collectively, these studies provide evidence of radon-induced lung cancer from long-term residential exposure. Continued monitoring of residential radon exposure is needed to more completely characterize exposure-response relationships. These assessments should include improved methods such as glass-based retrospective radon detectors (Field et al. 1999b; Steck et al. 2002; Sun 2008) and validation of such methods to more accurately estimate exposure scenarios. In addition, extensive data regarding radon exposure in non-residential buildings are needed.

Biomarkers of Exposure and Effect.

Exposure. Potential biomarkers of exposure may include the presence of radon progeny in urine, blood, bone, teeth, or hair. Although the detection of radon progeny in these media is not a direct measurement of an exposure level, estimates may be derived from mathematical models. Quantification of exposure to radon is further complicated by the fact that radon is a ubiquitous substance and background levels of radon and radon progeny are needed to quantify higher than “average” exposures.

Effect. It has been reported that chromosome aberrations in the peripheral blood lymphocytes may be a biological dose-response indicator of radiation exposure (Bilban and Jakopin 2005; Brandom et al. 1978; Pohl-Rüling et al. 1976; Smerkovsky et al. 2001, 2002). In addition, the frequency of abnormalities in sputum cytology has been utilized as an early indicator of radiation damage to lung tissue (Band et al. 1980); this has not been recommended regarding exposure to radon. However, more extensive research is

needed in order to correlate these effects with radon exposure levels and subsequent development of lung cancer or other adverse effects.

Absorption, Distribution, Metabolism, and Excretion. The toxicokinetics of inhaled and ingested radon and radon progeny has been fairly well studied, but information regarding the toxicokinetics of radon and radon progeny following dermal exposure is limited. Additional information on the deposition patterns in airways for radon progeny and the relationship of these deposition patterns to the onset of respiratory disease could help to enhance understanding of the disease process and delineate health protective measures to reduce deposition.

Comparative Toxicokinetics. Similar target organs have been identified in both humans and laboratory animals exposed to radon and radon progeny. More information on respiratory physiology, target cells, lung deposition, and absorption of radon and its progeny in different animal species is needed to clarify observed differences in species-sensitivity and tumor types. For example, rats generally develop lung tumors in the bronchioalveolar region of the lung while humans develop lung tumors in higher regions (tracheobronchial area). These studies could identify the appropriate animal model for further study of radon-induced adverse effects, although differences in anatomy and physiology of the respiratory system between animals and humans require careful consideration. Most of the information available on the toxicokinetics of radon and progeny has been obtained from studies of inhalation exposure. Studies on the transport of radon and progeny following oral and dermal exposures would be of use for comparing different routes of exposure, although oral and dermal exposure routes do not appear to be of particular toxicity concern.

Methods for Reducing Toxic Effects. Lung cancer is generally considered to be the only toxicity concern following long-term exposure to radon and radon progeny. The high-energy alpha emissions from radon progeny deposited in the lung are the source of toxicity concern. The sequence of events leading from irradiation of living cells is generally believed to involve ionization that causes cellular damage that includes DNA breakage, accurate or inaccurate repair, apoptosis, gene mutations, chromosomal change, and genetic instability. Cigarette smoke, crystalline silica dust, and arsenic have been reported to interact with radon and its progeny to potentiate their effects. The quality of breathing air in mines was addressed decades ago and the concentrations of radon, its progeny, silica dust, arsenic, and other mine pollutants that contribute to lung cancer were effectively reduced.

Methods for reducing the potential for radon-induced toxic effects consist of reducing or eliminating smoking, as well as periodically testing for radon in indoor air and reducing radon concentrations to below the EPA recommended action level of 4 pCi/L, using active soil depressurization (ASD) in existing homes and radon-reducing features in new home construction. In some cases, an active soil pressurization system (ASP) may be necessary (see Section 6.5 for explanatory information regarding ASD and ASP systems. Laws are being enacted to eliminate or limit smoking in public areas and business locations. Continued research is needed to develop effective smoking reduction and stop smoking campaigns and to develop and implement additional techniques for reducing radon levels in homes and public buildings.

Children's Susceptibility. If data needs, relating to both prenatal and childhood exposures, and developmental effects expressed either prenatally or during childhood, are identified, they are discussed in detail in the Developmental Toxicity subsection above.

Age-related differences in susceptibility to the effects of exposure to radon and radon progeny have not been demonstrated. Differences in lung morphometry and breathing rates in children may result in higher estimated radiation doses relative to adults (NCRP 1984a; Samet et al. 1989). However, available information from children employed as miners in China does not provide evidence of increased susceptibility to the effects of exposure to radon (Lubin et al. 1990; NIH 1994).

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

3.12.3 Ongoing Studies

Additional research known to be underway includes pooling of results from Iowa and Missouri residential radon studies using glass-based detectors that are undergoing final calibration (Field, personal communication) and pooling of results from the residential radon studies that contributed to the results of Lubin et al. (2004; China studies), Krewski et al. (2005, 2006; North American studies) and Darby et al. (2005, 2006; European studies).

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4. CHEMICAL, PHYSICAL, AND RADIOLOGICAL INFORMATION

4.1 CHEMICAL IDENTITY

Radon is a naturally occurring radionuclide. The largest source of radon in the environment is due to the ambient levels produced by the widespread distribution of uranium, thorium, and their decay products in the soil (Buttafuoco et al. 2007; Weast 1980). Radon is a decay product of radium and part of the uranium and thorium decay chains (see Figure 4-1) (Buttafuoco et al. 2007; O'Neil et al. 2006). The chemical identity of radon isotopes and identification numbers for several of the radon isotopes (^{218}Rn, ^{219}Rn, ^{220}Rn, ^{222}Rn, ^{226}Rn, ^{229}Rn, and ^{230}Rn) are listed in Table 4-1.

4.2 PHYSICAL, CHEMICAL, AND RADIOLOGICAL PROPERTIES

Radon is the densest of all the gases. Important physical and chemical properties of radon are listed in Table 4-2. The radioactive properties of the important, short-lived daughters of ^{222}Rn are listed in Table 4-3. Figure 4-1 depicts the ^{238}U decay series containing ^{222}Rn. Figure 4-2 depicts the ^{232}Th decay series containing ^{220}Rn (thoron). Figure 4-3 depicts the ^{235}U decay series containing ^{219}Rn (actinon).

Table 4-1. Chemical Identity of Radon

Characteristic	Radon	Reference
Isotope(s)	Recognized isotopes: ^{195}Rn through ^{228}Rn Naturally-occurring isotopes: ^{222}Rn (radon) ^{220}Rn (thoron) ^{219}Rn (actinon)	DOE 2008
Registered trade name(s)	No data	
Chemical formula	Rn	
Chemical structure	Monatomic	
Identification numbers:		
CAS Registry	10043-92-2 Radon 51712-92-6 (^{230}Rn) 51712-91-5 (^{229}Rn) 16369-95-2 (^{226}Rn) 14859-67-7 (^{222}Rn) 22481-48-7 (^{220}Rn) 14835-02-0 (^{219}Rn) 15411-71-9 (^{218}Rn)	ChemIDPlus 2012
NIOSH RTECS	No data	
EPA Hazardous Waste	No data	
OHM/TADS	No data	
DOT/UN/NA/IMDG	No data	
HSDB	6369 (radon radioactive)	HSDB 2008
NCI	No data	

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

Table 4-2. Physical, Chemical, and Radiological Properties of Radon

Property	Radon	Reference
Molecular weight	222 (radon), 220 (thoron), 219 (actinon)	Cothern 1987a
Color	Colorless	Lewis 2001
Physical state	Gas at 0 °C and 760 mm Hg	Lewis 2001
Melting point	-71 °C	Lide 2005
Boiling point	-61.8 °C	Lewis 2001
Density at -20 °C	$9.96x10^{-3}$ g/cm^3	Cothern 1987a
Odor[b]	Odorless	O'Neil et al. 2006
Odor threshold:		
Water	Odorless	
Air	Odorless	
Solubility:		
Water at 20 °C	230 cm^3/L	O'Neil et al. 2006
Organic solvents	Organic liquid, slightly soluble in alcohol	Weast 1980
Vapor pressure at 25 °C[a]	395.2 mm Hg	Cothern 1987a
Henry's Law constant	No data	
Autoignition temperature	Noble gas; does not autoignite	
Flash point	Noble gas; does not burn	
Flammability limits	Noble gas; is not flammable	
Half-life:		
^{222}Rn	3.8235 days	DOE 2008
^{220}Rn	55.6 seconds	DOE 2008
^{219}Rn	3.96 seconds	DOE 2008
Decay energies (MeV), and intensities (%)		
^{222}Rn	Alpha particles: 4.826 (0.0005%) 4.986 (0.078%) 5.48948 (99.920%) Gamma rays: 0.510 (0.076%)	DOE 2008
^{220}Rn	Alpha particles: 5.747 (0.114%) 6.288 (99.886%) Gamma rays: 0.5497 (0.114%)	DOE 2008

Table 4-2. Physical, Chemical, and Radiological Properties of Radon

Property	Radon	Reference
^{219}Rn	Alpha particles (15 reported): 6.425 (7.5%) 6.530 (0.12%) 6.553 (12.9%) 6.819 (79.4%) Gamma rays (dozens reported): 0.0111 (9.6% 0.0769 (5.0%) 0.0793 (8.4%) 0.2712 (10.8%)	U.S. DHEW 1970
Specific activity, nλ/mass (Ci/g):		
^{222}Rn	1.538×10^{5}	Based on DOE 2008
^{220}Rn	9.135×10^{8}	Based on DOE 2008
^{219}Rn	1.301×10^{10}	Based on DOE 2008
Decay products:	Radon progeny (daughters)	
^{222}Rn (see Figure 4-1)	^{218}Po ^{214}Pb ^{214}Bi ^{214}Po ^{210}Tl ^{210}Pb ^{210}Bi ^{210}Po ^{206}Tl ^{206}Pb	DOE 2008
^{220}Rn (see Figure 4-2)	^{216}Po ^{212}Pb ^{212}Bi ^{212}Po ^{208}Tl ^{208}Pb	DOE 2008
^{219}Rn (see Figure 4-3)	^{215}Po ^{215}At ^{211}Pb ^{211}Bi ^{211}Po ^{207}Tl ^{207}Pb	DOE 2008

MeV = million electron volts

Table 4-3. Radioactive Properties of ^{222}Rn and Its Short-lived Progeny

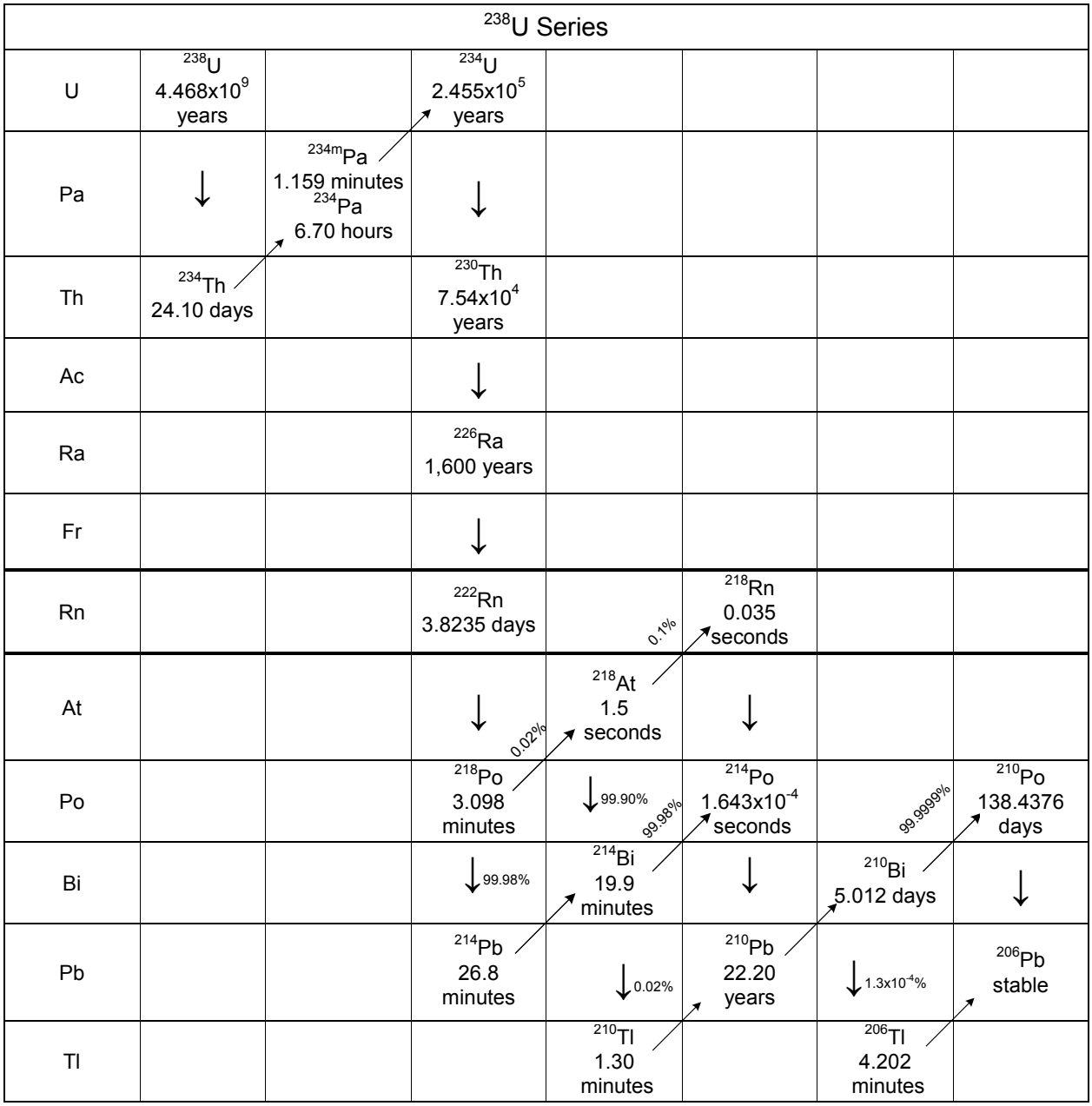
Isotope	Historical symbol	Principal radiation(s)	Q-Value of principal decay mode (MeV)	Half-life	Specific activity (Ci/g)
^{222}Rn	Rn	α	5.5903	3.8235 days	$1.54x10^{5}$
^{218}Po[a]	RaA	α	6.1147	3.098 minutes	$2.78x10^{8}$
^{218}At	At	α	6.874	1.5 seconds	$3.45x10^{10}$
^{214}Pb	RaB	β,γ	1.023	26.8 minutes	$3.28x10^{7}$
^{214}Bi	RaC	β,γ	5.6168	19.9 minutes	$4.41x10^{7}$
^{214}Po[a]	RaC'	α	7.8335	164.3 μseconds	$3.21x10^{14}$
^{210}Tl	RaC"	β	5.489	1.30 minutes	$6.89x10^{8}$

[a]Isotopes of primary radiological interest due to the potential for retention in the lung and subsequent alpha decay.

MeV = million electron volts

Source: DOE 2008

Figure 4-1. ^{238}U Decay Series Showing Sources and Decay Products*



*All of the single transitions are 100%; other branching ratios are shown in the decay series.

↓ alpha (α) decay; ↗ beta (β^-) decay or internal transition (IT)

Source: NNDC 2012b

Figure 4-2. ^{232}Th Decay Series Showing Sources and Decay Products

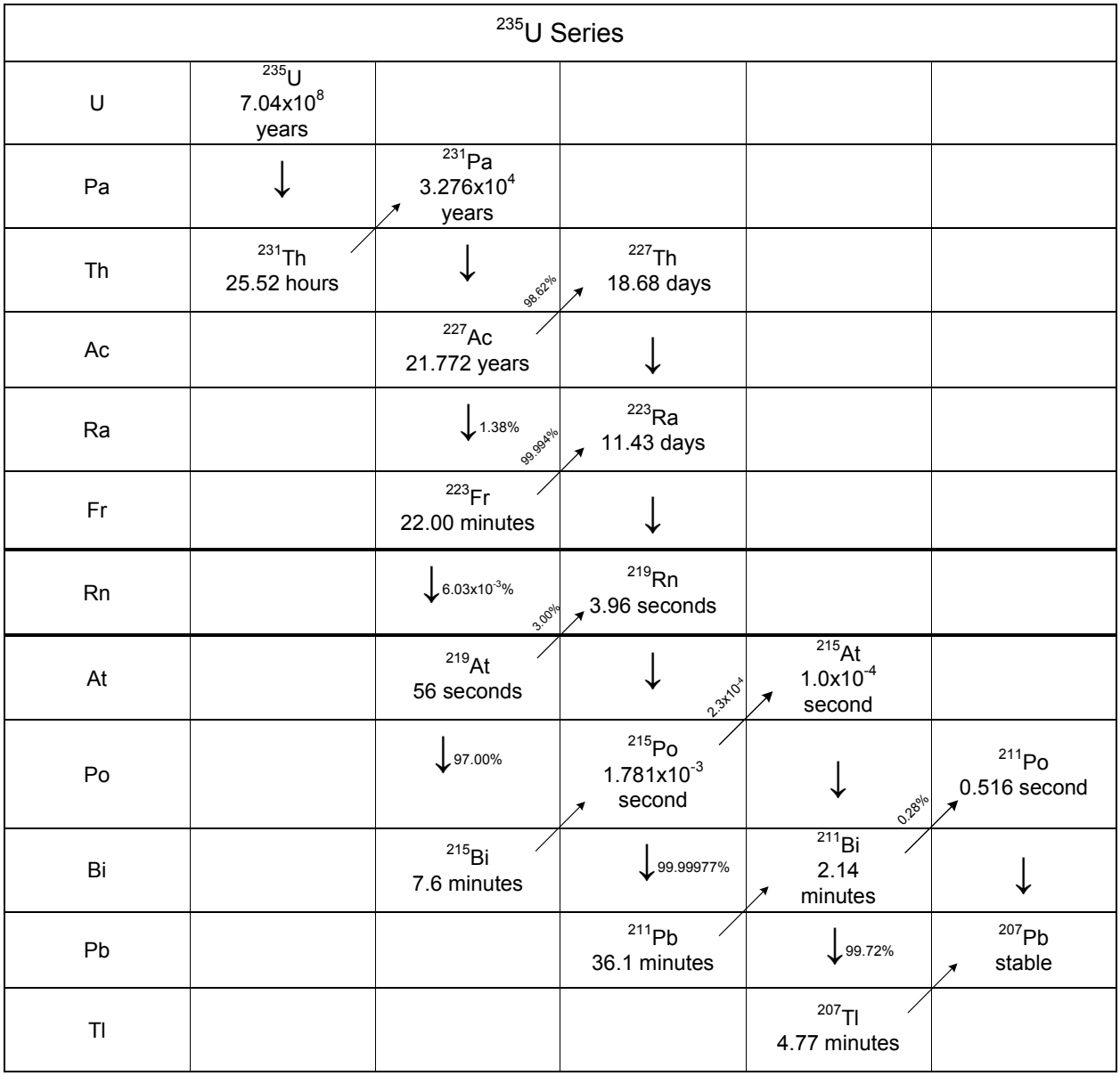
^{232}Th Series					
U					
Pa					
Th	^{232}Th 1.40x10^{10} years		^{228}Th 1.9116 years		
Ac	↓	^{228}Ac 6.15 hours	↓		
Ra	^{228}Ra 5.75 years		^{224}Ra 3.6319 days		
Fr			↓		
Rn			^{220}Rn 55.6 seconds		
At			↓		
Po			^{216}Po 0.145 seconds	98.62%	^{212}Po 2.99x10^{-7} seconds
Bi			↓	^{212}Bi 60.55 minutes	↓
Pb			^{212}Pb 10.64 hours	↓ 35.94%	^{208}Pb stable
Tl				^{208}Tl 3.053 minutes	

*All of the single transitions are 100%; other branching ratios are shown in the decay series.

↓ alpha (α) decay; ↗ beta (β^-) decay or internal transition (IT)

Source: NNDC 2012b

Figure 4-3. ^{235}U Decay Series Showing Sources and Decay Products



*All of the single transitions are 100%; other branching ratios are shown in the decay series.

↓ alpha (α) decay; ↗ beta (β^-) decay or internal transition (IT)

Source: NNDC 2012b

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

5.1 PRODUCTION

No information is available in the TRI database on facilities that manufacture or process radon because this chemical is not required to be reported under Section 313 of the Emergency Planning and Community Right-to-Know Act (Title III of the Superfund Amendments and Reauthorization Act of 1986) (EPA 1998).

Radon is a naturally occurring element; the isotope of primary health concern is ^{222}Rn. The largest source of radon in the environment is widely distributed uranium and its decay products in the soil (Buttafuoco et al. 2007; UNSCEAR 2000; Weast 1980). Radon is a decay product of radium and part of the uranium decay chain (see Figure 4-1) (Buttafuoco et al. 2007; O'Neil et al. 2006; UNSCEAR 2000). Every square mile of surface soil, to a depth of 6 inches, contains approximately 1 gram of radium, which slowly releases radon to the atmosphere (Weast 1980) when conditions of secular equilibrium exist.

The total production rate of radon in soil equates to the decay rate or concentration of radium present, which can range from 10 to 100 Bq/kg (270–2,700 pCi/kg) in the surface soil and from ~15 to ~50 Bq/kg (~400–~1,350 pCi/kg) in rock (Buttafuoco et al. 2007). The release of radon from the soil-gas or water to ambient air is affected by the soil porosity, meteorological factors, variations in atmospheric pressure, and concentration of radon in the soil-gas or water (WHO 1983). The concentration of radon in soil gas is affected by grain size, mineralogy, porosity, density permeability, and moisture, radium, and uranium content of the soil (Ericson and Pham 2001; Price et al. 1994; USNRC 1981). Meteorological factors, such as temperature and precipitation, may both enhance and inhibit transport of radon from the soil into other media. Radon progeny in the air can be removed by rainfall, soil moisture, and snow (UNSCEAR 2000). Alternatively, radon and its progeny may be temporarily increased at ground level after being brought to the surface by precipitation. If this is by rainfall, then the radon itself is rapidly released back into the atmosphere causing a spike in near-surface levels but leaving the particulate progeny behind in the water or on the surface. If this is by snowfall, then the progeny decay quickly, and any trapped radon builds up progeny toward equilibrium until snowmelt releases the remaining radon. Surface freezing can retard the radon emanation rate (Bunzl et al. 1998; Fujiyoshi et al. 2002). Vertical temperature gradients in which temperature decreases with elevation above the ground can help release radon from the soil, while temperature inversions inhibit this movement. The mechanism of radon transport in soil is described more fully in Section 6.3.1.

Outdoor radon levels vary significantly with geographic location. The ambient outdoor radon level goes through a daily cycle of concentrations ranging from approximately 0.03 to 3.50 pCi/L (Martin and Mills 1973) with the average level in the United States, based on a natural residential radon survey, being about 0.4 pCi L of outdoor air (EPA 2008b). Radon levels can be highly elevated in indoor spaces (UNSCEAR 2000). Indoor radon levels in the United States were found to range from approximately 0 to >80 pCi/L (3,000 Bq/m^3) (Fleischer 1986; Steck et a. 1999; White et al. 1992). EPA estimates that the average indoor radon level is 1.25 pCi/L in the United States (EPA 2003; Marcinowski et al. 1994).

The amount of naturally occurring radon released to the atmosphere is increased in areas with uranium and thorium ore deposits and granite formations, which have a high concentration of natural uranium. It is the presence of granite formations that has greatly increased radon concentrations in eastern Pennsylvania and parts of New York and New Jersey (EPA 2003; NAS 1999b; NCRP 1984a; Nero 1987), although elevated radon levels were also found in other parts of the country (map available at http://www.epa.gov/radon/zonemap.html) (EPA 2011a). Large granite outcroppings, such as the mountain in Stone Mountain, Georgia, are sources of additional airborne radon in that region. Sources of radon in the global atmosphere include natural emissions from radium in soil and water, tailings from metal mines (uranium, thorium, silver, tin, and phosphorus), agricultural lands utilizing phosphate fertilizers, and from construction materials and the burning of coal (EPA 2003; NAS 1999b; NCRP 1984a; Nero 1987). In a few locations, tailings have been used for yard fill, garden soil, sand for masonry work, or landfills and were subsequently built on, resulting in possible increased exposure to radon (Eichholz 1987). There is also an increased radon concentration in spring water due to the deposition of radium isotopes in the sinter areas around hot springs, where it is coprecipitated with calcium carbonate or silica (NCRP 1975). In groundwater, radon is present due to migration from rock and soil into surrounding groundwater (Hess et al. 1985; Lam et al. 1994).

Radon is not distributed commercially (Hwang et al. 2005). It has been produced commercially for use in radiation therapy, but for the most part, it has been replaced by radionuclides made in accelerators and nuclear reactors. Although no longer used, radiopharmaceutical companies and a few hospitals had pumped the radon from a radium source into tubes called “seeds” or “needles”, which may be implanted in patients (Cohen 1979). Due to the short half-life, research laboratories and universities typically produce radon in the laboratory for experimental studies (Hwang et al. 2005). Radon gas is collected by bubbling air through a radium salt solution (Hwang et al. 2005; Lewis 2001). The evolved gas containing radon, hydrogen, and oxygen is cooled to condense the radon and the gaseous hydrogen and oxygen are removed (Hwang et al. 2005).

5.2 IMPORT/EXPORT

Radon is not imported into or exported from the United States.

5.3 USE

While there are currently few significant technical uses for radon (Hwang et al. 2005), it does have several potentially useful applications. Medical uses of radon in the United States began as early as 1914. Treatments were primarily for malignant tumors. The radon was encapsulated in gold seeds and then implanted into the site of malignancy. During the period of 1930–1950, radon seeds were used for dermatological disorders, including acne. Radon therapy was still being studied and applied as recent as 1980 (Morken 1980).

Radium-223 (^{223}Ra), an isotope of radium that is a calcium surrogate and bone seeker, and which decays to ^{219}Rn, is being studied for possible use as a radiopharmaceutical in the treatment of skeletal metastases (NIST 2010). ^{223}Ra decays into ^{219}Rn, making this isotope a significant contributor to the radiation dose delivered to the tumor.

Water or air containing naturally high levels of ^{222}Rn has been used for therapeutic treatment of various diseases, such as arthritis (Becker 2003; Dobbin 1987; Pohl-Rüling and Fischer 1982). Small "radon mines" (caves with a high radon concentration in the air, such as abandoned mines) have been used as a health treatment (Cohen 1979). People would seek medical cures through exposure to radon gas for ailments ranging from arthritis, asthma, and allergies to diabetes and ulcers (Dobbin 1987), as well as for cancer treatment (Dobbin 1987; Lewis 2001). Radon "spas," with their commensurately high radon levels, have been used in Europe for the treatment of hypertension and a number of other disorders. In the former Soviet Union., for example, radon baths were often prescribed by the National Health System (Uzunov et al. 1981).

Radon may be utilized in the prediction of earthquakes (Cothern 1987b). Large quantities of radon have been found to migrate to the atmosphere from the earth from active fault zones, varying with atmospheric conditions and potentially with seismic activity (Buttafuoco et al. 2007). The emission of radon from soil and the concentration measured in groundwater appear to be good indicators of crustal activity. Other uses of radon include the study of atmospheric transport, the exploration for petroleum or uranium (Cothern 1987b), as a tracer in leak detection, for flow-rate measurement, and in radiography. Radon is

also used in chemical research (Lewis 2001) to initiate and influence reactions, as a label in surface study reactions, for radium and thorium determination, and in determining the behavior of filters (O'Neil et al. 2006).

As a tracer, radon can also be used in the identification and quantification of non-aqueous phase liquid (NAPL) contamination of the subsurface (Semprini et al. 2000). In the subsurface, naturally occurring ^{222}Rn exists as a dissolved gas in the saturated zone. While groundwater radon concentrations vary with the mineral composition of the substrate, they rapidly equilibrate in the absence of NAPL. The groundwater radon concentration, however, may be much less when NAPL is present due to its affinity for partitioning into NAPL. Reduced radon concentration correlates to the amount of NAPL in the subsurface pores. Scientists may then predict the location and saturation levels of NAPL by examining the distribution of radon in the subsurface (Semprini et al. 2000).

5.4 DISPOSAL

Disposal of radon would only be applicable to those facilities producing and/or using it for medical or experimental purposes where its release may be controlled. Regulations regarding the land disposal of radionuclides, as set forth in 10 CFR 61 (USNRC 2008), do not apply to radium, radon, or its daughters. Since radon is naturally occurring, it is not regulated by the U.S. Nuclear Regulatory Commission (USNRC) with the exception of emissions from uranium mill tailings. Uranium mill tailings contain radium, the precursor to radon. The Uranium Mill Tailings Radiation Control Act of 1978 (UMTRCA) established programs to control the disposal and stabilization of uranium mill tailings to minimize public health hazards associated with the decay of radium within the tailings (EPA 1995). Any other regulation of radon is up to the individual states. The allowable release rate of radon from the surface is 20 pCi/m^2/ second. See Chapter 8 for a listing of regulations concerning radon.

Radon emanation is not regulated under 10CFR20 for facilities operating under a USNRC license, but its flux or emanation rate is restricted by EPA regulation to 20 pCi/m^2/second (EPA 2011c). The two primary isotopes from natural sources have short half-lives and typically slow diffusion rates, so most ambient radon is produced in the top 30 cm or 1 foot of soil. Radon emanation rates from typical soil can be on the order of several pCi/m^2/second (Cember and Johnson 2009), but some mill tailings sites exceed the 20 pCi/m^2/second limit. In such cases, disposal involves moving the tailings or reducing the levels by adding a retarding layer over the tailings, such as a several foot thick layer of clay or shale soil (EPA 2008a). In small use facilities, radon may be compressed and stored in tanks until it decays or, if the

quantity is small, it may be adsorbed on activated charcoal (Cember 1983). Particulate matter may be removed from the gas by a variety of different devices including detention chambers, adsorbent beds, and liquefaction columns. After filtration, the remaining radioactive particulates are discharged into the atmosphere for dispersion of the nonfilterable low levels of activity (Cember 1983).

Discharge via combustion stream from a natural gas incinerator power plant may contain high levels of radon when the natural gas is retrieved from an area with high concentrations of radium. Radon can be released to the environment from fossil-fueled power plants since radon cannot be scrubbed from the combustion stream by standard methods. The average concentration of radon in the combustion stream of a plant reported by Ericson and Pham (2001) was 370 pCi /L (13,700 Bq/m^3). Federal and State of California regulations do not control radioactive emissions such as these, which are considered to be "natural" emissions (Ericson and Pham 2001).

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6. POTENTIAL FOR HUMAN EXPOSURE

6.1 OVERVIEW

The presence of radon at any site can be a consequence of its natural occurrence in the environment plus any releases from anthropogenic hazardous waste.

The results of the 1992 EPA National Residential Radon Survey (EPA 1992b) estimated that 1 in 15 homes had an elevated radon level (i.e., a level at or above the EPA action level of 4 pCi/L). At the time, an estimated 5.8 million homes had an elevated radon level. The source of radon in homes is from naturally occurring (geologic) sources. For more information, refer to EPA's A Citizen's Guide to Radon (EPA 2009a).

^{222}Rn is a naturally occurring radioactive noble gas that is part of the ^{238}U decay chain, and is the daughter of ^{226}Ra. Similarly, ^{219}Rn and ^{220}Rn are in the ^{235}U and ^{232}Th decay chains and immediate daughters of ^{223}Ra and ^{224}Ra. ^{218}Rn is in the ^{238}U decay chain and the immediate daughter of ^{218}At. As radium decays, radon is formed and is released into small air or water-containing pores between soil and rock particles. If this occurs within radon's diffusion length of the soil surface, the radon may be released to ambient air (EPA 2003). Similarly, radon may migrate into groundwater. If this groundwater reaches the surface, some of the radon gas will release into the ambient air, but small amounts remain dissolved in the water. By far, the major sources of radon are its formation in and release from soil and groundwater, with soil contributing the greater amount (EPA 2003; Planinić et al. 1994). Radon is also released from the near surface water of oceans, tailings from mines (particularly uranium, phosphate, silver, and tin mines), coal residues, the combustion of fossil fuels (coal, oil, and natural gas), and building products (concrete, drywall, and brick) (Ericson and Pham 2001; Nero 1987). Global radon emissions from soil are estimated to be 2,400 million Ci ^{222}Rn (8,880x10^{16} Bq), followed by release from groundwater (500 million Ci), oceans (34 million Ci), phosphate residues (3 million Ci), uranium mill tailings (2 million Ci), coal residues (0.02 million Ci), natural gas emissions (0.01 million Ci), coal combustion (0.009 million Ci), and human exhalation (1x10^{-5} million Ci) annually (Fishbein 1992). Monitoring data in this chapter are reported for ^{222}Rn unless otherwise specified. The two other naturally occurring radioactive isotopes of radon, ^{219}Rn and ^{220}Rn, are not discussed due to their short half-lives (3.96 and 55.6 seconds, respectively; see Figures 4-2 and 4-3) (DOE 2008).

The ultimate fate of radon is transformation through radioactive decay. Radon decays only by normal radioactive processes (i.e., an atom of radon emits an alpha particle resulting in an atom of polonium,

which itself undergoes radioactive decay to other radon daughters or progeny) (EPA 2003). There are no sinks for radon, since its radioactive half-life is so short (3.8 days) (O'Neil et al. 2006).

In soil, radium atoms decay to radon, which can be released from the soil mineral matrix and transported through the soil column, ultimately being released to air. Alpha recoil is the process by which radon, when it is formed by radium emitting an alpha particle, actually recoils in the opposite direction from the path of particle ejection. Alpha recoil is important because this process dislodges radon from the edge of the soil mineral matrix and allows it to enter pore space between the soil grains. After radon is released into the pore spaces, its ultimate release to ambient air is a function of the soil porosity, soil moisture content, and meteorological factors, such as precipitation, atmospheric pressure, and the temperature versus altitude profile. Once radon is released to ambient air, its dispersion is primarily determined by atmospheric stability, including vertical temperature gradients and effects of wind. Transport of radon in indoor air is almost entirely controlled by the ventilation flow path and rate. Generally, the indoor radon concentrations increase as ventilation rates decrease. These transport processes are discussed in more detail in Section 6.3.1.

In groundwater, radon moves by diffusion and, primarily, by the mechanical flow of the water. Radon solubility in water is relatively low and, with its short radioactive half-life of 3.825 days (O'Neil et al. 2006), much of it will decay before it can be released from groundwater. Groundwater supplies in the United States have been surveyed for radon levels. In larger aquifers, average radon concentrations were reported to be 240 pCi (8.8 Bq)/L of water, while in smaller aquifers and wells, average levels were considerably higher (780 pCi/L of water; 28.9 Bq/L) (Cothern et al. 1986). These differences in radon levels between large and small groundwater supplies are a reflection of the types of rock and soil, as well as their uranium concentrations, through which the groundwater flows (Agency for Toxic Substances and Disease Registry 2011). Granitic rock, which is associated with high radon levels, does support large aquifers, although small aquifers may be present (Field and Kross 1998). For public groundwater-derived water supplies, the average radon concentration is estimated at 540 pCi/L (20 Bq/L), although some wells have been found to have radon concentrations up to 400 times the average concentration (up to $1x10^7$ Bq/m^3; 270,000 pCi/L). Surface water tends to have the lowest radon concentrations (NAS 1999b). Additional detail on radon in water is provided in Section 6.4.2.

Radon levels in ambient air vary with the type of soil and underlying bedrock of the area. The average outdoor radon concentration in the United States is about 0.4 pCi/L (14.8 Bq/m^3) (NAS 1999b). Measurements in Iowa and Minnesota show higher levels, with average outdoor concentrations of 0.60–

0.82 pCi/L (22.2–30.3 Bq/m^3) (Steck et al. 1999). Indoor concentrations as high as 2,000 pCi/L (74,000 Bq/m^3) have been observed in certain locations in the United States (EPA 2008b). Based on the National Residential Radon Survey, EPA estimates that the average indoor radon level is 1.25 pCi/L (46.25 Bq/m^3) in the United States (EPA 2003; Marcinowski et al. 1994); however, several locations in the country have been documented where the average indoor air levels are several times greater than the national average (Field 2005; Steck et al. 1999). The 1992 National Residential Radon Survey indicated that radon levels above the EPA recommended action level of 4 pCi/L could be present in 1 in 15 homes. At the time of the survey (1990), it was estimated that about 5.8 million homes had a higher radon level. For more information, refer to EPA's A Citizen's Guide to Radon (EPA 2009a).

Measurements of radon in soil are expressed in terms of levels in soil-gas. However, these measurements do not directly relate to rates of radon released to the atmosphere. Factors that affect radon soil-gas levels include soil properties such as radium content, mineral composition, moisture content, density, and soil porosity. Radon concentrations in soil may also be affected by meteorological conditions on the surface, such as snow (Fujiyoshi et al. 2002).

The primary pathway for human exposure to radon is inhalation from soil gas intrusion to dwellings and buildings; however, indoor radon levels can also originate from water usage, outdoor air infiltration, and the presence of building materials containing radium (EPA 2003). The committed dose from radon and its progeny is estimated by complex mathematical models and simplified tables have been published by EPA as Federal Guidance Report No. 13 (EPA 1999a). Exposure, both occupational and environmental, will be discussed primarily in terms of radon or radon progeny levels in the air. However, some estimates of daily intake can be made. For example, using an average indoor air radon concentration of 1.25 pCi/L (EPA 2003; Marcinowski et al. 1994) and an assumed breathing rate of 20 m^3/day, the radon daily intake from indoor air is 25,000 pCi/day. Using an estimated outdoor concentration of 0.4 pCi/L (NAS 1999b) and the same inhalation rate, the radon daily intake from outdoor air is 8,000 pCi/day.

Radon releases from groundwater also contribute to exposure. The daily intake of radon originating from drinking water only is estimated at 100–600 pCi (3.7–22.2 Bq)/day both from ingestion of drinking water and inhalation of radon released from drinking water (Cothern et al. 1986).

The highest occupational exposures to radon typically result from employment in underground uranium and other hard rock mining, or in phosphate mining due to the high airborne levels of radon and its progeny (NIOSH 2006). For example, an abandoned uranium mine located in Hungary had an average

radon concentration of 410 kBq/m^3 (11,100 pCi/L) at a depth of 15–55 m below the surface (Somlai et al. 2006). Although persons engaged in uranium mining are believed to receive the greatest exposures, the number of persons employed in uranium mining has greatly decreased. Furthermore, continuous improvements in engineering controls have lessened radon exposure in underground mines (NIOSH 1987). Measurements of radon progeny in U.S. mines from 1976 to 1985 showed annual mean concentrations of 0.11–0.36 working level (WL). A working level is "any combination of short-lived radon progeny in 1 liter of air that will ultimately release $1.3x10^5$ million electron volts of alpha energy during decay to lead-210" (NIOSH 1987). However, levels in phosphate mines measured during the same period showed a larger range of mean levels (0.12–1.20 WL) (NIOSH 1987). In 2006, assessments of radon exposure during phosphate plant operations resulted in an estimated mean concentration of 0.003 WL, based on limited data (NIOSH 2006).

While certain professions pose a higher risk of occupational exposure to radon (employment at underground mines for instance), exposure to high concentrations can occur in any location with geologic radon sources (Field 1999). A list of common occupations that have the potential for high radon and progeny exposure was developed by Field (1999). These occupations include mine workers (uranium, hard rock, and vanadium mines) and employees of water treatment plants, and radioactively contaminated sites can include uranium mill sites and associated mill tailing piles, phosphate fertilizer plants, oil refineries, power plants, and natural gas and oil piping facilities. Locations that are not contaminated, but at which elevated natural radon levels exist, can include natural caverns, utility and subway tunnels, excavation sites, health mines and spas, and fish hatcheries (EPA 2003; Field 1999; Fisher et al. 1996). Higher exposures can occur to farmers, radon mitigation professionals, and scientists studying radon or other radionuclides, although exposure to local radon sources occurs to everyone present, and elevated exposures can occur in any occupation (Field 1999).

6.2 RELEASES TO THE ENVIRONMENT

Manufacturing and processing facilities are required to report Toxics Release Inventory (TRI) to the EPA if specific criteria are met (EPA 2005). The TRI requirements do not apply to radon.

6.2.1 Air

There is no information on releases of radon to the atmosphere from manufacturing and processing facilities because these releases are not required to be reported (EPA 1998).

Because of the extended half-lives of uranium and radium and their abundance in the earth's surface, radon is continually being formed in soil and released to air. This normal emission of radon from ^{226}Ra in soils is the largest single source of radon in the global atmosphere (NAS 1999b; NCRP 1984a; Planinić et al. 1994). Using an average soil emanation rate of 1,600 pCi/cm^2-year and an estimated global surface area of $1.5x10^{18}$ cm^2, Harley (1973) estimated soil emanation of radon to be on the order of $2.4x10^9$ Ci ($8.9x10^{19}$ Bq)/year. Some solubilized radon is removed from the soil by plants through evapotranspiration where it is subsequently released to the atmosphere by diffusion through the leaf (Kozak et al. 2003; Taskayev et al. 1986).

Radon levels in outdoor air are affected by the composition of the substrate in the region. A monitoring study of radon in outdoor air conducted at 50 sites with varying geological characteristics in the state of Nevada indicated that the median statewide concentration of radon was essentially that of the nationwide average level of 0.4 pCi/L (Price et al. 1994). However, concentrations as large as 1.4 pCi/L were observed and these high levels usually correlated with silica rich igneous rocks (rhyolite and granite). Groundwater radon concentrations are also affected by the type of substrate. According to a study of North Carolina groundwater from private wells, areas with soil comprised on sand, silt, sandstones, and shales tend to have lower groundwater radon concentrations (67–1,700 pCi/L [2.5–63 Bq/L]) than groundwater in areas with metamorphic and granitic rocks (21–59,000 pCi/L [0.8–2,200 Bq/L]) (Watson et al. 1993).

Groundwater that is in contact with radium-containing rock and soil will be a receptor of radon emanating from the surroundings. When the groundwater reaches the surface by natural or mechanical means, this radon will start to be released to air. Although most of the radon present in groundwater will decay before reaching the surface, groundwater is considered to be the second largest source of environmental radon and is estimated to contribute $5x10^8$ Ci ($1.85x10^{19}$ Bq)/year to the global atmosphere (Fishbein 1992; NCRP 1984a). Radon is also released from oceans, but only from the near surface water, and in amounts that are an order of magnitude less than that from groundwater. As radium in oceans is largely restricted to bottom sediments, most radon would decay before water could carry it to the surface. Radon emissions from oceans were estimated as $3.4x10^7$ Ci/year (Fishbein 1992).

Radon in indoor air may also originate from volatilization of radon gas from water supplies used within homes for drinking, bathing, cooking, etc. Approximately 1–5% of the radon in indoor air was estimated to originate from water (Lam et al. 1994). Radon can also be released from water during the aeration and backwashing portions of the water treatment process. In a study of the water treatment process, exposure

to ^{222}Rn was measured at 31 Iowa water treatment plants found to have the largest decrease in ^{222}Rn water concentrations between raw and finished water. Workers were estimated to be exposed to an average annual air concentration of 3.4 pCi/L (126 Bq/m^3) ranging from 0.4 to 133 pCi/L (15–4,921 Bq/m^3). Facilities with the highest ^{222}Rn air concentrations treated groundwater containing moderate ^{226}Ra concentrations using aeration and iron filters. The estimated worker exposures were below the OSHA limit of 4 WLM/year based on short exposure intervals, even though exposures were overestimated by assuming radon-progeny equilibrium (Fisher et al. 1996)

Tailings from uranium mines and residues from phosphate mines each contribute to global radon in the approximate amount of 2–3x10^6 Ci (7.4x10^{16}–1.11x10^{17} Bq)/year, or a combined total of approximately 5x10^6 Ci (1.85x10^{17} Bq)/year. An abandoned mine in Hungary, with a subsurface radon concentration of 410 kBq/m^3 (11,100 pCi/L), was thought to have a significant effect on the air concentration of radon in houses above the mine. Indoor air concentrations, which averaged 667 Bq/m^3 (18.0 pCi/L), were likely elevated due to gas concentration within fissures reaching from the mine to the surface (Somlai et al. 2006). Fishbein (1992) reported that 3x10^6 Ci of ^{222}Rn is emitted from phosphate residues and 2x10^6 Ci of ^{222}Rn originates from uranium mill tailings each year.

Coal residues and fossil fuel (coal, oil, and natural gas) combustion products each contribute to atmospheric radon levels to a minor extent (NCRP 1984a). The portion from coal residues, such as fly ash, is very small. As natural gas retrieved from an area with concentrations of radium may contain high levels of radon, discharge via a combustion stream from a natural gas incinerator power plant may also have high radon levels. Emissions from one plant were measured as having an average concentration of 370 pCi/L (13,700 Bq/m^3). Radon is a noble gas, so it is not feasible to scrub it from any combustion stream. As of 2001, federal and State of California regulations did not control radioactive emissions such as these, which are considered to be “natural” emissions. Liquefied natural gas products from these sites may contain radon and progeny (Ericson and Pham 2001). Fishbein (1992) reported that coal residue and natural gas emissions release 20,000 and 10,000 Ci of ^{222}Rn each year, respectively, while coal combustion results in 900 Ci of ^{222}Rn production annually.

6.2.2 Water

There is no information on releases of radon to the water from manufacturing and processing facilities because these releases are not required to be reported (EPA 1998).

The amount of radon released to groundwater is a function of the chemical concentration of ^{226}Ra in the surrounding soil or rock and in the water itself (Hess et al. 1985). Radon can dissolve in groundwater following radioactive decay of the radium. High radon concentrations are associated with groundwater running over granitic rock or through alluvial soils originating from granite (Hess et al. 1985; Lam et al. 1994). The physical characteristics of the rock matrix are also important since it is believed that much of the radon released diffuses along microcrystalline imperfections in the rock matrix (Hess et al. 1985). Radon can also enter surface water through decay of radium.

6.2.3 Soil

There is no information on releases of radon to the soil from manufacturing and processing facilities because these releases are not required to be reported (EPA 1998).

As stated in Section 6.2.1, soil is the primary source of radon (NCRP 1984a; Planinić et al. 1994). As such, radon is not released to soil but is the result of radioactive decay of ^{226}Rn within the soil. Hopke (1987) states that normal soil-gas radon measurements are in the range of 270–675 pCi/L of air (10,000–25,000 Bq/m^3). However, levels exceeding 10,000 pCi/L of air (370,000 Bq/m^3) have been documented.

6.3 ENVIRONMENTAL FATE

6.3.1 Transport and Partitioning

The transport of radon from subsurface soil to air is a complex process that is dependent upon characteristics of the soil and meteorological conditions.

Emanation is the process by which radon is transported from the edge of a solid soil matrix to a gas or liquid pore space between the soil grains (Michel 1987). The mechanism by which this process occurs is primarily through alpha recoil. When a ^{226}Ra atom decays, it emits either a 4.6 or 4.8 MeV alpha particle, which results in the formation of a radon atom. The alpha particle takes a virtually straight line path in one direction, heavily ionizing the matrix in one direction and temporarily weakening the local mineral structure. At the same time, the radon atom experiences a 4.6 or 4.8 MeV equal, yet opposite reaction push, called a recoil, that physically moves the atom away from its original location. This recoil aids in moving a radon atom near the surface of a grain to a soil pore. The rate of emanation is typically slower in very dry soils since alpha recoil may also result in moving the recoiled atoms into an adjacent wall of another soil particle rather than an open pore space. On the other hand, if there is a small amount of water

in the pore space, the kinetic energy of the recoiling atom can be dissipated and radon atoms can be slowed sufficiently before becoming embedded into an adjacent soil particle. In a model developed to calculate radon emanation in soil, Sasaki et al. (2004) estimated that the alpha recoil range for radon was 0.02–0.07 μm in common minerals, 0.1 μm in water, and 63 μm in air. Once held within the pore space, radon may be transported by diffusion and convection to the surface where it is ultimately released to air.

The actual release of radon from the pore space or soil-gas to ambient air is called exhalation, while its release from water is called evaporation. The rates of these processes are functions of many variables including the concentration of radon in the soil-gas or water, soil porosity and moisture, meteorological factors (such as temperature and precipitation), and variations in atmospheric pressure (NAS 1999b; WHO 1983). Soil moisture has an important but varying effect on radon release to the air. While lower levels of soil moisture greatly increase emanation by preventing recoil atoms from embedding into adjacent walls of soil particles as described above, saturated soil conditions in which the pores are filled with water tend to slow the rate of diffusion to the surface since the diffusion coefficient of radon is about 3 orders of magnitude lower in water as compared to air (Markkanen and Arvela 1992; Michel 1987; WHO 1983). The influence of moisture and temperature on the radon exhalation rate in concrete, alum shale, and alum shale bearing soil was studied in laboratory experiments (Stranden et al. 1984). The results indicated that for each material, increasing the rate of moisture up to a certain point increased the radon exhalation rate from the material due to enhanced emanation. For concrete samples, the maximum exhalation rate occurred at a moisture content of 4.5–5.5%, for the alum shale, the maximum rate occurred at 10–15%, and for the soil samples, the maximum exhalation rate occurred at 20–30% moisture content (Stranden et al. 1984). As the moisture content increased beyond these levels, a dramatic decrease in the exhalation rate was observed. The authors concluded that when the pores were completely filled with water, the reduced rate of diffusion significantly attenuated the exhalation rate of radon from the material. If the porosity of the samples is high as in the case of the soil, more water can be absorbed by the sample before the pores are filled and the maximum rate of radon exhalation will occur at a higher moisture content than for low porosity materials.

Vertical temperature gradients in the atmosphere can create slight vacuum conditions that pull radon from the soil, or temperature inversions that inhibit this movement. Therefore, meteorological events may both enhance and inhibit transport of radon from the soil into other media. For instance, radon may be released from the soil surface into water from melting snow (Fujiyoshi et al. 2002). Alternatively, winter conditions may cause radon-containing soil-gas to become trapped in frozen soil, thus decreasing transmission of radon to the atmosphere (Bunzl et al. 1998).

Diurnal and seasonal changes affect the behavior of radon at the interface between soil and ambient air by impacting temperature and atmospheric mixing (NAS 1999b; UNSCEAR 2000). Once radon reaches a height of approximately 1 meter above the soil surface, its dispersion is predominantly determined by atmospheric stability (Cohen 1979). This stability is a function of vertical temperature gradient, direction and force of the wind, and turbulence. Temperature inversions in the early morning act to produce a stable atmosphere which keeps radon in the soil or near the ground or water surface. Solar radiation breaks up the inversion, leading to upward dispersion of radon which reverses with radiant cooling in late afternoon (Gesell 1983; NAS 1999b; UNSCEAR 2000). In general, radon levels in air typically decrease exponentially with altitude (Cohen 1979). In a study by Chandrashekara et al. (2006), outdoor radon concentrations at 1 meter above the ground were found to increase during the night, peak in the very early morning, and decrease during the day. In the United States, radon concentrations typically reach their maximum in the summer to early winter, whereas from late winter to spring, concentrations are usually at a minimum as a result of meteorological changes and soil moisture conditions (NAS 1999b).

Sources of indoor radon include entry of amounts released beneath the structure, entry in utilities such as water and natural gas, and release from building materials. Normally, the greatest contribution is that from radon released from soil or rock (Nero 1987; Planinić et al. 1994). Entry occurs primarily by bulk flow of soil-gas driven by small pressure differences between the lower and upper parts of the house interior and the outdoors. The pressure differences are primarily due to differences in indoor/outdoor temperature and the effects of wind (Nero 1987).

In cases where uranium or other metal mine or mill tailings are used for construction purposes, the primary source of indoor radon can be from these materials (Agency for Toxic Substances and Disease Registry 2006). Mill tailings are a rather uniform sand that may be superior to local supplies in quality and price. They have been used for under slab foundations, for concrete and mortar mix (used in laying foundations, block, brick, and stone work), and even as a supplement for vegetable gardens. Radon buildup in such homes, along with direct gamma emissions from radium and radon progeny, contribute to elevated radiation exposure.

Transport of radon in indoor air is primarily a function of the outflow ventilation rate of the enclosure. Most residential heating and air conditioning systems operate in a total recirculation mode, which doesn't contribute to a ventilation rate. Under most conditions, the indoor radon concentration increases in direct proportion to the decrease in ventilation rates (WHO 1983). However, in some indoor radon studies,

radon concentrations showed greater variability than could be accounted for by ventilation rates. This was said to suggest that the strength of the radon source was the main cause of the wide range in observed indoor radon levels (Nero 1987). Behavior of radon in enclosed areas has also been extensively studied and predicted by modeling (Bowring 1992; Eichholz 1987; Kitto 2003).

Transport is primarily a function of the fraction of attachment of radon daughters to dust and dirt particles in the air, the concentration and size of the particles, and the rate of deposition. A major complication of modeling both radon and radon daughter transport indoors is that the outflow ventilation rate acts both to increase flow of radon into the structure and to remove radon and radon daughters from the structure through cracks and openings (Nero 1987). Air circulation rate also acts on the movement of air indoors causing variations in radon concentrations from room to room, as well as within a room.

Mechanisms for transport of radon in groundwater are complex. Just as transport in air is primarily governed by air flow patterns, the transport of radon in groundwater is accomplished by diffusion and, primarily, by the mechanical flow patterns of groundwater (Watson et al. 1993). As previously stated, the diffusion coefficient of radon in water is sufficiently low so that diffusion is only important for movement in very small and poorly ventilated spaces (such as pore spaces). The solubility of radon in water is relatively low (230 cm^3/L of water at 20 °C) and, due to radon's relatively short half-life, much of it will have decayed to polonium and other non-volatile progeny before the groundwater reaches the surface. However, that remaining in solution can be released to ambient air once it is encountered. In areas where groundwater has high levels of radon, release from groundwater may significantly affect ambient air levels.

6.3.2 Transformation and Degradation

6.3.2.1 Air

Regardless of the surrounding media, radon is a noble gas that transforms only by radioactive decay. There are no sinks for radon, and it is estimated that only negligible amounts escape to the stratosphere (Harley 1973). Therefore, the transformation of ^{222}Rn proceeds by alpha-emission with a half-life of 3.8235 days (NNDC 2012b). The half-lives of its first four progeny are much shorter, ranging from 164.3 µsec for ^{214}Po to 26.8 minutes for ^{214}Pb. The half-lives and progeny for ^{219}Rn, ^{220}Rn, and ^{222}Rn (as well as for all known radionuclides) are internationally maintained by DOE (NNDC 2012a) and are shown in Figures 4-1 through 4-3. NIST has developed and provides precise radon emanation rate standards in encapsulated solution form (currently, SRMs 4971, 4972, 4973, and 4974) for use in

calibrating radon monitors. Since ^{222}Rn standards are required for home radon testing, NIST has worked to transfer the U.S. national standards to secondary calibration laboratories (Kotrappa et al. 2005; NIST 2010).

6.3.2.2 Water

Radon undergoes natural radioactive decay in water by the mechanisms described in Chapter 4.

6.3.2.3 Sediment and Soil

Radon undergoes natural radioactive decay in soil by the mechanisms described in Chapter 4.

6.3.2.4 Other Media

Though radon is inert, it can react with highly electronegative elements, such as oxygen, fluorine, and chlorine, to form relatively stable compounds (Hwang et al. 2005; O'Neil et al. 2006). For example, radon reacts with fluorine to form radon fluoride, which has a fairly low volatility (Chernick et al. 1962).

6.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

Reliable evaluation of the potential for human exposure to radon depends in part on the reliability of supporting analytical data from environmental samples and biological specimens. Concentrations of radon in unpolluted atmospheres and in pristine surface waters are typically within the limits of current analytical methods. In reviewing data on radon levels monitored or estimated in the environment, it should also be noted that the amount of chemical identified analytically is not necessarily equivalent to the amount that is available. The analytical methods available for monitoring radon in a variety of environmental media are detailed in Chapter 7.

6.4.1 Air

Outdoor radon levels vary with geographic location and their proximity to radon sources in rocks and soil, water bodies, mines or mill tailings, and fossil-fuel combustion facilities (NAS 1999b). Gesell (1983) provided a compilation of data on radon levels in outdoor air. Measurements were taken over the continental United States, Hawaii, and Alaska. The highest concentrations were found in the Colorado Plateau, which is a region containing high levels of uranium as well as mines and uranium tailings. Measurements in this region ranged from 0.5 to 0.75 pCi/L of air (18.5–30 Bq/m^3). Average values from

the continental United States ranged from 0.12 to 0.3 pCi/L of air (4.4–11 Bq/m^3). More recent estimates based on an analysis of the available data of radon concentrations outdoors and on the transfer from water to air approximate the average outdoor air concentration over the entire United States as approximately 0.4 pCi/L (14.8 Bq/m^3) (NAS 1999b).

Price et al. (1994) reported the statewide median outdoor air concentration in Nevada to be 0.4 pCi/L (15 Bq/m^3), with a range of 0.07–1.40 pCi/L (2.6–52 Bq/m^3) for 50 sites. The ranges correlated to various concentrations of radon in soil as well as uranium and progeny in rocks. In Iowa and Minnesota, Steck et al. (1999) reported average outdoor radon concentrations of 0.82 pCi/L (30 Bq/m^3) and 0.60 pCi/L (22 Bq/m^3), respectively. Values in Iowa ranged from 0.2 to 1.5 pCi/L (7–55 Bq/m^3), while those in Minnesota ranged from 0.1 to 1.5 pCi/L (4–55 Bq/m^3).

Radon concentrations in air decrease with height from the soil surface (NAS 1999b). Several investigators have measured radon levels in the troposphere. Machta and Lucas (1962) measured 0.007 pCi/L of air (0.26 Bq/m^3) at 25,000 feet. Comparable measurements have been taken over Alaska and the southwestern United States (Harley 1973). Radon concentrations measured at a few centimeters above the ground surface may be a factor of 10 higher than measurements from 1 meter above the surface, although this factor would vary with atmospheric conditions (UNSCEAR 2000). The changes in radon concentration with height are thought to be the result of atmospheric conditions (mixing and turbulence) (NAS 1999b).

Numerous studies have been conducted to measure the radon concentrations of indoor air. Nero et al. (1986) reanalyzed up to 38 small data sets, of which 22 were considered unbiased. Biased data were those collected from areas where high radon concentrations were expected. On the basis of the unbiased data, the geometric mean of indoor radon levels was reported to be approximately 0.9 pCi/L of air (33 Bq/m^3). The arithmetic mean concentration was 1.5 pCi/L of air (56 Bq/m^3). Distribution studies of household levels indicated that from 1 to 3% of single-family houses may exceed 8 pCi/L of air (296 Bq/m^3). In this study, many of the measurements were made in main-floor living rooms or average living areas (Nero et al. 1986). On average the relative air concentrations of radon in residential dwellings are 1.8, 1.0, 0.9, and 0.5 pCi/L (66.6, 37, 33.3, and 18.5 Bq/m^3) for the basement, first, second, and third floors, respectively (Planinić et al. 1994), indicating that radon concentrations decrease with distance from the earth's surface. The National Residential Radon Survey conducted in 1989 and 1990 (published in 1992) determined that the indoor average concentration of radon for U.S. homes was approximately 1.25 pCi/L (46.3 Bq/m^3) (Marcinowski et al. 1994). Approximately 6% of homes studied

(5.8 million homes in 1990) had radon levels exceeding the EPA's recommended action level of 4 pCi/L (148 Bq/m^3) (Marcinowski et al. 1994).

A screening assessment conducted by the EPA of 55,000 homes located in 38 different states indicated that six counties in the Three Mile Island vicinity of Pennsylvania (Cumberland, Dauphin, Lancaster, Lebanon, Perry, and York) had the highest regional average indoor air levels of radon (17.8 pCi/L) (Field 2005). The author suggested that these high radon levels are the main source of radiation exposure to residents in this area and have not often been accounted for in epidemiological studies of residents in this area. Homes built in contact with bedrock may have a higher likelihood of elevated radon concentrations in indoor air. Brookins (1991) reported high indoor radon levels in residential dwellings of Albuquerque, New Mexico. These values correspond to high soil radon levels in the area, although they may have also been affected by the type of building materials used in the homes. Four of five adobe buildings showed radon levels >4 pCi/L (ranging from 2.0 to 10.7 pCi/L), while smaller percentages of homes utilizing other construction methods had elevated levels.

In an EPA assisted survey of indoor radon concentrations within 30 states, concentrations were found to vary widely between states. Additionally, houses with livable basements had higher radon concentrations than houses without basements. The mean concentration for those with basements ranged from 1.8 pCi/L (67 Bq/m^3) in Arizona and California to 9.4 pCi/L (348 Bq/m^3) in Iowa. Those without basements had mean concentrations ranging from 0.5 pCi/L (19 Bq/m^3) in Louisiana to 5.5 pCi/L (204 Bq/m^3) in Iowa (White et al. 1992).

Indoor radon levels were measured in homes located in the Reading Prong area of Pennsylvania. This area has an unusual abundance of homes with high radon concentrations that is presumed to be from geologically produced emanation of radon. Indoor levels of radon in this area ranged from 4–20 pCi/L (150–740 Bq/m^3) in 29% of the homes to >80 pCi/L (3,000 Bq/m^3) in 1% of the homes (Fleischer 1986). During a hot spot survey, indoor residential radon levels, also in the Reading Prong area, ranged from 0.2 to 360 pCi/L (Lewis 1996).

6.4.2 Water

In a nationwide survey by the EPA, almost 2,500 public drinking water supplies were sampled (nonrandom) with most of these serving greater than 1,000 people (Cothern et al. 1986). Average concentrations for U.S. groundwater were estimated to be 240 pCi/L of water (8.8 Bq/L) for larger

systems (>1,000 persons served) and 780 pCi/L of water (28.9 Bq/L) for smaller systems. The nationwide average for all groundwater samples tested in this study was 351 pCi/L (13 Bq/L). The highest levels reported were in smaller groundwater systems in Maine that averaged 10,000 pCi/L (370 Bq/L); lowest average levels were found in larger systems in Tennessee with levels of 24 pCi/L (0.9 Bq/L). Small, private groundwater systems appear to have higher radon concentrations than larger systems (Swistock et al. 1993; Watson et al. 1993). The average radon concentration in groundwater-derived public water supplies is approximately 540 pCi/L (20 Bq/L), although some public water supplies have been found to have radon concentrations up to $1x10^7$ Bq/m^3 (270,000 pCi/L) (NAS 1999b). Longtin (1988, 1990) has compiled the results of a comprehensive monitoring study (1984–1986) regarding the levels of radon, radium, and uranium in public drinking water supplies in the United States. The results indicated that over 72% of the sites sampled had radon concentrations greater than the minimum reporting limit of 100 pCi/L (3.7 Bq/L), and a maximum concentration of 25,700 pCi/L (951 Bq/L) was observed. The USGS conducted a comprehensive groundwater monitoring study (1992–2003) of aquifers across the United States for the presence of radon and various trace elements (USGS 2011). The median concentration of radon (n=3,877) was 430 pCi/L (15.8 Bq/L), with a maximum level of 220,000 pCi/L (8,140 Bq/L).

The relationship between radon concentrations in groundwater and system size (concentrations tend to increase with decreasing system size) was previously reported by Hess et al. (1985). This correlation may reflect a relationship between system size and aquifer composition. Those rock types that are associated with high radon levels (granitic rock) do not form aquifers large enough to support large systems. However, smaller systems may tap into such aquifers. Additionally, radon concentrations tend to decrease as the well depth increases, which may be attributed to the substrate composition at the various depths (Field and Kross 1998).

Crystalline aquifers of igneous and metamorphic rocks generally have higher radon levels than other aquifer types. Aquifers comprised of granites or alluvial soils derived from granite consistently show the highest levels (Lam et al. 1994; Michel 1987), though sandstone and feldspar substrates are also correlated to high radon levels (Lam et al. 1994). Average radon levels in water from granite aquifers are usually ≥2,703 pCi/L of water (100 Bq/L) (Michel 1987). This is indicated in the data of Cothern et al. (1986) which report the following trends in groundwater radon levels: in New England and the Piedmont and Appalachian Mountain Provinces, where igneous and metamorphic rocks form the aquifers, concentrations are in the range of 1,000–10,000 pCi/L of water (37–370 Bq/L); in the sandstone and sand aquifers that extend from the Appalachian Mountains west to the Plains, concentrations are generally

<1,000 pCi/L of water (37 Bq/L). NAS (1999b) also reported high radon concentrations in public water supplies for New England, the Appalachian states, and the Rocky Mountain states, as well as areas of the Southwest and Great Plains. A granitic substrate in the San Joaquin Valley of California contributes to high radon concentration in groundwater. The groundwater of several California counties contains levels of radon as high as 1,000–10,000 pCi/L (Lam et al. 1994).

A study of groundwater from 48 Pennsylvania counties indicated a median radon concentration of 1,100 pCi/L for all samples, with a maximum concentration of 141,270 pCi/L. The highest concentrations were present in samples obtained from Southeastern Pennsylvania, which includes geologic formations typical of high radon emission (Swistock et al. 1993). In North Carolina, the arithmetic mean radon concentration tested in groundwater supplies of 400 homes was 1,800 pCi/L (67 Bq/L) (Watson et al. 1993).

It has been reported that the radon concentration in surface waters is usually <4,000 Bq/m^3 (108 pCi/L) NAS (1999b).

6.4.3 Sediment and Soil

Because radon is a gas, its occurrence in soil is most appropriately referred to as its occurrence in "soil-gas," which is the gas or water-filled space between individual particles of soil. Factors that affect radon soil-gas levels include radium content and distribution, soil porosity, moisture, and density. However, soil as a source of radon is seldom characterized by radon levels in soil-gas, but is usually characterized directly by emanation measurements or indirectly by measurements of members of the ^{238}U series (NRC 1981). Radon content is not a direct function of the radium concentration of the soil, but radium concentration is an important indicator of the potential for radon production in soils and bedrock. However, Michel (1987) stated that average radium content cannot be used to estimate radon soil-gas levels, primarily due to differences in soil porosity. Similarly, Fujiyoshi et al. (2002) found that radium content may not control radon concentration in soil. In the study, radium concentrations were fairly consistent across various sites though the radon concentrations varied.

Despite such caveats, theoretical rates of radon formation in soil have been estimated as demonstrated by the following (Nevissi and Bodansky 1987):

> Consider a cube which is 1 meter in each dimension. Using rounded numbers, if the average density of the soil is 2.0 grams per cubic-centimeter and the average radium-226

concentration is 1.0 pCi/g (0.037 Bq/g), the cube will contain 2 million grams of soil and $2x10^{-6}$ Ci ($7.4x10^4$ Bq) of radium-226. This corresponds to the production of $7.4x10^4$ radon atoms per cubic-meter per second and the escape of 7,400 atoms per square-meter per second, in rough correspondence to the average measured value. In alternative units, the figure of 0.5 pCi per square-meter per second corresponds to the emission of 16 Ci of radon per square-kilometer per year.

For a discussion of ^{238}U and ^{226}Ra levels in soil, see the ATSDR Toxicological Profiles for uranium and radium (Agency for Toxic Substances and Disease Registry 1999a, 2011).

Brookins (1991) reported the average concentration of radon in soil-gas in the United States is approximately 100 pCi/L. However, this value does not compare well with two soil-gas measurements for U.S. locations found in the literature: one from Spokane, Washington, with soil-gas radon levels of 189–1,000 pCi/L (7,000–37,000 Bq/m^3) in soils formed from coarse glacial outwash deposits with 2.3 ppm uranium, and the other from Reading Prong, New Jersey, with soil-gas radon levels of 1,081–27,027 pCi/L of air (40,000–1,000,000 Bq/m^3) (Michel 1987). Hopke (1987) states that normal soil-gas radon measurements are in the range of 270–675 pCi/L (10,000–25,000 Bq/m^3).

Radon levels in soil-gas can fluctuate greatly, both temporally and spatially (Bunzl et al. 1998). A Bavarian study found that the concentration of radon in soil-gas of a high gravel content soil was higher at a depth of 0.5 m than at 1.0 m during the winter months, whereas in the summer, concentrations at the 1.0-m depth were higher. Bunzl et al. (1998) reasoned that high levels exhibited during the winter months were most likely the result of frozen soil conditions, whereby transmission of radon to the atmosphere is decreased and thus, levels in soil-gas are increased. The annual mean concentration at a depth of 0.5 m was observed to be 17.1 kBq/m^3 (462 pCi/L) while the mean level at a depth of 1.0 m was 15.2 kBq/m^3 (411 pCi/L) (Bunzl et al. 1998). At a depth of 38 cm, radon levels were found to range from 40 to 890 pCi/L in Albuquerque, New Mexico. The average summer value was 360 pCi/L, while the average winter levels were 200 pCi/L (Brookins 1991).

6.4.4 Other Environmental Media

Limited information exists to indicate that plants absorb both ^{226}Ra and ^{222}Rn from the soil layer and that these compounds are translocated to above ground plant parts (Taskayev et al. 1986). However, there is little information on the quantitative contribution of this process to exposure from ingestion of plant crops or of emanation rates from these plants. A measurement of the emission rates of radon from field corn was located in the literature. ^{222}Rn flux from leaves was reported to be $2.47x10^{-4}$ pCi

($9.15x10^{-6}$ Bq)/cm^2/second. This rate was 1.8 times greater than the exhalation rate from local soil (Pearson 1967). Solubilized radon can be removed from the soil by plants through evapotranspiration, where it is subsequently released to the atmosphere by diffusion through the leaf. Kozak et al. (2003) designed a flow and transport model to describe the transport or radon and radium through soil and vegetation.

6.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

In the following section, exposure to radon is discussed in terms of environmental levels rather than in terms of actual or estimated dose. The estimation of whole body or target tissue dose of radionuclides is extremely complex and must be accomplished by mathematical models for the specific radionuclide. Although such models are available to estimate whole body and target tissue dose for radon, discussion of these lies outside the scope of this document. For a discussion of these models, the reader is referred to NCRP (1984a) or NAS (1999a).

The general population is exposed to radon by inhalation, both outdoors and indoors, as well as by ingestion. Radon concentrations in outdoor air often correspond to soil gas levels (Price et al. 1994), although concentrations vary widely with geographical location, depending on factors such as the radium content, soil porosity, and moisture content. Comparing data from multiple studies, NAS (1999b) reports that the mean radon concentrations range from 1 to 63 Bq/m^3 (0.027–1.7 pCi/L) with the highest values reported in Iowa and Maine, with an overall average radon concentration of 0.32 pCi/L (12 Bq/L). Measurements in Iowa and Minnesota show average outdoor concentrations of 0.60–0.82 pCi/L (Steck et al. 1999). The average outdoor air concentration of radon over the entire United States is approximately 0.4 pCi/L (NAS 1999b). Due to the gaseous nature of radon, radon levels will decrease with increasing height from the soil surface; however, Price et al. (1994) reported that radon concentrations in Nevada obtained at heights of 0.5, 1.0, and 2.0 m from the surface were not statistically different from each other. This indicates that adults and children sitting or standing in the same location are exposed to similar concentrations.

Average radon levels indoors are found to be higher than ambient outdoor levels (Steck et al. 1999). When the general population encounters elevated concentrations of radon, it generally is while indoors, such as at home, school, or work where concentrations exceed the EPA-recommended action level of 4 pCi/L (CDC 1999). The National Residential Radon Survey conducted in 1989 and 1990 (published in 1992) determined that the indoor average annual concentration for U.S. homes was approximately

1.25 pCi/L (EPA 2003; Marcinowski et al. 1994). Approximately 6% of homes studied (5.8 million homes in 1990) had radon levels exceeding the EPA's action level of 4 pCi/L (Marcinowski et al. 1994). Two large indoor monitoring efforts in the United States reported arithmetic mean levels ranging from 1.5 to 4.2 pCi/L of air (55–157 Bq/m^3) (Alter and Oswald 1987; Nero et al. 1986). The data from Alter and Oswald (1987) are limited in that the dwellings do not represent a random sample and individual measurement values were reported rather than average concentrations from a residence.

The composition and physical properties of concrete, such as porosity, can affect the rate by which radon moves through an intact concrete slab and enters a home. Renken and Rosenberg (1995) estimated that a typical basement with a 1,500 ft^2 (140 m^2) concrete slab would have approximately 7.1 Bq/hour of radon diffusing through the concrete slab. Decreasing the porosity, permeability, and diffusion coefficient of the concrete mix can result in less radon gas diffusing through the slab and into the home.

Although the primary source of indoor radon is from soil, release of radon from water may contribute to indoor levels (Fishbein 1992; Lam et al. 1994). Nazaroff et al. (1987) performed an analysis that combined information on water use, efficiency of radon release from water, house volumes, and ventilation rates to determine the impact on indoor radon levels. Their analysis estimated that use of groundwater contributes an average of 2% to the mean indoor radon concentration in houses. Lam et al. (1994) concluded that groundwater may contribute 1–5% of indoor radon. As with levels in other media, levels of radon in groundwater vary greatly. In areas with high groundwater levels, the relative contribution to indoor radon levels will increase accordingly. Cothern et al. (1986) report a daily intake of radon originating from drinking water of 100–600 pCi (3.7–22.2 Bq)/day, assuming that consumption was 2 L/day of groundwater. Additionally, small groundwater systems appear to have higher radon concentrations than larger systems (Swistock et al. 1993).

The contribution of building materials to indoor radon (other than homes where metal mine or mill tailings have been used in construction) is estimated to be low in comparison with amounts which originate from soil and rock. In general, among common building materials, concrete and gypsum board release more radon than other materials.

The type of concrete used in a house slab can affect the rate at which radon diffuses from the ground through a basement slab and into the home. Renken and Rosenberg (1995) assessed porosity, permeability, and diffusion constants through three mix types. Diffusion constants in increasing order were 4.96×10^{-4} $cm^2 second^{-1}$ for a typical basement slab concrete mix, 9.09×10^{-4} $cm^2 second^{-1}$ for concrete

with an increased water:cement ratio, and $1.43x10^{-3}$ $cm^2second^{-1}$ for concrete with substituted fly ash. The respective porosities for these slabs were 0.12, 0.17, and 0.20. It was concluded that controlling the porosity of a concrete slab can reduce the rate of radon transmission into a house.

Active soil depressurization (ASD) was assessed for its effectiveness in mitigating radon in a home with basement concentrations averaging 7,580 Bq/m^3 (205 pCi/L). The system reduced levels to 520 Bq/m^3 (14 pCi/L). After a more powerful fan was installed to increase vacuum, radon levels in the basement unexpectedly increased to 1,070 Bq/m^3 (29 pCi/L). Upon reversal of the fan direction to produce an active soil pressurization system (ASP), the large fan reduced levels to 63 Bq/m^3 (1.7 pCi/L). Reinstallation of the small fan into the ASP system further reduced the radon level to 44 Bq/m^3 (1.2 pCi/L). The indications are that an overly forceful ASD vacuum can break the ground seal, reducing its effectiveness, and that ASP might be more effective than ASD in some cases (Kearney and Mason 2011).

Persons who are occupationally exposed to radon typically are those employed in mining and milling, primarily underground mining of uranium and hard rock (NIOSH 1987), but which also include silver, tin, bertrandite and beryl ores, and other mines (Kaczynski 2011; Lubin et al. 1994). Exposure to radon in underground mines has been shown by numerous studies to be a high risk factor for developing lung cancer (EPA 2003), particularly for miners in China, the Czech Republic, the United States, and Canada (Lubin et al. 1994). Exposures in above-ground mines and in mills are typically lower.

NIOSH reports that in 2005, 22,838 workers were employed in underground metal and nonmetal mines in the United States, with 29,705 workers employed at all underground mines (including metal, nonmetal, coal, and stone mines) (NIOSH 2008a). In 2005, 263 metal mines and 739 nonmetal mines were reported (NIOSH 2008b). The number of underground uranium mines has decreased from 300 in 1980 to 16 in 1984 (NIOSH 1987) to 17 in 1992 (EPA 1995), although the number may have increased to <100 in 2003 (IAEA 2004). The number of employees in underground uranium mines has decreased from 9,000 in 1979 to 448 in 1986 (NIOSH 1987), although figures were not available for later years. Measurements of radon progeny concentrations in these mines from 1976 to 1985 showed annual geometric mean concentrations in uranium mines of 0.11–0.36 WL (equivalent to 22–72 pCi/L of air [800–2,664 Bq/m^3] assuming an equilibrium factor of 0.5), with 95^{th} percentile levels ranging up to 2.73 WL (546 pCi/L of air; 20,202 Bq/m^3). Annual geometric mean levels in phosphate mines for the same period were 0.12–1.20 WL (24–240 pCi/L of air [888–8,880 Bq/m^3]) with 95^{th} percentile levels as high as 1.69 WL (338 pCi/L of air; 12,506 Bq/m^3). Measurements in uranium/vanadium mines showed annual geometric

mean concentrations similar to those in uranium mines. However, 95th percentile levels ranged up to 4.80 WL (960 pCi/L of air [$3.6x10^4$ Bq/m^3]), which was the highest annual concentration reported among the different types of mines (NIOSH 1987). Estimates of annual cumulative radon progeny exposures indicated that of the 1,405 underground uranium miners working in 1984, 28% had exposures >1 WL (200 pCi/L of air; 7,400 Bq/m^3). As uranium is a minor impurity in bertrandite and beryl ores, radon may be present above ambient levels where these ores are processed, such as at a beryllium extraction facility located in Delta, Utah (Kaczynski 2011).

Radon exposure in underground mines has been vastly reduced by installation of improved engineering controls. In New Mexico mines, the median annual exposure in 1967 of 5.4 WLM was reduced to 0.5 WLM by 1980 due to these improvements (Eichholz 1987). For 1982, Samet et al. (1986) reported a mean WLM of 0.7. A WLM expresses both intensity and duration of exposure (see Chapter 3 for further discussion).

MSHA regulates safety practices and worker protection in the mining industry. OSHA has established air monitoring requirements for underground mines and exposure limits for mine workers. These involve monitoring mine exhaust air for radon daughters, with values >0.1 WL for areas where uranium is mined (or between 0.1 and 0.3 WL for areas where uranium is not mined) requiring periodic monitoring of air representative of the workers' breathing zones (MSHA 2011c). Workers are not to be exposed to concentrations exceeding 1.0 WL in any active mine area (MSHA 2011b). In cases where accepted engineering control measures have not been implemented or when work conditions require, higher-level exposure is permitted under an appropriate respiratory protection program (MSHA 2001d). The goal is to ensure that no underground mine worker receives >4 WLM in any calendar year (MSHA 2011a).

Occupational exposure to radon can extend beyond mining. Water-plant operators may be exposed to high levels of radon gas created during the water treatment process. This occurs when radon emanates from water to air during the aeration process or when filter material to strip out uranium or radium is removed for disposal as radioactive waste. The geometric annual mean air concentration of radon in 31 water plants was 3.4 pCi/L (126 Bq/m^3), with a maximum value of 133 pCi/L (4,921 Bq/m^3) (Fisher et al. 1996). A high exposure risk is also present for employees at radioactive contaminated sites, nuclear waste repositories, natural caverns, phosphate fertilizer plants, oil refineries, utility and subway tunnels, excavators, power plants, natural gas and oil piping facilities, health mines and spas, fish hatcheries, and hospitals (EPA 2003; Field 1999; Fisher et al. 1996). Higher exposure risks are also present for farmers,

radon mitigation professionals, and scientists, although exposure to local radon sources can occur in any occupation (Field 1999).

6.6 EXPOSURES OF CHILDREN

This section focuses on exposures from conception to maturity at 18 years in humans. Differences from adults in susceptibility to hazardous substances are discussed in Section 3.7, Children's Susceptibility.

Children are not small adults. A child's exposure may differ from an adult's exposure in many ways. Children drink more fluids, eat more food, breathe more air per kilogram of body weight, and have a larger skin surface in proportion to their body volume. A child's diet often differs from that of adults. The developing human's source of nutrition changes with age: from placental nourishment to breast milk or formula to the diet of older children who eat more of certain types of foods than adults. A child's behavior and lifestyle also influence exposure. Children crawl on the floor, put things in their mouths, sometimes eat inappropriate things (such as dirt or paint chips), and spend more time outdoors. Children also are closer to the ground, and they do not use the judgment of adults to avoid hazards (NRC 1993).

Exposure levels at schools were utilized to provide an estimate of radon levels to which children may be exposed during the school day. However, limited U.S. data were available to address radon exposure of children.

The EPA recommends that all schools test for radon and mitigate areas with elevated concentrations. EPA's 1990 National School Radon Survey obtained radon measurements from 927 randomly selected schools across the United States. Based on these measurements, it is estimated that approximately 15,000 U.S. schools have at least one room with a potential for long-term elevation of radon levels. Radon is often unevenly distributed within a building. Overall, short-term radon concentrations in roughly 2.7% of all ground contact schoolrooms were >4 pCi/L, indicating 73,000 schoolrooms with a potential radon problem (EPA 1993c).

Additionally, higher respiration rates of children may influence the extent of radon and radon progeny inhaled. MacDonald and Laverock (1998) studied the exposure levels of soil-dwelling mammals in a radon-rich environment, concluding that larger mammals with higher lung capacities were least affected by radon. Most affected were smaller mammals with higher respiration rates. Using this logic, small

children with high respiration rates, as compared to adults, may receive relatively higher radiation doses from inhaled radon and radon progeny.

Kendall and Smith (2005) examined the doses of radon and its decay products inhaled or ingested by 1-year-old infants and 10-year-old children in the United Kingdom. The largest internal doses were found to be associated with the organ of intake (the respiratory tract and stomach). Dose coefficients (or the dose per unit intake factors) were found to be higher for children than for adults, although the overall annual doses were fairly consistent between children and adults (likely due to the smaller amount of air and water consumed by children).

6.7 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

Populations with potentially high exposures include those occupationally exposed. Those who use excavation equipment or are employed at underground mines (uranium, hard rock, and vanadium), water treatment plants, radioactively contaminated sites, natural caverns, phosphate fertilizer plants, oil refineries, utility and subway tunnels, fossil fueled power plants, natural gas and oil piping facilities, health mines and spas, and fish hatcheries have the potential to be more highly exposed to radon (EPA 2003; Field 1999; Fisher et al. 1996). Higher exposures are also possible for farmers, radon mitigation professionals, and scientists (Field 1999).

High radon exposure can occur in any location with geologic radon sources (see http://www.epa.gov/radon/zonemap.html) (EPA 2011a; Field 1999). High outdoor air radon concentrations were reported in Iowa, Main, and Minnesota NAS (1999b). NAS (1999b) also reported high radon concentrations in public water supplies for New England, the Appalachian states, and the Rocky Mountain states, as well as areas of the Southwest and Great Plains. Though the average radon concentration in groundwater-derived public water supplies is approximately 540 pCi/L (20 Bq/L), some public water supplies have been found to have radon concentrations up to $1x10^7$ Bq/m^3 (270,000 pCi/L) (NAS 1999b).

Communities that are very near uranium or phosphate mill tailing piles may have increased environmental radon levels. In addition, in some areas, mill tailings have been used as fill dirt, garden soil, sub-base for concrete slabs, and sand mix for brick mortar in home construction (for example, in Monticello, Utah) (Agency for Toxic Substances and Disease Registry 1997). Persons in these communities could be exposed to levels of radon exceeding typical indoor background levels.

6.8 ADEQUACY OF THE DATABASE

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

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

6.8.1 Identification of Data Needs

Physical and Chemical Properties. Information is available on the physical and chemical properties of radon, and parameters that influence the behavior of radon in the environment have been determined. Therefore, no data needs are identified concerning physical and chemical properties of radon.

Production, Import/Export, Use, Release, and Disposal. According to the Emergency Planning and Community Right-to-Know Act of 1986, 42 U.S.C. Section 11023, industries are required to submit substance release and off-site transfer information to the EPA. The TRI, which contains this information for 2006, became available in March of 2008. This database is updated yearly and should provide a list of industrial production facilities and emissions.

The production of radon occurs directly from a radium source either in the environment or in a laboratory environment. The disposal of gaseous radioactive effluents has been documented. Increased radon concentrations have been detected in waste generated by uranium and phosphate mining; therefore, these sites should be monitored on a continual basis. Although there are regulations for disposal of radionuclides in general, there are none that specifically address disposal of materials due to their radon

content. If such regulations were promulgated, they would be developed by states since the Federal government has no authority in this area.

Environmental Fate. Information is available on the environmental fate of radon in air and water and on the transport of radon in environmental media. Factors that affect the partitioning of radon from soil or water to air have been identified. Movement of radon into and within homes and the influence of meteorological conditions and other parameters on this movement should continue to be investigated. Transformation of radon has been adequately characterized. There is limited information on the uptake and release of radon by plants. Additional research of this phenomenon is needed in order to determine the relative contribution plants provide to atmospheric levels. Exposure from smoking tobacco should be explored.

Bioavailability from Environmental Media. Radon and radon progeny are known to be released from air and water and information is available, which characterizes the relative contribution of various media to levels of radon in air and water.

Food Chain Bioaccumulation. Since radon is a noble gas, it will not bioaccumulate. However, bioaccumulation has been reported for radon progeny such as ^{210}Pb in cephalopods (Khan and Wesley 2011) and ^{210}Po in marine birds (Skwarzec and Fabisiak 2007), mushrooms (Skwarzec and Jakusik 2003), cephalopods (Khan and Wesley 2011), and coastal sand dune wild legumes (Bhat et al. 2005).

Exposure from Environmental Media. Reliable monitoring data for the levels of radon in contaminated media at hazardous waste sites might be helpful, particularly if uranium mine tailings have been disposed of at these sites.

Information is available regarding the levels of radon in indoor air, outdoor air, and water. Continued comprehensive data on levels of radon in ambient air are needed in order to assess potential human exposure. The measurement of indoor and ambient radon levels are not mandated, and EPA has found that most homeowners do not choose to spend the money to have these measurements made.

Exposure Levels in Humans. EPA maintains information on those states and jurisdictions that have enacted Radon-Resistant New Construction building codes (EPA 2011g). Large-scale monitoring of radon in public buildings (e.g., schools) was conducted in the 1990s. Limited information for the United States in general is available on remediation activities conducted in response to those measurements and

the resulting radon levels, or on radon levels in building constructed since that time. Radon is a naturally occurring gas and is ubiquitous in the environment; therefore, humans are constantly exposed to some level of radon. The primary pathway for human exposure to radon is inhalation from soil gas intrusion to dwellings and buildings. Outdoor radon levels vary with geographic location and their proximity to radon sources in rocks and soil, water bodies, mines or mill tailings, and fossil-fuel combustion facilities. Since the half-life of radon is short, its measurement in biological samples, such as serum, urine, blood, etc., is not practical. Concentrations of radon progeny are measurable in urine, blood, bone, teeth, and hair, and these levels can be used to provide some indication of exposure; however, they are not direct measurements of levels of exposure. These estimates may be derived through use of mathematical models.

This information is necessary for assessing the need to conduct health studies on these populations.

Exposures of Children. Limited information is available to address radon exposure of children, particularly within the United States. Some communities require testing of schools for radon and abatement if levels are ≥4 pCi/L (NJDEP 2004). Available data were not always in agreement, and thus, conclusions were difficult to assess. Studies are needed to better characterize exposure levels specific to children in the United States.

Child health data needs relating to susceptibility are discussed in Section 3.12.2, Identification of Data Needs: Children's Susceptibility.

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

The Hanford Environmental Foundation in Richland, Washington, maintains a registry of United States uranium miners and millers. The data in the registry are derived from autopsy material and include exposure information. Since uranium decays to radon, this exposure registry on miners and millers may provide information on radon exposure. The NIOSH dose reconstruction and worker compensation programs should also be addressed.

6.8.2 Ongoing Studies

No ongoing studies were identified.

7. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting, measuring, and/or monitoring radon and its progeny. The intent is not to provide an exhaustive list of analytical methods. Rather, the intention is to identify well-established methods that are used as the standard methods of analysis. Many of the analytical methods used for environmental samples are the methods approved by federal agencies and organizations such as EPA and the National Institute for Occupational Safety and Health (NIOSH). Other methods presented in this chapter are those that are approved by groups such as the Association of Official Analytical Chemists (AOAC), the American Public Health Association (APHA), the National Radon Safety Board (NRSB), and the National Radon Proficiency Program (NRPP), which is operated jointly by the National Environmental Health Association (NEHA) and the American Association of Radon Scientists and Technologists (AARST). Additionally, analytical methods are included that modify previously used methods to obtain lower detection limits and/or to improve accuracy and precision.

7.1 BIOLOGICAL MATERIALS

Table 7-1 lists various methods used to detect radon progeny in biological samples. Since the half-life of radon is short, its measurement in biological samples, such as serum, urine, blood, etc., is not practical. Measurements of the longer lived radon progeny ^{210}Pb and ^{210}Po in biological samples may be used as an indication of radon exposure; however, ingestion of these isotopes from food and drinking water or direct exposure from other environmental media are considered the primary sources of exposure for these isotopes. Therefore, while this chapter discusses the analysis of ^{210}Pb and ^{210}Po in biological media, their presence in the body arises from a variety of sources, not just direct inhalation of radon, and should not be considered unique biomarkers of radon exposure.

A method of estimating individual, chronic human exposure to natural waterborne radionuclides using *in vivo* skull measurements and *in vitro* urine measurements of ^{210}Pb and natural uranium (^{234,235,238}U) is described by Muikku et al. (2003). Four, high-purity broad energy Ge detectors, situated near the top and back of the head, measure the activity of the 186 keV ^{235}U and 46 keV ^{210}Pb gamma rays. Urine samples were analyzed with inductively coupled plasma mass spectrometry (ICP-MS) for uranium content (Muikku et al. 2003). A similar technique was used by Eisenbud et al. (1969), who concluded that *in vivo* skull measurements of ^{210}Pb allow cumulative exposure to radon daughters to be estimated in uranium miners. *In vivo* measurements of ^{210}Pb in the knee have also been reported (by measuring the 46 keV

Table 7-1. Analytical Methods for Determining Radon Progeny in Biological Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Reference
Tooth	Clean and dry tooth; dry overnight and grind to fine powder; separate enamel from dentin and compress into pellets; coat with titanium nitride	PIXE for total lead content in teeth	0.5 ppm	Anttila 1987
Urine, blood, hair, feces	Wet ash in HNO_3-$NaClO_4$, electrostatic precipitation	Alpha spectometry	0.1 pCi ($3.7x10^{-3}$ Bq)	Gotchy and Schiager 1969
Urine, blood, hair	Wet ashing with concentrated nitric acid and hydrogen peroxide, followed by drying and dissolution in hydrochloric acid solution	Alpha particle counting of ^{209}Po (4.866 MeV) and ^{210}Po (5.305 MeV) using silicon surface barrier detectors	1.1–1.5 mBq/L (24-hour counting time)	Al-Arifi et al. (2006)
Blood	Wet ash and plate on disk	Autoradio-graphy of alpha tracks, using nuclear emulsion	No data	Weissbuch et al. 1980
Bone	Wash with acetone, hydrogen peroxide and isopropanol followed by drying and homogenization to a grain size of 1–3 mm	Gamma ray spectrometry (46.5 keV ^{210}Pb) using HPGe detector	0.4–0.7 mBq per gram of sample	Johnston et al. 2005
Bone	Extract fat with anhydrous benzene; wet ash using nitric acid and perchloric acid	Alpha particle counting ^{210}Po using a ZnS(Ag) scintillation counter	No data	Blanchard et al. 1969
Bone	*In vivo*	Whole body gamma ray spectroscopy (46 keV ^{210}Pb)	No data	Eisenbud et al. 1969
Tissue	Immediate measurement of dissected tissue samples following inhalation exposure	Gamma ray activity using a NaI(Tl) scintillation counter	No data	Nussbaum and Hursh 1957
Tissue (Brain)	Homogenize tissue in trichloroacetic acid solution followed by centrifugation	Alpha particle counting of ^{210}Po and beta particle counting of ^{210}Bi	$1x10^{-5}$ Bq per gram tissue	Momčilović et al. 1999

HPGe = High purity germanium; PIXE = proton induced X-ray emission analysis

gamma ray); however, calibration for the skull is generally simpler than for the knee (Johnston et al. 2005).

Urine analysis and whole body counting have been used to measure levels of radon progeny in humans. It is generally known that ^{210}Pb is deposited primarily in bone with a relatively long biological half-life, which enables it to reach transient radioactive equilibrium conditions with its descendant, ^{210}Po (Clemente et al. 1984). The short half-lives of radon and the daughters, ^{218}Po through ^{214}Po, preclude their detection through normal bioassay techniques that typically require a day or more after the sample has been collected before counting can commence (Gotchy and Schiager 1969).

Al-Arifi et al. (2006) discussed an analytical method for measuring levels of ^{210}Po in samples of blood, urine, and hair for various populations using a high resolution alpha spectrometer. Although the main route of ^{210}Po intake by the human body is the ingestion of food, smoking, ingestion of drinking water, and inhalation of radon may also contribute to the body burden.

Radon exposure in humans is typically assessed by monitoring air levels indoors, outdoors, and under occupational settings as discussed in Section 7.2.

7.2 ENVIRONMENTAL SAMPLES

Most methods of measuring radon and its decay products in environmental samples are based on the detection of alpha particles emitted during the radioactive decay process, although some methods are based on the detection of emitted gamma rays. Detailed reviews of the measurement of radon and its progeny in environmental samples can be found in NCRP (1988), George (1988), and European Commission (1995). EPA issued updates regarding radon measurement techniques in 1992 and provided general guidelines for optimal measurement conditions, device placement, and documentation of results (EPA 1992a). EPA has also issued technical guidance for measuring radon concentrations in residences (EPA 1993b).

There are several generalizations about the measurement of radon that apply regardless of the specific measurement technique used. Radon concentrations in the same location may differ by a factor of 2 over a period of 1 hour. Also, the concentration in one room of a building may be significantly different than the concentration in an adjoining room. Therefore, improvements in sampling methodology would be helpful. Since the accuracy and level of uncertainty of individual measurements are important, especially

when assessing the implications of elevated readings, the measurement uncertainty should be reported for each sample analysis result.

Air radon and radon progeny measurement devices fall broadly into two categories: passive devices and continuous monitor devices (AARST 2006). Passive radon monitors allow air to diffuse into a sensor chamber and do not require any power to operate. However, passive monitors only provide average concentrations for the entire sampling time period (usually at least 48 hours) and typically require laboratory analysis to determine radon concentrations. Continuous radon monitors (CRMs) measure radon gas and continuous working level monitors (CWMs) measure radon progeny. These continuous monitoring devices can record and review radon concentrations in time increments of ≤1 hour, but may require a power source. CRMs are commercially available to home inspectors or radon testing professionals. The principles by which radon detectors operate are described in the following paragraphs.

Activated charcoal adsorption devices are inexpensive, passive detectors used for monitoring radon in air samples. Commercially available devices are often sold at hardware or home improvement stores for estimating radon levels in households or buildings. A typical detector consists of a circular, 6–10 cm diameter container that is approximately 2.5 cm deep and filled with 25–100 g of activated charcoal (EPA 1992a). One side of the container is fitted with a screen that encloses the charcoal sample and allows air to diffuse in. The passive nature of these detectors allows for the continuous adsorption and desorption of radon, and the adsorbed radon undergoes radioactive decay during the measurement period. Following a brief exposure period (2–7 days), the charcoal detectors are returned to a laboratory and analyzed directly by counting gamma rays emitted by the radon decay products on the charcoal using a sodium iodide gamma detector. The detector may be used in conjunction with a multi-channel gamma spectrometer or with a single-channel analyzer with the window set to include the appropriate gamma energy window. The detector system and detector geometry must be the same used to derive the calibration factors for the device (EPA 1992a). Alternatively, the sample may be desorbed by an aromatic solvent (typically toluene or benzene) and analyzed using liquid scintillation counting using an appropriate fluor solution.

Indoor radon levels are also frequently measured using alpha track detection devices (EPA 1992a). The detector consists of a small piece of plastic or film enclosed in a container with a filter-covered opening or similar design to allow radon, but not its progeny, to enter. Some common materials used in this capacity for radon detection are the cellulose nitrate film (LR-115), the thermoset polymer plastic (CR-39), and the polycarbonate plastic (Makrofol) (European Commission 1995). Radon gas diffuses into the container and alpha particles emitted by the radon and its subsequently-produced progeny strike the detector and

produce submicroscopic damage tracks to the enclosed plastic material. Following the analysis period, the plastic detectors are placed in a caustic solution that accentuates the damage tracks so they can be counted using a microscope or an automated counting system. The number of tracks per unit area is correlated to the radon concentration in air, using a conversion factor derived from data generated at a laboratory. The number of tracks per unit of analyzed detector area produced per unit of time (minus the background) is proportional to the radon concentration. When compared to charcoal adsorption detectors, alpha track detectors have the advantage that they can be used for measurements over long time frames and thus, they measure true time-integrated average concentrations (EPA 1992a). Inexpensive alpha track radon detection kits are commercially available to the general public to estimate radon exposure in a dwelling. Unlike the activated charcoal test kits that have a brief exposure period, the alpha track monitors are typically used for 90 days to 1 year and provide a better estimate of the annual radon exposure.

Electret ion chamber (EC) radon detectors are passive detectors that use an electrostatically charged disk to collect ions formed in the chamber by radiation generated from radon and radon progeny (EPA 1992a). Radon diffuses into the chamber through filtered openings and ions that are generated continuously by the decay of radon, and its progeny are drawn to the surface of the electret, which subsequently reduces its surface voltage. The change of voltage measured by an electrostatic voltmeter is related to the average radon concentration based on the duration of the exposure period.

Flow through alpha scintillation cells (Lucas type cells) are frequently used to measure radon concentrations in air for field measurements and in occupational settings (NCRP 1988). The cell consists of a silver activated zinc sulfide (ZnS) phosphor screen that emits photons of visible light when impacted by alpha particles (Lucas 1957). Air is drawn continuously through the cell by an air pump and the cell is coupled to a photomultiplier tube for continuous analysis. The scintillations or flashes of light caused by the alpha particles from radon and its progeny, which strike the ZnS screen, are recorded by the photomultiplier tube. Using appropriate calibration and decay scheme factors, the radon gas concentration may be determined from the rate at which the pulses are recorded (European Commission 1995).

Personal and occupational exposure to radon is frequently assessed using personal dosimeters. An early personal radon dosimeter used in occupational settings by miners, called a radon film badge, was described by Geiger (1967). It consisted of a plastic holder, which encompassed a nuclear track film to detect emitted alpha particles. Radon gas diffused through the central opening of the badge and into the

film emulsion. The number of alpha particles was determined by counting the tracks in the processed film emulsion. Another example of a passive radon dosimeter based on alpha particle etched track detection used to assess personal exposure is described by Taheri et al. (2006). This particular dosimeter employs a polycarbonate detector and a porous fiberglass filter to collect the radon progeny, ^{218}Po and ^{214}Po. A thin aluminum foil is placed between the filter and the detector in order to attenuate the energy of the emitted alpha particles.

Retrospective radon detection methods using surface traps or volume traps provide a means of estimating long-term radon exposure at a building or residence. By determining the historical average concentration, the methodology provides an estimate of the indoor radon level to which a person was exposed over a period of time. For surface trap methods, the activity is measured at the surface of objects, such as glass, that were present in the location of interest during the exposure assessment period. The average radon concentration over several decades is related to the surface activity of the glass. This results from the radon progeny ^{210}Pb, which has a long half-life (22.26 years) and is found implanted within the glass (or other hard surface) due to the kinetic energy transferred by alpha decay to the radon progeny atoms plating out on the surface (Lagarde et al. 2002; Mahaffey et al. 1993; Samuelsson 1988; Steck and Field 1999). A field study conducted from 2005 to 2007 in 38 homes in Iowa occupied by either smokers or nonsmokers using surface trap CR-39 chip retrospective radon detectors indicated that radon progeny (^{214}Po and ^{218}Po) deposited on the surface of these detectors was effective for predicting the airborne radon progeny dose rate for individuals and estimating long-term exposure in nonsmoking environments. The operation of ceiling fans or fireplaces in monitoring areas adversely affected the measurements (Sun 2008).

Pressyanov et al. (2003) explored the use of compact disks as retrospective radon detectors. After exposure, a surface layer was removed and electrochemically etched marks were counted. The study results indicated that compact disks may be useful for retrospectively obtaining radon measurements for levels above 3 Bq/m^3 (0.08 pCi/L).

Radon volume trap detectors also provide a convenient method to estimate average radon concentrations in dwellings over several years in time (Oberstedt and Vanmarcke 1996). Sponge-like materials, such as mattresses and cushions, build-up ^{210}Pb, which reaches an equilibrium with the alpha emitter ^{210}Po, which is used to estimate the average radon concentration over the exposure period. Laboratory tests employing polyester foam samples to simulate mattress material of differing densities and rigidity were exposed to a radon source (Oberstedt and Vanmarcke 1996). Following the initial exposure period, the materials were

stored in a radon-free environment for at least one half-life of ^{210}Po (138 days). The ^{210}Po was separated from the polyester materials in a series of extraction steps and the activity was analyzed by alpha spectrometry. The results indicated that home dwelling materials, such as cushions and mattress material, could be used as an accurate and sensitive retrospective radon monitor. Wooden furniture material has also been tested as a volume trap; however, the natural varying background concentrations of ^{210}Po in different wood types make these materials a less attractive retrospective detection system.

A standard test method for the detection of radon in drinking water has been developed by the American Society for Testing and Materials (ASTM) based on scintillation counting of radon and its progeny (ASTM 1999). A sample of unaerated water is injected into a vial containing toluene or a scintillation cocktail mix and analyzed using a commercially available liquid scintillation spectrometer. This method has a reported detection limit of 0.040 Bq/L (1.1 pCi/L).

A method for measuring radon in soil gas that utilizes liquid scintillation counting for determining concentration is given by Wadach and Hess (1985). A description of this method may be found in Table 7-2. A detection system for continuous soil radon concentration measurements was developed using a continuous monitor RM-3. The system detects radon based on an airflow ionization chamber. Details are available in Fronka et al. (2008).

The accuracy of any measurement will depend upon the calibration of the instrument used. The calibration of an instrument determines its response to a known amount or concentration of radioactivity. This allows a correlation to be made between the instrument reading and the actual amount or concentration present. A range of activities of ^{226}Ra standard reference materials (SRM) is available from the National Institute of Standards and Technology (NIST) polyethylene-encapsulated ^{226}Ra/^{222}Rn emanation standards (PERE). These are used to produce an accurate concentration of ^{222}Rn in air, such as for calibrating passive radon detection systems. Ionization pulse chambers are often used for instrumental calibration and measurement systems in interlaboratory comparisons (NCRP 1988). NIST developed a ^{226}Ra-^{222}Rn generator for use as a transfer standard for radon-in-water measurement calibrations (Hutchinson et al. 1984, 1986). Modifications to this standard generator and its long-term performance have been evaluated and described using 4π-αβ liquid scintillation spectrometry of gravimetrically determined aliquants dispensed from the generator (Collé and Kishore 1997). Analytical methods for measuring radon in environmental samples are given in Table 7-2. To quantify the sensitivity of a particular analytical method, the lower limits of detection (LLD) are given when possible. The LLD is typically defined as the minimum activity that would result in a quantifiable signal on some analytical

Table 7-2. Analytical Methods for Determining Radon and Progeny in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Radon					
Air	Adsorb onto activated charcoal; 2–7 days	Gamma spectroscopy	No data	No data	Cohen and Nason 1986
Air	Adsorb onto activated charcoal followed by direct analysis; extract with toluene add 1–2 mL fluor	Gamma counting of 0.295 and 0.352 γ MeV lines of ^{214}Pb; liquid scinilation analysis of desorbed sample	No data	94% of true concentration	Prichard and Marlen 1983
Air	Scintillation cell method; allow air to enter detection chamber through millipore filter until equlibrated, or collect sample in bag (Mylar or Tedlar); transer to chamber as soon as possible	ZnS(Ag) scintillation/ photomultiplier tube	No data	No data	Crawford-Brown and Michel 1987
Air	Two-filter method: draw air into fixed length tube with entry and exit filters; monitor exit filter activity	ZnS(Ag) scintillation/ photomultiplier tube	No data	90%	Schery et al. 1980
Air	Diffuse through a filter into a cup containing alpha track material (cellulose nitrate film) for up to 1 year; etch in acidic or basic solution operated upon an alternating electric field	Solid state nuclear track detector Microscopic examination of damaged material	14 pCi/m^3 (0.519 Bq/m^3)	No data	NCRP 1988
Air	Adsorb onto compact disks; remove surface layer at 25 °C with aqueous 45% KOH and 40% methanol; apply electrochemical etching	Marks counted using video camera	No data	No data	Pressyanov et al. 2003
Air	Dissolve material in nitric acid followed by additional digestion in hydrochloric acid. Auto deposit polonium on a silver plate during drying with an infrared source	Volume trap detector using alpha spectrometer	54 pCi/L		Oberstedt and Vanmarcke 1996

Table 7-2. Analytical Methods for Determining Radon and Progeny in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Glass	Attach dosimetry-grade track registration material (CR-39 and LANTRAK®) to ordinary smooth glass without visible coatings or colorings that has been in an unobstructed location without strong air currents; leave in place for long periods (several weeks to a year)	Chemically etch the dosimeter, read ^{210}Po tracks manually with microscope, determine cumulative radon gas exposure as kym^{-1} (i.e., $kBq\text{-}ym^{-1}/Bqm^{-2}$)[a]	~0.3 kym^{-1}	NA	Steck et al. 2002
Soil	Dry in 55 °C oven for 24 hours; place 5 g in 20 mL borosilicate glass scintillation; cover with 10 mL distilled water; allow soil to become wet; add 5 mL high-efficiency mineral oil; allow to age 30 days	Scintillation counter	No data	No data	Rangarajan and Eapen 1987; Wadach and Hess 1985
Soil	None	Track etch detector buried 30 cm deep	No data	No data	Rangarajan and Eapen 1987
Drinking Water	Draw an aliquot of unaerated water into a syringe and inject in a scintillation vial containing the liquid scintillation cocktail solution	ASTM Method D5072 (Scintillation counter)	0.04 Bq/L (1.1 pCi/L)	94–96%	ASTM 1999
Water	Pass carrier gas through samples in a bubbler flask to purge out dissolved radon; transfer radon to evacuated scintillation cell	Scintillation counter	1.4 pCi/L (52 Bq/m^3)	90%	Crawford-Brown and Michel 1987

Table 7-2. Analytical Methods for Determining Radon and Progeny in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Water	Inject into glass vial containing liquid scintillation solution; shake vigorously	Liquid scintillation counter	10 pCi/L (370 Bq/m^3)	No data	Crawford-Brown and Michel 1987
Water	Direct measurement	Gamma ray spectroscopy	10 pCi/L for 1-L sample (370 Bq/m^3)	No data	Yang 1987
Air	CR-39 chip bathed in 6.25N sodium hydroxide at 75 °C oven for 6 hours	Alpha track density determined by microscopy	No data	No data	Sun 2008

[a]Unit of measure (kym^{-1}) equals radon gas exposure in kiloBecquerel-years per m^3 ($kBqym^{-3}$) divided by surface activity in Becquerels per m^2 (Bqm^{-2}).

TLD = thermoluminescent dosimeter

instrument that would yield a net count for which there is confidence at a predetermined level (usually the 95th percentile confidence limit) that activity is present (Harley and Pasternack 1982; NCRP 1988). In order to calculate the LLD, the measurement system characteristics, detection system efficiency, background count rate, sampling volume, and sampling period must be known.

The EPA Radiation and Indoor Environments National Laboratory (RIENL) provides radon measurement technical support for the radon monitoring proficiency testing programs in the United States (as supported by NIST) and for tribal, state, and local governments, federal agencies, and private industry (EPA 2011b). The National Environmental Health Association-National Radon Proficiency Program (NEHA-NRPP) operates a radon proficiency test (PT) and contractor certification program for those who want to become a Certified Radon Professional (NEHA-NRPP 2008). NIST has developed and provides precise radon emanation rate standards (currently, SRMs 4971, 4972, and 4973) for use in calibrating radon monitors. Since ^{222}Rn standards are required for home radon testing, NIST has worked to transfer the U.S. national standards (which are still based on the international standards produced by Marie Curie in 1912) to secondary calibration laboratories (NIST 2011).

7.3 ADEQUACY OF THE DATABASE

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

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

7.3.1 Identification of Data Needs

Methods for Determining Biomarkers of Exposure and Effect.

Exposure. Methods are available to measure the presence of radon progeny in urine, blood, bone, teeth, and hair. However, these radon progeny detected in biological systems arise from ingestion of these progeny from food and drinking water as well as from the inhalation of radon. Therefore, these methods cannot be considered as specific biomarkers for radon inhalation.

Effect. The frequency of abnormalities in sputum cytology has been utilized as a possible early indicator of radiation damage to lung tissue (Band et al. 1980; Brandom et al. 1978; Saccomanno et al. 1974). The accuracy and precision of this measurement is not known.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Analytical methods are available that allow for the quantification of radon in air, water, and soil. However, methods for the measurement of radon concentrations in soil-gas are limited. The ability to accurately measure soil-gas is needed to provide a better understanding of the emanation rate of radon gas from soil.

7.3.2 Ongoing Studies

Researchers at the University of Iowa are involved in ongoing studies that include pooling results from Iowa and Missouri residential radon studies using glass-based detectors that are undergoing final calibration (field, personal communication) and pooling results from the residential radon studies that contributed to the results of Krewski et al. (2005, 2006; North American studies) and Darby et al. (2005, 2006; European studies).

8. REGULATIONS, ADVISORIES, AND GUIDELINES

Recommendations for radiation protection for people in the general population as a result of exposure to radon in the environment are found in the International Commission on Radiological Protection (ICRP) Publication 65 (ICRP 1994a). National guidelines for occupational radiation protection are found in the "Federal Radiation Protection Guidance for Occupational Exposure" (EPA 1987b). The 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 1994a).

The basic philosophy of radiation protection is the concept of ALARA (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, guides for Annual Limits on Intake (ALIs) have been calculated (USNRC 2011). The ALI 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).

MRLs are substance specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors and other responders to identify contaminants and potential health effects that may be of concern at hazardous waste sites.

No inhalation or oral MRLs were derived for radon.

The international and national regulations, advisories, and guidelines regarding radon in air, water, and other media are summarized in Table 8-1.

The EPA IRIS database (IRIS 2012) has withdrawn its cancer classification for radionuclides, but the EPA Office of Air and Radiation believes that all radionuclides, including radon and its radioactive progeny, should be considered to be known carcinogens, and has assigned them to Group A (EPA 2012b). The EPA has not derived reference concentrations (RfCs) or reference doses (RfDs) for radon (IRIS 2012). EPA has not promulgated a maximum contaminant level (MCL) for radon in drinking water. In 1991, EPA proposed an MCL, but was directed in 1996 to withdraw it and did so in 1997. In 1999, EPA again proposed an MCL (EPA 1999b), but finalized the current radionuclides in drinking water rule in 2000 without a value for radon (EPA 2000) and this status has not changed. The EPA website contains a

wealth of information, including a publication entitled A Citizen's Guide to Radon (EPA 2009a). This guide includes information on the health risk from inhaling radon and its progeny, methods for radon testing in homes, methods and techniques for reducing the radon level, and a recommendation to use a certified radon mitigation specialist to ensure that appropriate methods are used to reduce radon levels. EPA recommends actions to take if the measured radon indoor level is ≥4 pCi/L and notes that radon levels <4 pCi/L still pose a health risk and can be reduced in many cases, and recommends not smoking as an additional way to reduce radon risk.

Table 8-1. Regulations, Advisories, and Guidelines Applicable to Radon

Agency	Description	Information	Reference
INTERNATIONAL			
Guidelines:			
IARC	Carcinogenicity classification		IARC 2008
	^{222}Rn and its decay products	Group 1[a]	
ICRP	Summary of values recommended		
	Nominal probability coefficient for radon- and radon-progeny-induced lung cancer	$5x10^{-4}$ per WLM (0.14 per J h m^{-3})	ICRP 2010
	Dose conversion convention, effective dose per unit of exposure		ICRP 1994a
	At home	1.1 mSv (mJ h m^{-3})	
	At work	1.4 mSv (mJ h m^{-3})	
	Action level (dwellings)		
	Radon concentration	200–600 (Bq m^{-3})[b]	
	Annual effective dose	3–10 mSv	
	Action level (workplace)		
	Radon concentration	500–1,500 (Bq m^{-3})[b]	
	Annual effective dose	3–10 mSv	
	Occupational annual limit on exposure		
	Per year, averaged over 5 years	14 (mJ h m^{-3})	
	In a single year	35 (mJ h m^{-3})	
WHO	Air quality guidelines		WHO 2000
	Risk estimates and recommended action level for radon progeny for exposure to 1 Bq/m^3		
	Lung cancer excess lifetime risk estimate	$3–6x10^{-5}$	
	Recommended level for remedial action in buildings	≥100 Bq/m^3 (2.7 pCi/L); annual average	
	Drinking water quality guidelines		WHO 2004
	Radon	100 Bq/L (2,700 pCi/L)	
NATIONAL			
Regulations and Guidelines:			
a. Air			
ACGIH	Guidelines for exposure to ionizing radiation		ACGIH 2007
	Radon daughters	4 WLM/year	

Table 8-1. Regulations, Advisories, and Guidelines Applicable to Radon

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
EPA	AEGL-1, -2, and -3	No data	EPA 2011e
	Hazardous air pollutant		EPA 2010b 42 USC 7412
	Radon	Yes	
	Effective dose equivalent to public from ^{222}Rn not to exceed 10 mrem/year	From operating uranium mine	EPA 2011i (40CFR61.22)
		From a DOE facility	EPA 2011j (40CFR61.92)
	^{222}Rn emissions rate from soil not to exceed 20 pCi/m^2-second average for entire source	From a DOE facility	EPA 2011k (40CFR61.192)
		From an inactive phosphogypsum stack	EPA 2011l (40CFR61.202)
		From a non-operational uranium mill tailings pile	EPA 2011m (40CFR61.222)
		From an existing uranium mill tailings pile	EPA 2011n (40CFR61.252)
	Standards for uranium byproduct materials shall apply to thorium byproduct materials	Provisions from soil for ^{222}Rn from uranium byproduct materials are applicable to ^{220}Rn from thorium byproduct materials	EPA 2011h (40CFR192.41)
	^{210}Po (^{222}Rn progeny)	Emissions from elemental phosphorus plant <2 Ci/year, or 4.5 Ci/year with scrubbers	EPA 2011o (40CFR61.122)
	Monitoring of radon in homes		EPA 2009a
	No action necessary	<4 pCi/L, 0.02 WL	
	Take necessary action to decrease indoor radon levels	≥4 pCi/L	
MSHA	Annual exposure limits		MSHA 2011a 30 CFR 57.5038
	Radon daughters	4 WLM in any calendar year underground	
	Maximum permissible concentration		MSHA 2011b 30CFR57.5039
	Radon daughters	1 WL in active workings underground	
NIOSH	REL (10-hour TWA)	No data	

Table 8-1. Regulations, Advisories, and Guidelines Applicable to Radon

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
OSHA	OSHA adopted the 1971 version of USNRC regulatory limits in 10CFR20 Appendix B for exposure to radon in air. Applies to employers. OSHA states that following the current 10CFR20 App B is a *de minimis* violation.	Adult workers: $1x10^{-7}$ µCi/mL (100 pCi/L) averaged over 40-hour work week of 7 consecutive days	OSHA 2011 29 CFR 1910.1096; OSHA 1971; OSHA 2002
		Workers under 18 years of age: $3x10^{-9}$ µCi/mL (3 pCi/L) averaged over 40-hour work week of 7 consecutive days	OSHA 2011 29CFR1910.1096 (c)(2); OSHA 1971, OSHA 2002
		Surveys are required in order to comply	OSHA 2011, 29CFR1910.1096 (e)(4)ii
		Post airborne radioactivity area signs when weekly average exceeds 25% of limit (i.e., 25 pCi/L adults, 0.75 pCi/L child workers)	OSHA 2011, 29CFR1910.1096 (e)(4)(i)(b)
USNRC	ALI for occupational exposure (values for oral ingestion)		USNRC 2011 10 CFR 20, Appendix B
	^{220}Rn (with daughters removed)	Not listed	
	^{220}Rn (with daughters present)	Not listed	
	^{222}Rn (with daughters removed)	Not listed	
	^{222}Rn (with daughters present)	Not listed	
	ALI for occupational exposure (values for inhalation)		
	^{220}Rn (with daughters removed)	20,000 µCi	
	^{220}Rn (with daughters present)	20 µCi (or 12 WLM)	
	^{222}Rn (with daughters removed)	10,000 µCi	
	^{222}Rn (with daughters present)	100 µCi (or 4 WLM)	
	Derived air concentrations for occupational exposure (values for inhalation)		
	^{220}Rn (with daughters removed)	$7x10^{-6}$ µCi/mL	
	^{220}Rn (with daughters present)	$9x10^{-9}$ µCi/mL (or 1.0 WL)	
	^{222}Rn (with daughters removed)	$4x10^{-6}$ µCi/mL	
	^{222}Rn (with daughters present)	$3x10^{-8}$ µCi/mL (or 0.33 WL)	
	Annual average effluent air concentration (no values provided for effluent water)		
	^{220}Rn (with daughters removed)	$2x10^{-8}$ µCi/mL	

Table 8-1. Regulations, Advisories, and Guidelines Applicable to Radon

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
	^{220}Rn (with daughters present)	$3x10^{-11}$ µCi/mL	
	^{222}Rn (with daughters removed)	$1x10^{-8}$ µCi/mL	
	^{222}Rn (with daughters present)	$1x10^{-10}$ µCi/mL	
b. Water			
EPA	Drinking water standards and health advisories for radon activity	None; EPA proposed an MCL for radon in 1991, withdrew it in 1997, and published the final rule in 2000 without a radon MCL	EPA 2011d, EPA 1997
	National recommended water quality criteria	No data	
c. Food		No data	
d. Other			
ACGIH	Carcinogenicity classification	No data	ACGIH 2007
EPA	Carcinogenicity classification		IRIS 2012
	^{222}Rn	Withdrawn in 1993	
	RfC		
	^{222}Rn	Not established	
	RfD		
	^{222}Rn	Not established	
	Superfund, emergency planning, and community right-to-know		EPA 2011f 40 CFR 302.4 App B
	Designated CERCLA hazardous substance		
	^{220}Rn[c]	0.1 Ci	
	^{222}Rn[c]	0.1 Ci	
NTP	Carcinogenicity classification		NTP 2011
	Ionizing radiation (includes ^{220}Rn and ^{222}Rn)	Known to be a human carcinogen	

[a]Group 1: carcinogenic to humans.
[b]Assuming 7,000 hours/year indoors or 2,000 hours/year at work and an equilibrium factor of 0.4.
[c]Designated CERCLA hazardous substance pursuant to Section 112 of the Clean Air Act.

ACGIH = American Conference of Governmental Industrial Hygienists; AEGL = Acute Exposure Guideline Levels; ALI = annual limit on intake; CERCLA = Comprehensive Environmental Response, Compensation, and Liability Act; CFR = Code of Federal Regulations; EPA = Environmental Protection Agency; IARC = International Agency for Research on Cancer; ICRP = International Commission on Radiological Protection; MCL = maximum contaminant level; MSHA = Mine Safety and Health Administration; NAS = National Academy of Sciences; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; REL = recommended exposure limit; RfC = inhalation reference concentration; RfD = oral reference dose; TWA = time-weighted average; USC = United States Code; USNRC = U.S. Nuclear Regulatory Commission; WHO = World Health Organization; WL = working level; WLM = working level months

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10. GLOSSARY

Some terms in this glossary are generic and may not be used in this profile.

Absorbed Dose, Chemical—The amount of a substance that is either absorbed into the body or placed in contact with the skin. For oral or inhalation routes, this is normally the product of the intake quantity and the uptake fraction divided by the body weight and, if appropriate, the time, expressed as mg/kg for a single intake or mg/kg/day for multiple intakes. For dermal exposure, this is the amount of material applied to the skin, and is normally divided by the body mass and expressed as mg/kg.

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

Absorbed Fraction—A term used in internal dosimetry. It is that fraction of the photon energy (emitted within a specified volume of material) which is absorbed by the volume. The absorbed fraction depends on the source distribution, the photon energy, and the size, shape and composition of the volume.

Absorption—The process by which a chemical penetrates the exchange boundaries of an organism after contact, or the process by which radiation imparts some or all of its energy to any material through which it passes.

> **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 absorption of the energy of an unscattered beam of x- or gamma-radiation per unit thickness (linear absorption coefficient), per unit mass (mass absorption coefficient), or per atom (atomic absorption coefficient) of absorber, due to transfer of energy to the absorber. The total absorption coefficient is the sum of individual energy absorption processes (see Compton Effect, Photoelectric Effect, and Pair Production).

Absorption Coefficient, Linear—A factor expressing the fraction of a beam of x- or gamma radiation absorbed in a unit thickness of material. In the expression $I=I_oe^{-\mu x}$, I_o is the initial intensity, I the intensity of the beam after passage through a thickness of the material x, and μ is the linear absorption coefficient.

Absorption Coefficient, Mass—The linear absorption coefficient per cm divided by the density of the absorber in grams per cubic centimeter. It is frequently expressed as μ/ρ, where μ is the linear absorption coefficient and ρ the absorber density.

Absorption Ratio, Differential—Ratio of concentration of a nuclide in a given organ or tissue to the concentration that would be obtained if the same administered quantity of this nuclide were uniformly distributed throughout the body.

Activation—The process of making a material radioactive by bombardment with neutrons or protons.

Activity—The number of radioactive nuclear transformations occurring in a material per unit time (see Curie, Becquerel). The term for activity per unit mass is specific activity.

Activity Median Aerodynamic Diameter (AMAD)—The diameter of a unit-density sphere with the same terminal settling velocity in air as that of the aerosol particle whose activity is the median for the entire size distribution of the aerosol.

Acute Exposure, Chemical—Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

Acute Exposure, Radiation—The absorption of a relatively large amount of radiation (or intake of a radioactive material) over a short period of time.

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

***Ad libitum*—**Available in excess and freely accessible.

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

Adsorption Ratio (K_d)—See Distribution Coefficient

Alpha Particle—A positively charged particle ejected spontaneously from the nuclei of some radioactive elements. It is identical to a helium nucleus, i.e., 2 neutrons and two protons, with a mass number of 4 and an electrostatic charge of +2.

Alpha Track—The track of ionized atoms (pattern of ionization) left in a medium by an alpha particle that has traveled through the medium.

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

Annual Limit on Intake (ALI)—The derived limit for the amount of radioactive material taken into the body of an adult worker by inhalation or ingestion in a year. It is the smaller value of intake of a given radionuclide in a year by the reference man that would result in a committed effective dose equivalent of 5 rem or a committed dose equivalent of 50 rem to any organ or tissue.

Atom—The smallest particle of an element that cannot be divided or broken up by chemical means. It consists of a central core called the *nucleus*, which contains *protons* and *neutrons* and an outer shell of *electrons*.

Atomic Mass (u)—The mass of a neutral atom of a nuclide, usually expressed in terms of "atomic mass units." The "atomic mass unit" is one-twelfth the mass of one neutral atom of carbon-12; equivalent to 1.6604×10^{-24} g.

Atomic Mass Number—See Mass Number.

Atomic Number—The number of protons in the nucleus of an atom. The "effective atomic number" is calculated from the composition and atomic numbers of a compound or mixture. An element of this atomic number would interact with photons in the same way as the compound or mixture. (Symbol: Z).

Atomic Weight—The weighted mean of the masses of the neutral isotopes of an element expressed in atomic mass units.

10. GLOSSARY

Attenuation—A process by which a beam from a source of radiation is reduced in intensity by absorption and scattering when passing through some material.

Attenuation Coefficient—The fractional reduction in the intensity of a beam of radiation as it passes through an absorbing medium. It may be expressed as reduction per unit distance, per unit mass thickness, or per atom, and is called the linear, mass, or atomic attenuation coefficient, respectively.

Auger Effect—The emission of an electron from the extranuclear portion of an excited atom when the atom undergoes a transition to a less excited state.

Background Radiation—The amount of radiation to which a member of the general population is exposed from natural sources, such as terrestrial radiation from naturally occurring radionuclides in the soil, cosmic radiation originating from outer space, and naturally occurring radionuclides deposited in the human body.

Becquerel (Bq)—International System of Units unit of activity and equals that quantity of radioactive material in which one transformation (disintegration) occurs per second (see Units).

Terabecquerel (TBq)—One trillion becquerel.
Gigabecquerel (GBq)—One billion becquerel.
Megabecquerel (MBq)—One million becquerel.
Kilobecquerel (kBq))—One thousand becquerel.
Millibecquerel (mBq)—One-thousandth of a becquerel.
Microbecquerel (µBq)—One-millionth of a becquerel.

Benchmark Dose (BMD)—Usually defined as the lower confidence limit on the dose that produces a specified magnitude of changes in a specified adverse response. For example, a BMD_{10} would be the dose at the 95% lower confidence limit on a 10% response, and the benchmark response (BMR) would be 10%. The BMD is determined by modeling the dose response curve in the region of the dose response relationship where biologically observable data are feasible.

Benchmark Dose Model—A statistical dose-response model applied to either experimental toxicological or epidemiological data to calculate a BMD.

Beta Particle—An electron that is emitted from the nucleus of an atom during one type of radioactive transformation. A beta particle has a mass and charge equal in magnitude to that of the electron. The charge may be either +1 or -1. Beta particles with +1 charges are called positrons (symbolized β^+), and beta particles with -1 charges are called negatrons (symbolized β^-).

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

Biologic Effectiveness of Radiation—See Relative Biological Effectiveness.

Biological Half-time—The time required for a biological system, such as that of a human, to eliminate by natural process half of the amount of a substance (such as a chemical substance, either stable or radioactive) that has entered it.

Biomagnification—The progressive increase in the concentration of a bioaccumulated chemical in organisms as that chemical is passed from the bottom to the top of the food web.

Biomarkers—Broadly defined as indicators signaling events in biologic systems or samples. They have been classified as markers of exposure, markers of effect, and markers of susceptibility.

Body Burden, Chemical—The total amount of a chemical found in an animal or human body.

Body Burden, Radioactivity—The amount of radioactive material found in an animal or human body.

Bone Seeker—Any compound or ion which migrates in the body and preferentially deposits into bone.

Branching—The occurrence of two or more modes by which a radionuclide can undergo radioactive decay. For example, ^{214}Bi can undergo alpha or beta minus decay, ^{64}Cu can undergo beta minus, beta plus, or electron capture decay. An individual atom of a nuclide exhibiting branching disintegrates by one mode only. The fraction disintegrating by a particular mode is the "branching fraction" for that mode. The "branching ratio" is the ratio of two specified branching fractions (also called multiple disintegration).

Bremsstrahlung—X rays that are produced when a charged particle accelerates (speeds up, slows down, or changes direction) in the strong field of a nucleus.

Buildup Factor—The ratio of the radiation intensity, including both primary and scattered radiation, to the intensity of the primary (unscattered) radiation.

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

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

Capture, K-Electron—Electron capture from the K shell by the nucleus of the atom. Also loosely used to designate any orbital electron capture process.

Carcinogen—A chemical or radiation that is capable of inducing cancer.

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

Case-Control Study—A type of epidemiological study which examines the relationship between a particular outcome (disease or condition) and a variety of potential causative agents (such as toxic chemicals). In a case-controlled study, a group of people with a specified and well-defined outcome is identified and compared to a similar group of people without outcome.

Case Report—Describes a single individual with a particular disease or exposure. These may suggest some potential topics for scientific research but are not actual research studies.

Case Series—Describes the experience of a small number of individuals with the same disease or exposure. These may suggest potential topics for scientific research, but are not actual research studies.

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

Ceiling Value—A concentration of a substance that should not be exceeded, even temporarily.

Charged Particle—A nuclear particle, atom, or molecule carrying a positive or negative charge.

Chronic Exposure—A long-term, continuous exposure to a chemical or radioactive material. For example, exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Cohort Study—A type of epidemiological study of a specific group or groups of people who have had a common insult (e.g., exposure to an agent suspected of causing disease or a common disease) and are followed forward from exposure to outcome. At least one exposed group is compared to one unexposed group.

Collective Dose—The sum of the individual doses received in a given period of time by a specified population from exposure to a specified source of radiation. Collective dose is expressed in units such as man-rem and person-sievert.

Compton Effect—An attenuation process observed for x- or gamma radiation in which an incident photon interacts with an orbital electron of an atom to produce a recoil electron and a scattered photon whose energy is less than the incident photon.

Containment—The confinement of a chemical or radioactive substance in such a way that it is prevented from being dispersed from its container or into the environment, or is released only at a specified rate.

Contamination—Deposition of a stable or radioactive substance in any place where it is not desired.

Cosmic Rays—High-energy particulate and electromagnetic radiations that originate outside the earth's atmosphere and interact with the atmosphere to produce a shower of secondary cosmic rays.

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

Counter, Gas-flow Proportional (GPC)—An instrument for detecting beta particle radiation. Beta particles are detected by ionization of the counter gas which results in an electrical impulse at an anode wire.

Counter, Geiger-Mueller (GM counter)—Highly sensitive, gas-filled radiation-measuring device that detects (counts) individual photons or particulate radiation.

Counter, Scintillation—The combination of a crystal or phosphor, photomultiplier tube, and associated circuits for counting light emissions produced in the phosphors by ionizing radiation. Scintillation counters generally are more sensitive than GM counters for gamma radiation.

Counting, Cerenkov—Relatively energetic β-particles pass through a transparent medium of high refractive index and a highly-directional, bluish-white light (“Cerenkov” light) is emitted. This light is detected using liquid scintillation counting equipment.

Cross-sectional Study—A type of epidemiological study of a group or groups which examines the relationship between exposure and outcome to a chemical or to chemicals at one point in time.

Curie (Ci)—A unit of radioactivity. One curie equals that quantity of radioactive material in which there are $3.7x10^{10}$ nuclear transformations per second. The activity of 1 gram of radium is approximately 1 Ci.

Attocurie (aCi)—One-thousandth of a femtocurie ($3.7x10^{-8}$ disintegrations per second).
Femtocurie (fCi)—One-billionth of a microcurie ($3.7x10^{-5}$ disintegrations per second).
Megacurie (MCi)—One million curies ($3.7x10^{16}$ disintegrations per second).
Microcurie (µCi)—One-millionth of a curie ($3.7x10^{4}$ disintegrations per second).
Millicurie (mCi)—One-thousandth of a curie ($3.7x10^{7}$ disintegrations per second).
Nanocurie (nCi)—One-billionth of a curie ($3.7x10^{1}$ disintegrations per second).
Picocurie (pCi)—One-millionth of a microcurie ($3.7x10^{-2}$ disintegrations per second).

Data Needs—Substance-specific informational needs that if met would reduce the uncertainties of human health assessment.

Daughter Products—See Progeny and Decay Product

Decay Chain or Decay Series—A sequence of radioactive decays (transformations) beginning with one nucleus. The initial nucleus, the parent, decays into a daughter or progeny nucleus that differs from the first by whatever particles were emitted during the decay. If further decays take place, the subsequent nuclei are also usually called daughters or progeny. Sometimes, to distinguish the sequence, the daughter of the first daughter is called the granddaughter, etc.

Decay Constant (λ)—The fraction of the number of atoms of a radioactive nuclide which decay in unit time (see Disintegration Constant).

Decay Product, Daughter Product, Progeny—A new nuclide formed as a result of radioactive decay. A nuclide resulting from the radioactive transformation of a radionuclide, formed either directly or as the result of successive transformations in a radioactive series. A decay product (daughter product or progeny) may be either radioactive or stable.

Decay, Radioactive—Transformation of the nucleus of an unstable nuclide by spontaneous emission of radiation, such as charged particles and/or photons (see Disintegration).

Decile—A method of splitting up a set of ranked data into 10 equally large subsections.

Delta Ray—An electron removed from an atom of a medium that is irradiated, or through which radiation passes, during the process of ionization (also called secondary electron). Delta rays cause a track of ionizations along their path.

Derived Air Concentration (DAC)—The concentration of radioactive material in air that, if breathed by the reference man for a working year of 2000 hours under conditions of light work (at a rate of 1.2 liters of air per hour), would result in an intake of one ALI (see Annual Limit on Intake).

Deterministic Effect—A health effect, the severity of which varies with the dose and for which a threshold is believed to exist (also called a non-stochastic effect).

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

Disintegration Constant—Synonymous with decay constant. The fraction of the number of atoms of a radioactive material that decays per unit time (see Decay Constant.)

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

Distribution Coefficient (K_d)—Describes the distribution of a chemical between the solid and aqueous phase at thermodynamic equilibrium, is given as follows:

$$K_d = \frac{[C]_s}{[C]_w}$$, Units = (L solution)/(kg solid),

where $[C]_s$ is the concentration of the chemical associated with the solid phase in units of (mg)/(kg solid), and $[C]_w$ is the concentration of the chemical in the aqueous phase in units of (mg)/(L solution). As the magnitude of K_d decreases, the potential mobility of the chemical to groundwater systems increases and vice versa.

Dose—A general term denoting the quantity of a substance, radiation, or energy absorbed. For special purposes it must be appropriately qualified. If unqualified, it refers to radiation absorbed dose.

> **Absorbed Dose—**The energy imparted to matter by ionizing radiation per unit mass of irradiated material at the place of interest. The unit of absorbed dose is the rad. One rad equals 100 ergs per gram. In SI units, the absorbed dose is the gray which is 1 J/kg (see Rad).
>
> **Cumulative Dose (Radiation)—**The total dose resulting from repeated or continuous exposures to radiation.

Dose Assessment—An estimate of the radiation dose to an individual or a population group usually by means of predictive modeling techniques, sometimes supplemented by the results of measurement.

Dose Equivalent (DE)—A quantity used in radiation safety practice to account for the relative biological effectiveness of the several types of radiation. It expresses all radiations on a common scale for calculating the effective absorbed dose. The NRC defines it as the product of the absorbed dose, the quality factor, and all other modifying factors at the location of interest. ICRP has changed its definition to be the product of the absorbed dose and the radiation weighting factor. (The unit of dose equivalent is the rem. In SI units, the dose equivalent is the sievert, which equals 100 rem.)

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

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

Dose, Radiation—The amount of energy imparted to matter by ionizing radiation per unit mass of the matter, usually expressed as the unit rad, or in SI units, the gray. 100 rad=1 gray (Gy) (see Absorbed Dose).

> **Committed Dose Equivalent ($H_{T,50}$)—**The dose equivalent to organs or tissues of reference (T) that will be received from an intake of radioactive material by an individual during the 50 years following the intake.

Committed Effective Dose Equivalent ($H_{E,50}$)—The sum of the products of the weighting factors applicable to each of the body organs or tissues that are irradiated and the committed dose equivalent to those organs or tissues.

Effective Dose —A dose value that attempts to normalize the detriment to the body (for cancer mortality and morbidity, hereditary effects, and years of life lost) from a non-uniform exposure to that of a uniform whole body exposure. Effective dose is calculated as the sum of products of the equivalent dose and the tissue weighting factor (w_T) for each tissue exposed. ($E = \sum D_{T,R}\ w_R\ w_{T)}$).

Effective Dose Equivalent (H_E)—This dose type is limited to internal exposures and is the sum of the products of the dose equivalent to the organ or tissue (H_T) and the weighting factors (w_T) applicable to each of the body organs or tissues that are irradiated. ($H_E = \sum w_T\ H_T$).

Equivalent Dose—A dose quantity that places the biological effect of all radiation types on a common scale for calculating tissue damage. Alpha particles, for example, are considered to cause 20 times more damage than gamma rays. Equivalent dose is calculated as the sum of products of the average absorbed dose (in gray) in an organ or tissue ($_{DT,R}$) from each type of radiation and the radiation weighting factor (w_R) for that radiation ($\sum D_{T,R}\ w_R$).

External Dose—That portion of the dose equivalent received from radiation sources outside the body.

Internal Dose—That portion of the dose equivalent received from radioactive material taken into the body.

Limit—A permissible upper bound on the radiation dose.

Maximum Permissible Dose (MPD)—The greatest dose equivalent that a person or specified part thereof shall be allowed to receive in a given period of time.

Median Lethal Dose (MLD)—Dose of radiation required to kill, within a specified period (usually 30 days), 50% of the individuals in a large group of animals or organisms. Also called the LD_{50}, or $LD_{50/30}$ if for 30 days.

Threshold Dose—The minimum absorbed dose that will produce a detectable degree of any given effect.

Tissue Dose—Absorbed dose received by tissue in the region of interest, expressed in rad (see Dose, Gray, and Rad).

Dose Rate—The amount of radiation dose delivered per unit time. Generically, the rate at which radiation dose is delivered to any material or tissue.

Dose-Response Relationship—The quantitative relationship between the amount of exposure to a toxicant and the incidence of the adverse effects.

Dosimetry—Quantification of radiation doses to cells, tissues, organs, individuals or populations resulting from radiation exposures.

Early Effects (of radiation exposure)—Effects that appear within 60 days of an acute exposure.

Electron—A stable elementary particle having an electric charge equal to $\pm 1.60210 \times 10^{-19}$ C (Coulombs) and a rest mass equal to 9.1091×10^{-31} kg. A positron is a positively charged "electron" (see Positron).

Electron Volt—A unit of energy equivalent to the energy gained by an electron in passing through a potential difference of one volt. Larger multiple units of the electron volt are frequently used: keV for thousand or kilo electron volts; MeV for million or mega electron volts (eV). 1 eV=1.6×10^{-12} erg.

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

Energy—Capacity for doing work. Gravitationally, "potential energy" is the energy inherent in a mass because of its spatial relation to other masses. Chemically or radiologically, "potential energy" is the energy released when a chemical reaction or radiological transformation goes to completion. "Kinetic energy" is the energy possessed by a mass because of its motion (SI unit: joules):

> **Binding Energy (Electron)—**The amount of energy that must be expended to remove an electron from an atom.
>
> **Binding Energy (Nuclear)—**The energy represented by the difference in mass between the sum of the component parts and the actual mass of the nucleus. It represents the amount of energy that must be expended to break a nucleus into its component neutrons and protons.
>
> **Excitation Energy—**The energy required to change a system from its ground state to an excited state. Each different excited state has a different excitation energy.
>
> **Ionizing Energy—**The energy required to knock an electron out of an atom. The average energy lost by electrons or beta particles in producing an ion pair in air or in soft tissue is about 34 eV.
>
> **Radiant Energy—**The energy of electromagnetic radiation, such as radio waves, visible light, x and gamma rays.

Enrichment, Isotopic—An isotopic separation process by which the relative abundances of the isotopes of a given element are altered, thus producing a form of the element that has been enriched in one or more isotopes and depleted in others. In uranium enrichment, the percentage of uranium-235 in natural uranium can be increased from 0.7% to >90% in a gaseous diffusion process based on the different thermal velocities of the constituents of natural uranium (^{234}U, ^{235}U, ^{238}U) in the molecular form UF_6.

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

Epidemiology—Refers to the investigation of factors that determine the frequency and distribution of disease or other health-related conditions within a defined human population during a specified period.

Equilibrium, Radioactive—In a radioactive series, the state which prevails when the ratios between the activities of two or more successive members of the series remains constant.

Secular Equilibrium—If a parent element has a very much longer half-life than the daughters (so there is not appreciable change in its amount in the time interval required for later products to attain equilibrium) then, after equilibrium is reached, equal numbers of atoms of all members of the series disintegrate in unit time. This condition is never exactly attained, but is essentially established in such a case as ^{226}Ra and its transformation series to stable ^{206}Pb. The half-life of ^{226}Ra is about 1,600 years; of ^{222}Rn, approximately 3.82 days, and of each of the subsequent members, a few minutes. After about a month, essentially the equilibrium amount of radon is present; then (and for a long time) all members of the series disintegrate the same number of atoms per unit time. At this time, the activity of the daughter is equal to the activity of the parent.

Transient Equilibrium—If the half-life of the parent is short enough so the quantity present decreases appreciably during the period under consideration, but is still longer than that of successive members of the series, a stage of equilibrium will be reached after which all members of the series decrease in activity exponentially with the period of the parent. At this time, the ratio of the parent activity to the daughter activity is constant.

Equilibrium, Electron—The condition in a radiation field where the energy of the electrons entering a volume equals the energy of the electrons leaving that volume.

Excitation—The addition of energy to a system, thereby transferring it from its ground state to an excited state. Excitation of a nucleus, an atom, or a molecule can result from absorption of photons or from inelastic collisions with other particles. The excited state of an atom is an unstable or metastable state and will return to ground state by radiation of the excess energy.

Exposure (Chemical)—Contact of an organism with a chemical or physical agent. Exposure is quantified as the amount of the agent available at the exchange boundaries of the organism (e.g., skin, lungs, gut) and available for absorption.

Exposure (Radiation)—Subjection to ionizing radiation or to a radioactive material. For example, exposure in air is a measure of the ionization produced in air by x or gamma radiation; the sum of the electric charges on all ions of one sign produced in air when all electrons liberated by photons in a volume of air are completely stopped in air (dQ), divided by the mass of the air in the volume (dm). The unit of exposure in air is the roentgen, or coulomb per kilogram (SI units). One roentgen is equal to 2.58×10^{-4} coulomb per kilogram (C/kg).

Fission, Nuclear—A nuclear transformation characterized by the splitting of a nucleus into at least two other nuclei with emission of several neutrons, accompanied by the release of a relatively large amount of energy.

Gamma Ray, Penetrating—Short wavelength electromagnetic radiation of nuclear origin.

Genetic Effect of Radiation—Inheritable change, chiefly mutations, produced by the absorption of ionizing radiation by germ cells. Genetic effects have not been observed in any human population exposed at any dose level.

Genotoxicity—A specific adverse effect on the genome of living cells that, upon the duplication of affected cells, can be expressed as a mutagenic, clastogenic or carcinogenic event because of specific alteration of the molecular structure of the genome.

Gray (Gy)—SI unit of absorbed dose, 1 J/kg. One gray equals 100 rad (see Units).

Half-life, Effective—See Half-Time, Effective.

Half-life, Radioactive—Time required for a radioactive substance to lose 50% of its activity by decay. Each radio-nuclide has a unique physical half-life. Known also as physical half-time and symbolized as T_r or T_{rad}.

Half-time, Biological—Time required for an organ, tissue, or the whole body to eliminate one-half of any absorbed substance by regular processes of elimination. This is the same for both stable and radioactive isotopes of a particular element, and is sometimes referred to as half-time, symbolized as t_{biol} or T_b.

Half-time, Effective—Time required for a radioactive element in an organ, tissue, or the whole body to be diminished 50% as a result of the combined action of radioactive decay and biological elimination, symbolized as T_e or T_{eff}.

$$\text{Effective half-time} = \frac{\text{Biological half-time} \times \text{Radioactive half-life}}{\text{Biological half-time} + \text{Radioactive half-life}}$$

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

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

Immunological Effects—Functional changes in the immune response.

Incidence—The ratio of individuals in a population who develop a specified condition to the total number of individuals in that population who could have developed that condition in a specified time period.

Intensity—Amount of energy per unit time passing through a unit area perpendicular to the line of propagation at the point in question.

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

Internal Conversion—Process in which a gamma ray knocks an electron out of the same atom from which the gamma ray was emitted. The ratio of the number of internal conversion electrons to the number of gamma quanta emitted in the de-excitation of the nucleus is called the "conversion ratio."

***In Vitro*—**Isolated from the living organism and artificially maintained, as in a test tube. Literally, "in glass."

***In Vivo*—**Occurring within the living organism. Literally, "in life."

Ion—Atomic particle, atom or chemical radical bearing a net electrical charge, either negative or positive.

Ion Pair—Two particles of opposite charge, usually referring to the electron and positive atomic or molecular residue resulting after the interaction of ionizing radiation with the orbital electrons of atoms.

Ionization—The process by which a neutral atom or molecule acquires a positive or negative charge.

Primary Ionization—(1) In collision theory: the ionization produced by the primary particles as contrasted to the "total ionization" which includes the "secondary ionization" produced by delta rays. (2) In counter tubes: the total ionization produced by incident radiation without gas amplification.

Specific Ionization—Number of ion pairs per unit length of path of ionizing radiation in a medium; e.g., per centimeter of air or per micrometer of tissue.

Total Ionization—The total electric charge of one sign on the ions produced by radiation in the process of losing its kinetic energy. For a given gas, the total ionization is closely proportional to the initial ionization and is nearly independent of the nature of the ionizing radiation. It is frequently used as a measure of absorption of radiation energy.

Ionization Density—Number of ion pairs per unit volume.

Ionization Path (Track)—The trail of ion pairs produced by an ionizing particle in its passage through matter.

Ionizing Radiation—Any radiation capable of knocking electrons out of atoms and producing ions. Examples: alpha, beta, gamma and x rays, and neutrons.

Isobars—Nuclides having the same mass number but different atomic numbers.

Isomers—Nuclides having the same number of neutrons and protons but capable of existing, for a measurable time, in different quantum states with different energies and radioactive properties. Commonly the isomer of higher energy decays to one with lower energy by the process of isomeric transition.

Isotopes—Nuclides having the same number of protons in their nuclei, and hence the same atomic number, but differing in the number of neutrons, and therefore in the mass number. Identical chemical properties exist in isotopes of a particular element. The term should not be used as a synonym for nuclide because isotopes refer specifically to different nuclei of the same element.

Stable Isotope—A nonradioactive isotope of an element.

Joule—The S.I. unit for work and energy. It is equal to the work done by raising a mass of one newton through a distance of one meter (J = Nm), which corresponds to about 0.7 ft-pound.

Kerma (k)—A measure of the kinetic energy transferred from gamma rays or neutrons to a unit mass of absorbing medium in the initial collision between the radiation and the absorber atoms. The SI unit is J/kg. The special name of this unit is the rad (traditional system of units) or Gray (SI).

Labeled Compound—A compound containing one or more radioactive atoms intentionally added to its structure. By observations of radioactivity or isotopic composition, this compound or its fragments may be followed through physical, chemical, or biological processes.

Late Effects (of radiation exposure)—Effects which appear 60 days or more following an acute exposure.

$LD_{50/30}$—The dose of a chemical or radiation expected to cause 50% mortality in those exposed within 30 days. For radiation, this is about 350 rad (3.5 gray) received by humans over a short period of time.

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

Lethal Concentration$_{(50)}$ (LC_{50})—A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population within a specified time, usually 30 days.

Lethal Dose$_{(Lo)}$ (LD_{Lo})—The lowest dose of a chemical introduced by a route other than inhalation that is expected to have caused death in humans or animals within a specified time, usually 30 days.

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

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

Linear Energy Transfer (LET)—A measure of the energy that a charged particle transfers to a material per unit path length.

> **Average LET—**The energy of a charged particle divided by the length of the path over which it deposits all its energy in a material. This is averaged over a number of particles.
>
> **High-LET—**Energy transfer characteristic of heavy charged particles such as protons and alpha particles where the distance between ionizing events is small on the scale of a cellular nucleus.
>
> **Low-LET—**Energy transfer characteristic of light charged particles such as electrons produced by x and gamma rays where the distance between ionizing events is large on the scale of a cellular nucleus.

Lowest-Observed-Adverse-Effect Level (LOAEL)—The lowest dose of chemical in a study, or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Lung Clearance Class (fast, F; medium, M; slow, S)—A classification scheme for inhaled material according to its rate of clearance from the pulmonary region of the lungs to the blood and the gastrointestinal tract.

Lymphoreticular Effects—Represent morphological effects involving lymphatic tissues such as the lymph nodes, spleen, and thymus.

Malformations—Permanent structural changes that may adversely affect survival, development, or function.

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

Minimal Risk Level—An estimate of daily human exposure to a substance that is likely to be without an appreciable risk of adverse noncancerous effects over a specified duration of exposure.

Modifying Factor (MF)—A value (greater than zero) that is applied to the derivation of a Minimal Risk Level (MRL) to reflect additional concerns about the database that are not covered by the uncertainty factors. The default value for a MF is 1.

Morbidity—State of being diseased; morbidity rate is the incidence or prevalence of disease in a specific population.

Mortality—Death; mortality rate is a measure of the number of deaths in a population during a specified interval of time.

Mutagen—A substance that causes changes (mutations) in the genetic material in a cell. Mutations can lead to birth defects, miscarriages, or cancer.

Necropsy—The gross examination of the organs and tissues of a dead body to determine the cause of death or pathological conditions.

Neurotoxicity—The occurrence of adverse effects on the nervous system following exposure to a substance.

Neutrino (v)—A neutral particle of infinitesimally small rest mass emitted during beta plus or beta minus decay. This particle accounts for conservation of energy in beta plus and beta minus decays. It plays no role in damage from radiation.

Noble Gas—Any of a group of rare gases that include helium, neon, argon, krypton, xenon, and radon. Because the outermost electron shell of atoms of these gases is full, they do not react chemically with other substances except under certain special conditions. Also called inert gas.

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

Nuclear Reactor—A power plant that heats the medium (typically water) by using the energy released from the nuclear fission of uranium or plutonium isotopes instead of burning coal, oil, or natural gas. All of these sources of energy simply heat water and use the steam which is produced to turn turbines that make electricity or propel a ship.

Nucleon—Common name for a constituent particle of the nucleus. Applied to a proton or neutron.

Nuclide—A species of atom characterized by the constitution of its nucleus. The nuclear constitution is specified by the number of protons (Z), number of neutrons (N), and energy content; or, alternatively, by the atomic number (Z), mass number A(N+Z), and atomic mass. To be regarded as a distinct nuclide, the atom must be capable of existing for a measurable time. Thus, nuclear isomers are separate nuclides, whereas promptly decaying excited nuclear states and unstable intermediates in nuclear reactions are not so considered.

Octanol-Water Partition Coefficient (K_{ow})—The equilibrium ratio of the concentrations of a chemical in n-octanol and water, in dilute solution.

Odds Ratio (OR)—The ratio of the odds of an event (e.g., lung cancer) occurring in one group (e.g., a group exposed to a particular substance) to the odds of the same event (e.g., lung cancer) occurring in another group (e.g., a group not exposed to the same substance). An odds ratio of greater than 1 is considered to indicate greater risk of disease in the exposed group compared to the unexposed.

> **Excess Odds Ratio—**The 'extra' or 'additional' odds of an effect due to exposure to some stressor above and beyond the odds of that effect occurring in the absence of the stressor, expressed as excess odds per some unit increase in the stressor.

Organophosphate or Organophosphorus Compound—A phosphorus-containing organic compound and especially a pesticide that acts by inhibiting cholinesterase.

Pair Production—An absorption process for x- and gamma radiation in which the incident photon is absorbed in the vicinity of the nucleus of the absorbing atom, with subsequent production of an electron and positron pair (see annihilation). This reaction can only occur for incident photon energies exceeding 1.02 MeV.

Parent—Any radionuclide nuclide which, upon disintegration, yields a new nuclide (termed the progeny or daughter), either directly or as a later member of a radioactive series.

Permissible Exposure Limit (PEL)—A maximum allowable atmospheric level of a substance in workplace air averaged over an 8-hour shift.

Pesticide—General classification of chemicals specifically developed and produced for use in the control of agricultural and public health pests.

Pharmacokinetic Model—A set of equations that can be used to describe the time course of a parent chemical or metabolite in an animal system. There are two types of pharmacokinetic models: data-based and physiologically-based. A data-based model divides the animal system into a series of compartments which, in general, do not represent real, identifiable anatomic regions of the body whereas the physiologically-based model compartments represent real anatomic regions of the body.

Pharmacokinetics—The dynamic behavior of a material in the body, used to predict the fate (disposition) of an exogenous substance in an organism. Utilizing computational techniques, it provides the means of studying the absorption, distribution, metabolism and excretion of chemicals by the body.

Physiologically Based Pharmacodynamic (PBPD) Model—A type of physiologically-based dose-response model which quantitatively describes the relationship between target tissue dose and toxic end points. These models advance the importance of physiologically based models in that they clearly describe the biological effect (response) produced by the system following exposure to an exogenous substance.

Physiologically Based Pharmacokinetic (PBPK) Model—A model comprising a series of compartments representing organs or tissue groups with realistic weights and blood flows. These models require a variety of physiological information: tissue volumes, blood flow rates to tissues, cardiac output, alveolar ventilation rates and, possibly membrane permeabilities. The models also utilize biochemical information such as air/blood partition coefficients, and metabolic parameters. PBPK models are also called biologically based tissue dosimetry models.

Photoelectric Effect—An attenuation process observed for x and gamma radiation in which an incident photon interacts with a tightly bound inner orbital electron of an atom delivering all of its energy to knock the electron out of the atom. The incident photon disappears in the process.

Photon—A quantum of electromagnetic energy (E) whose value is the product of its frequency (ν) in hertz and Planck's constant (h). The equation is: $E = h\nu$.

Population dose—See Collective dose.

Positron—A positively charged electron.

Potential, Ionization—The energy expressed as electron volts (eV) necessary to separate one electron from an atom, resulting in the formation of an ion pair.

Power, Stopping—A measure of the ability of a material to absorb energy from an ionizing particle passing through it; the greater the stopping power, the greater the energy absorbing ability (see Linear Energy Transfer).

Prevalence—The number of cases of a disease or condition in a population at one point in time.

Progeny—The decay product or daughter products resulting after a radioactive decay or a series of radioactive decays. The progeny can also be radioactive, and the chain continues until a stable nuclide is formed.

Prospective Study—A type of cohort study in which the pertinent observations are made on events occurring after the start of the study. A group is followed over time.

Proton—Elementary nuclear particle with a positive electric charge equal numerically to the charge of the electron and a rest mass of 1.007 mass units.

q_1*—The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The q_1* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually µg/L for water, mg/kg/day for food, and $\mu g/m^3$ 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 (Q)—The linear-energy-transfer-dependent factor by which absorbed doses are multiplied to obtain (for radiation protection purposes) a quantity that expresses - on a common scale for all ionizing radiation - the approximate biological effectiveness of the absorbed dose.

Type of radiation	Quality Factor
X, gamma, or beta	1
Alpha particles	20
Neutrons of unknown energy	10
High energy protons	10

Rad—The traditional unit of absorbed dose equal to 100 ergs per gram, or 0.01 joule per kilogram (0.01 Gy) in any medium (see Absorbed Dose).

Radiation—The emission and propagation of energy through space or through a material medium in the form of waves (e.g., the emission and propagation of electromagnetic waves, or of sound and elastic waves). The term radiation or radiant energy, when unqualified, usually refers to electromagnetic radiation. Such radiation commonly is classified according to frequency, as microwaves, infrared, visible (light), ultraviolet, and x and gamma rays (see Photon.) and, by extension, corpuscular emission, such as alpha and beta radiation, neutrons, or rays of mixed or unknown type, as cosmic radiation.

Radiation, Annihilation—Photons produced when an electron and a positron unite and cease to exist. The annihilation of a positron-electron pair results in the production of two photons, each of 0.51 MeV energy.

Radiation, Background—See Background Radiation.

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

Radiation, External—Radiation from a source outside the body.

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

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

Radiation, Monoenergetic—Radiation of a given type in which all particles or photons originate with and have the same energy.

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

Radiation, Secondary—A particle or ray that is produced when the primary radiation interacts with a material, and which has sufficient energy to produce its own ionization, such as bremsstrahlung or electrons knocked from atomic orbitals with enough energy to then produce ionization (see Delta Rays).

Radiation Weighting Factor (also called Quality Factor)—In radiation protection, a factor (1 for x-rays, gamma rays, beta particles; 20 for alpha particles) weighting the absorbed dose of radiation of a specific type and energy for its effect on tissue.

Radioactive Material—Material containing radioactive atoms.

Radioactivity—Spontaneous nuclear transformations that result in the formation of new elements. These transformations are accomplished by emission of alpha or beta particles from the nucleus or by the capture of an orbital electron. Each of these reactions may or may not be accompanied by a gamma photon.

Radioactivity, Artificial—Man-made radioactivity produced by particle bombardment or nuclear fission, as opposed to naturally occurring radioactivity.

Radioactivity, Induced—Radioactivity produced in a substance after bombardment with neutrons or other particles. The resulting activity is "natural radioactivity" if formed by nuclear reactions occurring in nature and "artificial radioactivity" if the reactions are caused by man.

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

Radioisotope—An unstable or radioactive isotope of an element that decays or disintegrates spontaneously, emitting radiation.

Radionuclide—Any radioactive isotope of any element. Approximately 5,000 natural and artificial radioisotopes have been identified.

Radiosensitivity—Relative susceptibility of cells, tissues, organs, organisms, or any living substance to the injurious action of radiation. Radiosensitivity and its antonym, radioresistance, are used comparatively, rather than absolutely.

Recommended Exposure Limit (REL)—A National Institute for Occupational Safety and Health (NIOSH) time-weighted average (TWA) concentration for up to a 10-hour workday during a 40-hour workweek.

Reference Concentration (RfC)—An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious noncancer health effects during a lifetime. The inhalation reference concentration is for continuous inhalation exposures and is appropriately expressed in units of mg/m^3 or ppm.

Reference Dose (RfD)—An estimate of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the NOAEL (from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a professional judgment of the entire database on the chemical. The RfDs are not applicable to non-threshold effects such as cancer.

Relative Biological Effectiveness (RBE)—The RBE is a factor used to compare the biological effectiveness of absorbed radiation doses (i.e., rad) due to different types of ionizing radiation. More specifically, it is the experimentally determined ratio of an absorbed dose of a radiation in question to the absorbed dose of a reference radiation (typically ^{60}Co gamma rays or 200 kVp x rays) required to produce an identical biological effect in a particular experimental organism or tissue (see Quality Factor).

Relative Risk (RR)— Risk as a ratio of the incidence among subjects exposed to a particular risk factor divided by the incidence among subjects who were not exposed to the risk factor.

Excess Relative Risk (ERR)— In epidemiology typically defined to be the difference between the proportion of subjects in a population with a particular disease who were exposed to a specified risk factor and the proportion of subjects with that same disease who were not exposed.

Rem—The traditional unit of dose equivalent that is used in the regulatory, administrative, and engineering design aspects of radiation safety practice. The dose equivalent in rem is numerically equal to the absorbed dose in rad multiplied by the quality factor (1 rem is equal to 0.01 sievert).

Reportable Quantity (RQ)—The quantity of a hazardous substance that is considered reportable under CERCLA. Reportable quantities are (1) 1 pound or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Sect. 311 of the Clean Water Act. Quantities are measured over a 24-hour period.

Reproductive Toxicity—The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

Roentgen (R)—A unit of exposure (in air) to ionizing radiation. It is the amount of x or gamma rays required to produce ions carrying 1 electrostatic unit of electrical charge in 1 cubic centimeter of dry air under standard conditions. Named after William Roentgen, a German scientist who discovered x rays in 1895.

Retrospective Study—A type of cohort study based on a group of persons known to have been exposed at some time in the past. Data are collected from routinely recorded events, up to the time the study is undertaken. Retrospective studies are limited to causal factors that can be ascertained from existing records and/or examining survivors of the cohort.

Risk—The possibility or chance that some adverse effect will result from a given exposure to a chemical.

Risk Factor—An aspect of personal behavior or lifestyle, an environmental exposure, or an inborn or inherited characteristic that is associated with an increased occurrence of disease or other health-related event or condition.

Risk Ratio—The ratio of the risk among persons with specific risk factors compared to the risk among persons without risk factors. A risk ratio greater than 1 indicates greater risk of disease in the exposed group compared to the unexposed group.

Self-Absorption—Absorption of radiation (emitted by radioactive atoms) by the material in which the atoms are located; in particular, the absorption of radiation within a sample being assayed.

Short-Term Exposure Limit (STEL)—The maximum concentration to which workers can be exposed for up to 15 minutes continually. No more than four excursions are allowed per day, and there must be at least 60 minutes between exposure periods. The daily TLV-TWA may not be exceeded.

SI Units—The International System of Units as defined by the General Conference of Weights and Measures in 1960. These units are generally based on the meter/kilogram/second units, with special quantities for radiation including the becquerel, gray, and sievert.

Sickness, Acute Radiation (Syndrome)—The complex symptoms and signs characterizing the condition resulting from excessive exposure of the whole body (or large part) to ionizing radiation. The earliest of these symptoms are nausea, fatigue, vomiting, and diarrhea, and may be followed by loss of hair (epilation), hemorrhage, inflammation of the mouth and throat, and general loss of energy. In severe cases, where the radiation dose is relatively high (over several hundred rad or several gray), death may occur within two to four weeks. Those who survive six weeks after exposure of a single high dose of radiation may generally be expected to recover.

Sievert (Sv)—The SI unit of any of the quantities expressed as dose equivalent. The dose equivalent in sieverts is equal to the absorbed dose, in gray, multiplied by the quality factor (1 sievert equals 100 rem). The sievert is also the SI unit for effective dose equivalent, which is the sum of the products of the dose equivalent to each organ or tissue and its corresponding tissue weighting factor.

Specific-Activity—Radioactivity per unit mass of a radionuclide, expressed, for example, as Ci/gram or Bq/kilogram.

Specific Energy—The actual energy per unit mass deposited per unit volume in a small target, such as the cell or cell nucleus, as the result of one or more energy-depositing events. This is a stochastic quantity as opposed to the average value over a large number of instance (i.e., the absorbed dose).

Standardized Mortality Ratio (SMR)—A ratio of the observed number of deaths and the expected number of deaths in a specific standard population.

Stochastic Effect—A health effect that occurs randomly and for which the probability of the effect occurring, rather than its severity, is assumed to be a linear function of dose without a threshold (also called a nondeterministic effect).

Stopping Power—The average rate of energy loss of a charged particle per unit thickness of a material or per unit mass of material traversed.

Surface-seeking Radionuclide—A bone-seeking internal emitter that deposits and remains on the bone surface for a long period of time, although it may eventually diffuse into the bone mineral. This contrasts with a volume seeker, which deposits more uniformly throughout the bone volume.

Target Organ Toxicity—This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

Target Theory (Hit Theory)—A theory explaining some biological effects of radiation on the basis that ionization, occurring in a discrete volume (the target) within the cell, directly causes a lesion which subsequently results in a physiological response to the damage at that location. One, two, or more “hits” (ionizing events within the target) may be necessary to elicit the response.

Teratogen—A chemical that causes birth defects.

Threshold Limit Value (TLV)—The maximum concentration of a substance to which most workers can be exposed without adverse effect. TLV is a term used exclusively by the ACGIH. Other terms used to express similar concepts are the MAC (Maximum Allowable Concentration) and PEL (Permissible Exposure Limits).

Time-Weighted Average (TWA)—An allowable exposure concentration averaged over a normal 8-hour workday or 40-hour workweek.

Tissue Weighting Factor (W_t)—Organ- or tissue-specific factor by which the equivalent dose is multiplied to give the portion of the effective dose for that organ or tissue. Recommended values of tissue weighting factors are:

Tissue/Organ	Tissue Weighting Factor
Gonads	0.70
Bone marrow (red)	0.12
Colon	0.12
Lung	0.12
Stomach	0.12
Bladder	0.05
Breast	0.05
Liver	0.05
Esophagus	0.05
Thyroid	0.05
Skin	0.01
Bone surface	0.01
Remainder (adrenals, brain, upper large intestine, small intestine, pancreas, spleen, thymus, and uterus)	0.05

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

Toxicokinetic—The absorption, distribution and elimination of toxic compounds in the living organism.

Toxicosis—A diseased condition resulting from poisoning.

Transformation, Nuclear—The process of radioactive decay by which a nuclide is transformed into a different nuclide by absorbing or emitting particulate or electromagnetic radiation.

Transition, Isomeric—The process by which a nuclide decays to an isomeric nuclide (i.e., one of the same mass number and atomic number) of lower quantum energy. Isomeric transitions (often abbreviated I.T.) proceed by gamma ray and internal conversion electron emission.

Tritium—The hydrogen isotope with one proton and two neutrons in the nucleus (Symbol: ^3H). It is radioactive and has a physical half-life of 12.3 years.

Unattached Fraction—That fraction of the radon daughters, usually ^{218}Po and ^{214}Po, which has not yet attached to a dust particle or to water vapor. As a free atom, it has a high probability of being exhaled and not retained within the lung. It is the attached fraction which is primarily retained.

Uncertainty Factor (UF)—A factor used in operationally deriving the RfD from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of human, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10.

Units, Prefixes—Many units of measure are expressed as submultiples or multiples of the primary unit (e.g., 10^{-3} curie is 1 mCi and 10^{3} becquerel is 1 kBq).

Factor	Prefix	Symbol	Factor	Prefix	Symbol
10^{-18}	atto	a	10^{3}	kilo	k
10^{-15}	femto	f	10^{6}	mega	M
10^{-12}	pico	p	10^{9}	giga	G
10^{-9}	nano	n	10^{12}	tera	T
10^{-6}	micro	μ	10^{15}	peta	P
10^{-3}	milli	m	10^{18}	exa	E
10^{-2}	centi	c			

Units, Radiological—

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

*International Units, designated (SI)

Working Level (WL)—Any combination of short-lived radon daughters in 1 liter of air that will result in the ultimate emission of 1.3×10^{5} MeV of potential alpha energy.

Working Level Month (WLM)—A unit of exposure to radon daughters corresponding to the product of the radon daughter concentration in Working Level (WL) and the exposure time in nominal months (1 nominal month = 170 hours). Inhalation of air with a concentration of 1 WL of radon daughters for 170 working hours results in an exposure of 1 WLM.

Xenobiotic—Any chemical that is foreign to the biological system.

X rays—Penetrating electromagnetic radiations whose wave lengths are very much shorter than those of visible light. They are usually produced by bombarding a metallic target with fast electrons in a high vacuum. X rays (called characteristic x rays) are also produced when an orbital electron falls from a high energy level to a low energy level.

Zero-Threshold Linear Hypothesis (or No-Threshold Linear Hypothesis)—The assumption that a dose-response curve derived from data in the high dose and high dose-rate ranges may be extrapolated through the low dose and low dose range to zero, implying that, theoretically, any amount of radiation will cause some damage.

APPENDIX A. ATSDR MINIMAL RISK LEVELS AND WORKSHEETS

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) [42 U.S.C. 9601 et seq.], as amended by the Superfund Amendments and Reauthorization Act (SARA) [Pub. L. 99–499], requires that the Agency for Toxic Substances and Disease Registry (ATSDR) develop jointly with the U.S. Environmental Protection Agency (EPA), in order of priority, a list of hazardous substances most commonly found at facilities on the CERCLA National Priorities List (NPL); prepare toxicological profiles for each substance included on the priority list of hazardous substances; and assure the initiation of a research program to fill identified data needs associated with the substances.

The toxicological profiles include an examination, summary, and interpretation of available toxicological information and epidemiologic evaluations of a hazardous substance. During the development of toxicological profiles, Minimal Risk Levels (MRLs) are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration for a given route of exposure. An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. MRLs are based on noncancer health effects only and are not based on a consideration of cancer effects. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors to identify contaminants and potential health effects that may be of concern at hazardous waste sites. It is important to note that MRLs are not intended to define clean-up or action levels.

MRLs are derived for hazardous substances using the no-observed-adverse-effect level/uncertainty factor approach. They are below levels that might cause adverse health effects in the people most sensitive to such chemical-induced effects. MRLs are derived for acute (1–14 days), intermediate (15–364 days), and chronic (365 days and longer) durations and for the oral and inhalation routes of exposure. Currently, MRLs for the dermal route of exposure are not derived because ATSDR has not yet identified a method suitable for this route of exposure. MRLs are generally based on the most sensitive chemical-induced end point considered to be of relevance to humans. Serious health effects (such as irreparable damage to the liver or kidneys, or birth defects) are not used as a basis for establishing MRLs. Exposure to a level above the MRL does not mean that adverse health effects will occur.

MRLs are intended only to serve as a screening tool to help public health professionals decide where to look more closely. They may also be viewed as a mechanism to identify those hazardous waste sites that

are not expected to cause adverse health effects. Most MRLs contain a degree of uncertainty because of the lack of precise toxicological information on the people who might be most sensitive (e.g., infants, elderly, nutritionally or immunologically compromised) to the effects of hazardous substances. ATSDR uses a conservative (i.e., protective) approach to address this uncertainty consistent with the public health principle of prevention. Although human data are preferred, MRLs often must be based on animal studies because relevant human studies are lacking. In the absence of evidence to the contrary, ATSDR assumes that humans are more sensitive to the effects of hazardous substance than animals and that certain persons may be particularly sensitive. Thus, the resulting MRL may be as much as 100-fold below levels that have been shown to be nontoxic in laboratory animals.

Proposed MRLs undergo a rigorous review process: Health Effects/MRL Workgroup reviews within the Division of Toxicology and Human Health Sciences (proposed), expert panel peer reviews, and agency-wide MRL Workgroup reviews, with participation from other federal agencies and comments from the public. They are subject to change as new information becomes available concomitant with updating the toxicological profiles. Thus, MRLs in the most recent toxicological profiles supersede previously published levels. For additional information regarding MRLs, please contact the Division of Toxicology and Human Health Sciences (proposed), Agency for Toxic Substances and Disease Registry, 1600 Clifton Road NE, Mailstop F-62, Atlanta, Georgia 30333.

For reasons discussed in Section 2.3, MRLs were not derived for radon.

APPENDIX B. USER'S GUIDE

Chapter 1

Public Health Statement

This chapter of the profile is a health effects summary written in non-technical language. Its intended audience is the general public, especially people living in the vicinity of a hazardous waste site or chemical release. If the Public Health Statement were removed from the rest of the document, it would still communicate to the lay public essential information about the chemical.

The major headings in the Public Health Statement are useful to find specific topics of concern. The topics are written in a question and answer format. The answer to each question includes a sentence that will direct the reader to chapters in the profile that will provide more information on the given topic.

Chapter 2

Relevance to Public Health

This chapter provides a health effects summary based on evaluations of existing toxicologic, epidemiologic, and toxicokinetic information. This summary is designed to present interpretive, weight-of-evidence discussions for human health end points by addressing the following questions:

1. What effects are known to occur in humans?

2. What effects observed in animals are likely to be of concern to humans?

3. What exposure conditions are likely to be of concern to humans, especially around hazardous waste sites?

The chapter covers end points in the same order that they appear within the Discussion of Health Effects by Route of Exposure section, by route (inhalation, oral, and dermal) and within route by effect. Human data are presented first, then animal data. Both are organized by duration (acute, intermediate, chronic). *In vitro* data and data from parenteral routes (intramuscular, intravenous, subcutaneous, etc.) are also considered in this chapter.

The carcinogenic potential of the profiled substance is qualitatively evaluated, when appropriate, using existing toxicokinetic, genotoxic, and carcinogenic data. ATSDR does not currently assess cancer potency or perform cancer risk assessments. Minimal Risk Levels (MRLs) for noncancer end points (if derived) and the end points from which they were derived are indicated and discussed.

Limitations to existing scientific literature that prevent a satisfactory evaluation of the relevance to public health are identified in the Chapter 3 Data Needs section.

Interpretation of Minimal Risk Levels

Where sufficient toxicologic information is available, ATSDR has derived MRLs for inhalation and oral routes of entry at each duration of exposure (acute, intermediate, and chronic). These MRLs are not meant to support regulatory action, but to acquaint health professionals with exposure levels at which adverse health effects are not expected to occur in humans.

MRLs should help physicians and public health officials determine the safety of a community living near a chemical emission, given the concentration of a contaminant in air or the estimated daily dose in water. MRLs are based largely on toxicological studies in animals and on reports of human occupational exposure.

MRL users should be familiar with the toxicologic information on which the number is based. Chapter 2, "Relevance to Public Health," contains basic information known about the substance. Other sections such as Chapter 3 Section 3.9, "Interactions with Other Substances," and Section 3.10, "Populations that are Unusually Susceptible" provide important supplemental information.

MRL users should also understand the MRL derivation methodology. MRLs are derived using a modified version of the risk assessment methodology that the Environmental Protection Agency (EPA) provides (Barnes and Dourson 1988) to determine reference doses (RfDs) for lifetime exposure.

To derive an MRL, ATSDR generally selects the most sensitive end point which, in its best judgement, represents the most sensitive human health effect for a given exposure route and duration. ATSDR cannot make this judgement or derive an MRL unless information (quantitative or qualitative) is available for all potential systemic, neurological, and developmental effects. If this information and reliable quantitative data on the chosen end point are available, ATSDR derives an MRL using the most sensitive species (when information from multiple species is available) with the highest no-observed-adverse-effect level (NOAEL) that does not exceed any adverse effect levels. When a NOAEL is not available, a lowest-observed-adverse-effect level (LOAEL) can be used to derive an MRL, and an uncertainty factor (UF) of 10 must be employed. Additional uncertainty factors of 10 must be used both for human variability to protect sensitive subpopulations (people who are most susceptible to the health effects caused by the substance) and for interspecies variability (extrapolation from animals to humans). In deriving an MRL, these individual uncertainty factors are multiplied together. The product is then divided into the inhalation concentration or oral dosage selected from the study. Uncertainty factors used in developing a substance-specific MRL are provided in the footnotes of the levels of significant exposure (LSE) tables.

Chapter 3

Health Effects

Tables and Figures for Levels of Significant Exposure (LSE)

Tables and figures are used to summarize health effects and illustrate graphically levels of exposure associated with those effects. These levels cover health effects observed at increasing dose concentrations and durations, differences in response by species, MRLs to humans for noncancer end points, and EPA's estimated range associated with an upper- bound individual lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. Use the LSE tables and figures for a quick review of the health effects and to locate data for a specific exposure scenario. The LSE tables and figures should always be used in conjunction with the text. All entries in these tables and figures represent studies that provide reliable, quantitative estimates of NOAELs, LOAELs, or Cancer Effect Levels (CELs).

The legends presented below demonstrate the application of these tables and figures. Representative examples of LSE Table 3-1 and Figure 3-1 are shown. The numbers in the left column of the legends correspond to the numbers in the example table and figure.

LEGEND

See Sample LSE Table 3-1 (page B-6)

(1) Route of Exposure. One of the first considerations when reviewing the toxicity of a substance using these tables and figures should be the relevant and appropriate route of exposure. Typically when sufficient data exist, three LSE tables and two LSE figures are presented in the document. The three LSE tables present data on the three principal routes of exposure, i.e., inhalation, oral, and dermal (LSE Tables 3-1, 3-2, and 3-3, respectively). LSE figures are limited to the inhalation (LSE Figure 3-1) and oral (LSE Figure 3-2) routes. Not all substances will have data on each route of exposure and will not, therefore, have all five of the tables and figures.

(2) Exposure Period. Three exposure periods—acute (less than 15 days), intermediate (15–364 days), and chronic (365 days or more)—are presented within each relevant route of exposure. In this example, an inhalation study of intermediate exposure duration is reported. For quick reference to health effects occurring from a known length of exposure, locate the applicable exposure period within the LSE table and figure.

(3) Health Effect. The major categories of health effects included in LSE tables and figures are death, systemic, immunological, neurological, developmental, reproductive, and cancer. NOAELs and LOAELs can be reported in the tables and figures for all effects but cancer. Systemic effects are further defined in the "System" column of the LSE table (see key number 18).

(4) Key to Figure. Each key number in the LSE table links study information to one or more data points using the same key number in the corresponding LSE figure. In this example, the study represented by key number 18 has been used to derive a NOAEL and a Less Serious LOAEL (also see the two "18r" data points in sample Figure 3-1).

(5) Species. The test species, whether animal or human, are identified in this column. Chapter 2, "Relevance to Public Health," covers the relevance of animal data to human toxicity and Section 3.4, "Toxicokinetics," contains any available information on comparative toxicokinetics. Although NOAELs and LOAELs are species specific, the levels are extrapolated to equivalent human doses to derive an MRL.

(6) Exposure Frequency/Duration. The duration of the study and the weekly and daily exposure regimens are provided in this column. This permits comparison of NOAELs and LOAELs from different studies. In this case (key number 18), rats were exposed to “Chemical x” via inhalation for 6 hours/day, 5 days/week, for 13 weeks. For a more complete review of the dosing regimen, refer to the appropriate sections of the text or the original reference paper (i.e., Nitschke et al. 1981).

(7) System. This column further defines the systemic effects. These systems include respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, and dermal/ocular. "Other" refers to any systemic effect (e.g., a decrease in body weight) not covered in these systems. In the example of key number 18, one systemic effect (respiratory) was investigated.

(8) NOAEL. A NOAEL is the highest exposure level at which no harmful effects were seen in the organ system studied. Key number 18 reports a NOAEL of 3 ppm for the respiratory system, which was used to derive an intermediate exposure, inhalation MRL of 0.005 ppm (see footnote "b").

(9) LOAEL. A LOAEL is the lowest dose used in the study that caused a harmful health effect. LOAELs have been classified into "Less Serious" and "Serious" effects. These distinctions help readers identify the levels of exposure at which adverse health effects first appear and the gradation of effects with increasing dose. A brief description of the specific end point used to quantify the adverse effect accompanies the LOAEL. The respiratory effect reported in key number 18 (hyperplasia) is a Less Serious LOAEL of 10 ppm. MRLs are not derived from Serious LOAELs.

(10) Reference. The complete reference citation is given in Chapter 9 of the profile.

(11) CEL. A CEL is the lowest exposure level associated with the onset of carcinogenesis in experimental or epidemiologic studies. CELs are always considered serious effects. The LSE tables and figures do not contain NOAELs for cancer, but the text may report doses not causing measurable cancer increases.

(12) Footnotes. Explanations of abbreviations or reference notes for data in the LSE tables are found in the footnotes. Footnote "b" indicates that the NOAEL of 3 ppm in key number 18 was used to derive an MRL of 0.005 ppm.

LEGEND

See Sample Figure 3-1 (page B-7)

LSE figures graphically illustrate the data presented in the corresponding LSE tables. Figures help the reader quickly compare health effects according to exposure concentrations for particular exposure periods.

(13) Exposure Period. The same exposure periods appear as in the LSE table. In this example, health effects observed within the acute and intermediate exposure periods are illustrated.

(14) Health Effect. These are the categories of health effects for which reliable quantitative data exists. The same health effects appear in the LSE table.

(15) Levels of Exposure. Concentrations or doses for each health effect in the LSE tables are graphically displayed in the LSE figures. Exposure concentration or dose is measured on the log scale "y" axis. Inhalation exposure is reported in mg/m^3 or ppm and oral exposure is reported in mg/kg/day.

(16) NOAEL. In this example, the open circle designated 18r identifies a NOAEL critical end point in the rat upon which an intermediate inhalation exposure MRL is based. The key number 18 corresponds to the entry in the LSE table. The dashed descending arrow indicates the extrapolation from the exposure level of 3 ppm (see entry 18 in the table) to the MRL of 0.005 ppm (see footnote "b" in the LSE table).

(17) CEL. Key number 38m is one of three studies for which CELs were derived. The diamond symbol refers to a CEL for the test species-mouse. The number 38 corresponds to the entry in the LSE table.

(18) Estimated Upper-Bound Human Cancer Risk Levels. This is the range associated with the upper-bound for lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. These risk levels are derived from the EPA's Human Health Assessment Group's upper-bound estimates of the slope of the cancer dose response curve at low dose levels (q_1*).

(19) Key to LSE Figure. The Key explains the abbreviations and symbols used in the figure.

SAMPLE

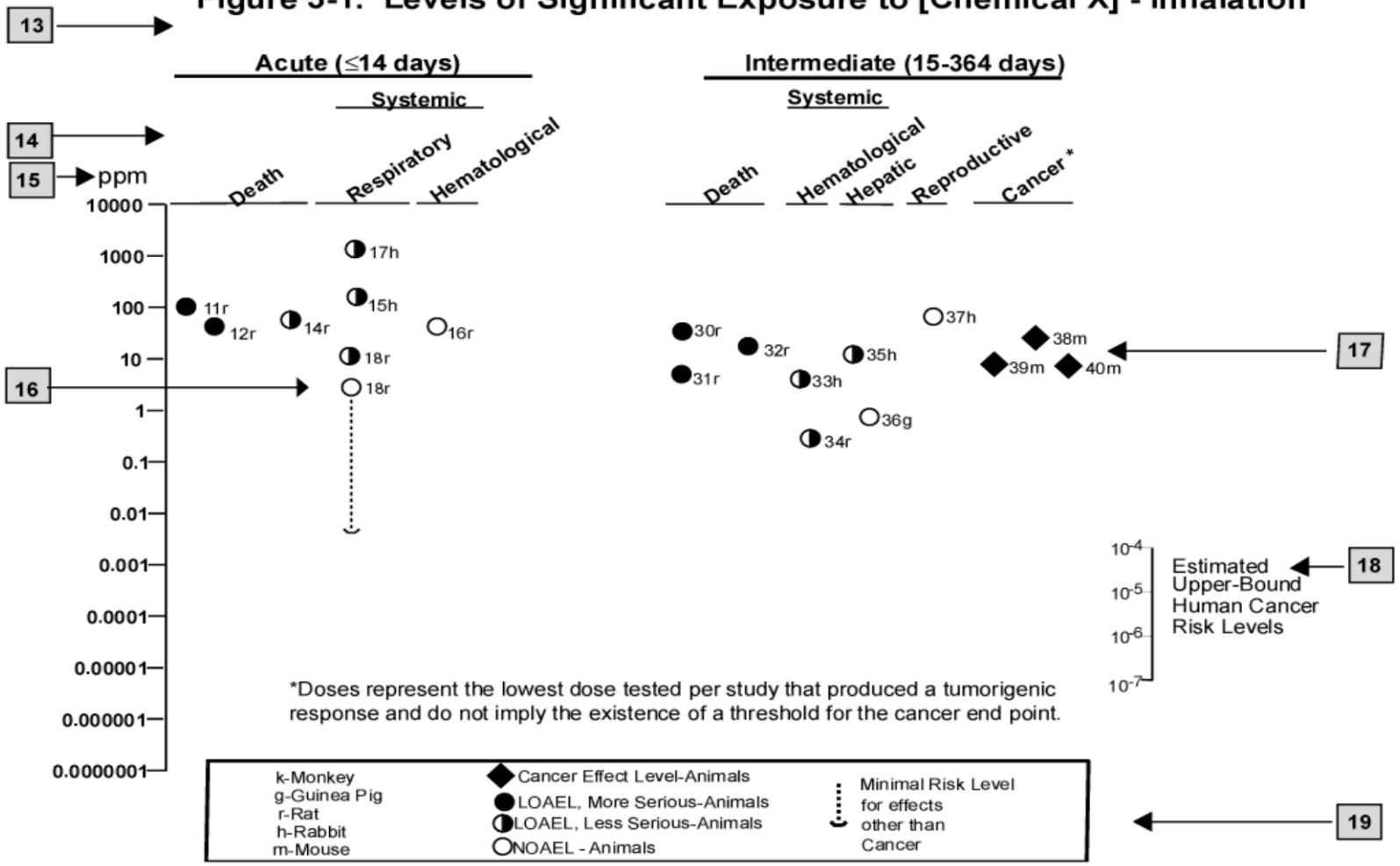
1 → **Table 3-1. Levels of Significant Exposure to [Chemical x] – Inhalation**

	Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect) Less serious (ppm)	Serious (ppm)	Reference
2 →	INTERMEDIATE EXPOSURE							
		5	6	7	8	9		10
3 →	Systemic	↓	↓	↓	↓	↓		↓
4 →	18	Rat	13 wk 5 d/wk 6 hr/d	Resp	3[b]	10 (hyperplasia)		Nitschke et al. 1981
	CHRONIC EXPOSURE							
	Cancer					11		
						↓		
	38	Rat	18 mo 5 d/wk 7 hr/d			20	(CEL, multiple organs)	Wong et al. 1982
	39	Rat	89–104 wk 5 d/wk 6 hr/d			10	(CEL, lung tumors, nasal tumors)	NTP 1982
	40	Mouse	79–103 wk 5 d/wk 6 hr/d			10	(CEL, lung tumors, hemangiosarcomas)	NTP 1982

12 → [a] The number corresponds to entries in Figure 3-1.
[b] Used to derive an intermediate inhalation Minimal Risk Level (MRL) of $5x10^{-3}$ ppm; dose adjusted for intermittent exposure and divided by an uncertainty factor of 100 (10 for extrapolation from animal to humans, 10 for human variability).

SAMPLE

Figure 3-1. Levels of Significant Exposure to [Chemical X] - Inhalation



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APPENDIX C. ACRONYMS, ABBREVIATIONS, AND SYMBOLS

AARST	American Association of Radon Scientists and Technologists
ACGIH	American Conference of Governmental Industrial Hygienists
ACOEM	American College of Occupational and Environmental Medicine
ADI	acceptable daily intake
ADME	absorption, distribution, metabolism, and excretion
AED	atomic emission detection
AFID	alkali flame ionization detector
AFOSH	Air Force Office of Safety and Health
ALT	alanine aminotransferase
AML	acute myeloid leukemia
AOAC	Association of Official Analytical Chemists
AOEC	Association of Occupational and Environmental Clinics
AP	alkaline phosphatase
APHA	American Public Health Association
ASD	active soil depressurization
AST	aspartate aminotransferase
atm	atmosphere
ATSDR	Agency for Toxic Substances and Disease Registry
AWQC	Ambient Water Quality Criteria
BAT	best available technology
BCF	bioconcentration factor
BEI	Biological Exposure Index
BMD	benchmark dose
BMD/C	benchmark dose or benchmark concentration
BMD_X	dose that produces a X% change in response rate of an adverse effect
$BMDL_X$	95% lower confidence limit on the BMD_X
BMDS	Benchmark Dose Software
BSC	Board of Scientific Counselors
C	centigrade
CAA	Clean Air Act
CAG	Cancer Assessment Group of the U.S. Environmental Protection Agency
CAS	Chemical Abstract Services
CDC	Centers for Disease Control and Prevention
CEL	cancer effect level
CELDS	Computer-Environmental Legislative Data System
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
Ci	curie
CI	confidence interval
CL	ceiling limit value
CLP	Contract Laboratory Program
cm	centimeter
CML	chronic myeloid leukemia
CPSC	Consumer Products Safety Commission
CRM	continuous radon monitor
CWA	Clean Water Act
CWM	continuous working level monitor
DHEW	Department of Health, Education, and Welfare
DHHS	Department of Health and Human Services

DNA	deoxyribonucleic acid
DOD	Department of Defense
DOE	Department of Energy
DOL	Department of Labor
DOT	Department of Transportation
DOT/UN/ NA/IMDG	Department of Transportation/United Nations/ North America/Intergovernmental Maritime Dangerous Goods Code
DWEL	drinking water exposure level
ECD	electron capture detection
ECG/EKG	electrocardiogram
EEG	electroencephalogram
EEGL	Emergency Exposure Guidance Level
EPA	Environmental Protection Agency
ERR	excess relative risk
F	Fahrenheit
F_1	first-filial generation
FAO	Food and Agricultural Organization of the United Nations
FDA	Food and Drug Administration
FEMA	Federal Emergency Management Agency
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FPD	flame photometric detection
fpm	feet per minute
FR	Federal Register
FSH	follicle stimulating hormone
g	gram
GC	gas chromatography
gd	gestational day
GLC	gas liquid chromatography
GPC	gel permeation chromatography
HPLC	high-performance liquid chromatography
HRGC	high resolution gas chromatography
HSDB	Hazardous Substance Data Bank
IARC	International Agency for Research on Cancer
IDLH	immediately dangerous to life and health
ILO	International Labor Organization
IRIS	Integrated Risk Information System
Kd	adsorption ratio
kg	kilogram
kkg	metric ton
K_{oc}	organic carbon partition coefficient
K_{ow}	octanol-water partition coefficient
L	liter
LC	liquid chromatography
LC_{50}	lethal concentration, 50% kill
LC_{Lo}	lethal concentration, low
LD_{50}	lethal dose, 50% kill
LD_{Lo}	lethal dose, low
LDH	lactic dehydrogenase
LH	luteinizing hormone
LOAEL	lowest-observed-adverse-effect level
LSE	Levels of Significant Exposure

LT_{50}	lethal time, 50% kill
m	meter
MA	*trans,trans*-muconic acid
MAL	maximum allowable level
mCi	millicurie
MCL	maximum contaminant level
MCLG	maximum contaminant level goal
MF	modifying factor
MFO	mixed function oxidase
mg	milligram
mL	milliliter
mm	millimeter
mmHg	millimeters of mercury
mmol	millimole
mppcf	millions of particles per cubic foot
MRL	Minimal Risk Level
MS	mass spectrometry
NAAQS	National Ambient Air Quality Standard
NAS	National Academy of Science
NATICH	National Air Toxics Information Clearinghouse
NATO	North Atlantic Treaty Organization
NCE	normochromatic erythrocytes
NCEH	National Center for Environmental Health
NCI	National Cancer Institute
ND	not detected
NFPA	National Fire Protection Association
ng	nanogram
NHANES	National Health and Nutrition Examination Survey
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute for Occupational Safety and Health
NIOSHTIC	NIOSH's Computerized Information Retrieval System
NLM	National Library of Medicine
nm	nanometer
nmol	nanomole
NOAEL	no-observed-adverse-effect level
NOES	National Occupational Exposure Survey
NOHS	National Occupational Hazard Survey
NPD	nitrogen phosphorus detection
NPDES	National Pollutant Discharge Elimination System
NPL	National Priorities List
NR	not reported
NRC	National Research Council
NRPP	National Radon Proficiency Program
NRSB	National Radon Safety Board
NS	not specified
NSPS	New Source Performance Standards
NTIS	National Technical Information Service
NTP	National Toxicology Program
ODW	Office of Drinking Water, EPA
OERR	Office of Emergency and Remedial Response, EPA
OHM/TADS	Oil and Hazardous Materials/Technical Assistance Data System

OPP	Office of Pesticide Programs, EPA
OPPT	Office of Pollution Prevention and Toxics, EPA
OPPTS	Office of Prevention, Pesticides and Toxic Substances, EPA
OR	odds ratio
OSHA	Occupational Safety and Health Administration
OSW	Office of Solid Waste, EPA
OTS	Office of Toxic Substances
OW	Office of Water
OWRS	Office of Water Regulations and Standards, EPA
PAH	polycyclic aromatic hydrocarbon
PBPD	physiologically based pharmacodynamic
PBPK	physiologically based pharmacokinetic
PCE	polychromatic erythrocytes
PEL	permissible exposure limit
pg	picogram
PHS	Public Health Service
PID	photo ionization detector
pmol	picomole
PMR	proportionate mortality ratio
ppb	parts per billion
ppm	parts per million
ppt	parts per trillion
PSNS	pretreatment standards for new sources
RADEP	RAdon Dose Evaluation Program
RBC	red blood cell
REL	recommended exposure level/limit
RfC	reference concentration
RfD	reference dose
RNA	ribonucleic acid
RQ	reportable quantity
RR	relative risk
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
SCE	sister chromatid exchange
SGOT	serum glutamic oxaloacetic transaminase
SGPT	serum glutamic pyruvic transaminase
SIC	standard industrial classification
SIM	selected ion monitoring
SMCL	secondary maximum contaminant level
SMR	standardized mortality ratio
SNARL	suggested no adverse response level
SPEGL	Short-Term Public Emergency Guidance Level
STEL	short term exposure limit
STORET	Storage and Retrieval
TD_{50}	toxic dose, 50% specific toxic effect
TLV	threshold limit value
TOC	total organic carbon
TPQ	threshold planning quantity
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
TWA	time-weighted average

UF	uncertainty factor
U.S.	United States
USDA	United States Department of Agriculture
USGS	United States Geological Survey
VOC	volatile organic compound
WBC	white blood cell
WHO	World Health Organization

>	greater than
≥	greater than or equal to
=	equal to
<	less than
≤	less than or equal to
%	percent
α	alpha
β	beta
γ	gamma
δ	delta
μm	micrometer
μg	microgram
q_1^*	cancer slope factor
–	negative
+	positive
(+)	weakly positive result
(–)	weakly negative result

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APPENDIX D

OVERVIEW OF BASIC RADIATION PHYSICS, CHEMISTRY, AND BIOLOGY

Understanding the basic concepts in radiation physics, chemistry, and biology is important to the evaluation and interpretation of radiation-induced adverse health effects and to the derivation of radiation protection principles. This appendix presents a brief overview of the areas of radiation physics, chemistry, and biology and is based to a large extent on the reviews of Mettler and Moseley (1985), Hobbs and McClellan (1986), Eichholz (1982), Hendee (1973), Cember (1996, 2009), and Early et al. (1979).

D.1 RADIONUCLIDES AND RADIOACTIVITY

The substances we call elements are composed of atoms. Atoms in turn are made up of neutrons, protons and electrons: neutrons and protons in the nucleus and electrons in a cloud of orbits around the nucleus. Nuclide is the general term referring to any nucleus along with its orbital electrons. The nuclide is characterized by the composition of its nucleus and hence by the number of protons and neutrons in the nucleus. All atoms of an element have the same number of protons (this is given by the atomic number) but may have different numbers of neutrons (this is reflected by the atomic mass numbers or atomic weight of the element). Atoms with different atomic mass but the same atomic numbers are referred to as isotopes of an element.

The numerical combination of protons and neutrons in most nuclides is such that the nucleus is quantum mechanically stable and the atom is said to be stable, i.e., not radioactive; however, if there are too few or too many neutrons, the nucleus is unstable and the atom is said to be radioactive. Unstable nuclides undergo radioactive transformation, a process in which a neutron or proton converts into the other and a beta particle is emitted, or else an alpha particle is emitted. Each type of decay is typically accompanied by the emission of gamma rays. These unstable atoms are called radionuclides; their emissions are called ionizing radiation; and the whole property is called radioactivity. Transformation or decay results in the formation of new nuclides some of which may themselves be radionuclides, while others are stable nuclides. This series of transformations is called the decay chain of the radionuclide. The first radionuclide in the chain is called the parent; the subsequent products of the transformation are called progeny, daughters, or decay products.

In general there are two classifications of radioactivity and radionuclides: natural and artificial (man-made). Naturally-occurring radioactive material (NORM) exists in nature and no additional energy is necessary to place them in an unstable state. Natural radioactivity is the property of some naturally occurring, usually heavy elements, that are heavier than lead. Radionuclides, such as radium and uranium, primarily emit alpha particles. Some lighter elements such as carbon-14 and tritium (hydrogen-3) primarily emit beta particles as they transform to a more stable atom. Natural radioactive atoms heavier than lead cannot attain a stable nucleus heavier than lead. Everyone is exposed to background radiation from naturally-occurring radionuclides throughout life. This background radiation is the major source of radiation exposure to man and arises from several sources. The natural background exposures are frequently used as a standard of comparison for exposures to various artificial sources of ionizing radiation.

Artificial radioactive atoms are produced either as a by-product of fission of uranium or plutonium atoms in a nuclear reactor or by bombarding atoms with particles (such as neutrons, protons, or heavy nuclei) at high velocity via a particle accelerator. Goals of these efforts can include producing medical isotopes or new elements. These artificially produced radioactive elements usually decay by emission of particles, such as alpha particles, positive or negative beta particles, and one or more high energy photons (gamma rays). Unstable (radioactive) atoms of any element can be produced.

Both naturally occurring and artificial radioisotopes find application in medicine, industrial products, and consumer products. Some specific radioisotopes, called fall-out, are still found in the environment as a result of nuclear weapons use or testing, or nuclear power plant accidents (e.g., Three Mile Island Unit 2, Chernobyl, and Fukushima Dai-ichi).

D.2 RADIOACTIVE DECAY

D.2.1 Principles of Radioactive Decay

The stability of an atom is the result of the balance of the forces of the various components of the nucleus. An atom that is unstable (a radionuclide) will release energy (decay) in various ways and transform to stable atoms or to intermediate radioactive species called progeny or 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 progeny decay products may be produced until stable atoms are formed. Radionuclides can be characterized by the type and energy of the radiation emitted, the rate of decay, and the mode of decay. The mode of decay indicates how a parent compound undergoes transformation. Radiations considered here are primarily of nuclear origin, i.e., they arise from nuclear excitation, usually caused by the capture of charged or uncharged nucleons by a nucleus, or by the radioactive decay or transformation of an unstable nuclide. The type of radiation may be categorized as charged or uncharged particles, protons, and fission products) or electromagnetic radiation (gamma rays and x rays). Table D-1 summarizes the basic characteristics of the more common types of radiation encountered.

D.2.2 Half-Life and Activity

For any given radionuclide, the rate of decay is a first-order process that is constant, regardless of the radioactive atoms present and is characteristic for each radionuclide. The process of decay is a series of random events; temperature, pressure, or chemical combinations do not affect the rate of decay. While it may not be possible to predict exactly which atom is going to undergo transformation at any given time, it is possible to predict, on average, the fraction of the radioactive atoms that will transform during any interval of time.

The *activity* is a measure of the quantity of radioactive material. For these radioactive materials it is customary to describe the activity as the number of disintegrations (transformations) per unit time. The unit of activity is the curie (Ci), which was originally related to the activity of one gram of radium, but is now defined as the disintegration or transformation rate occurring in a quantity of radioactive material. The definition is:

1 curie (Ci) $= 3.7 \times 10^{10}$ disintegrations (transformations)/second (dps) or
$= 2.22 \times 10^{12}$ disintegrations (transformations)/minute (dpm).

The SI unit of activity is the becquerel (Bq); 1 Bq = that quantity of radioactive material in which there is 1 transformation/second. Since activity is proportional to the number of atoms of the radioactive material, the quantity of any radioactive material is usually expressed in curies, regardless of its purity or concentration. The transformation of radioactive nuclei is a random process, and the number of transformations is directly proportional to the number of radioactive atoms present. For any pure radioactive substance, the rate of decay is usually described by its radiological half-life, $t_{½}$, i.e., the time it takes for a specified source material to decay to half its initial activity. The specific activity is an indirect measure of the rate of decay, and is defined as the activity per unit mass or per unit volume. The higher the specific activity of a radioisotope, the faster it is decaying.

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

$$A = A_o e^{-0.693t/t_{½}},$$

where A = the activity in dps or curies or becquerels,
A_o = the activity at time zero,
t = the time at which measured, and
$t_{½}$ = the radiological half-life of the radionuclide ($t_{½}$ and t must be in the same units of time).

The time when the activity of a sample of radioactivity becomes one-half its original value is the radioactive half-life and is expressed in any suitable unit of time.

APPENDIX D

Table D-1. Characteristics of Nuclear Radiations

Radiation	Rest mass[a]	Charge	Typical energy range	Path length[b]		Comments
				Air	Solid	
Alpha (α)	4.00 amu	+2	4–10 MeV	5–10 cm	25–80 μm	Identical to ionized He nucleus
Negatron (β^-)	5.48×10^{-4} amu; 0.51 MeV	–1	0–4 MeV	0–10 m	0–1 cm	Identical to electron
Positron (β^+)	5.48×10^{-4} amu; 0.51 MeV	+1	0-4 MeV	0–10 m	0–1 cm	Identical to electron except for sign of charge
Neutron	1.00866 amu; 939.565 MeV	0	0–15 MeV	b	b	Half life: 10.183 min
X ray (e.m. photon)	–	0	5 keV–100 keV	b	b	Photon from transition of an electron between atomic orbits
Gamma (γ) (e.m. photon)	–	0	10 keV–3 MeV	b	b	Photon from nuclear transformation

[a] The rest mass (in amu) has an energy equivalent in MeV that is obtained using the equation $E=mc^2$, where 1 amu = 932 MeV.
[b] Path lengths are not applicable to x- and gamma rays since their intensities decrease exponentially; path lengths in solid tissue are variable, depending on particle energy, electron density of material, and other factors.

amu = atomic mass unit; e.m. = electromagnetic; MeV = MegaElectron Volts

The specific activity is a measure of activity, and is defined as the activity per unit mass or per unit volume. This activity is usually expressed in curies per gram and may be calculated by

$$\text{curies/gram} = 1.3 \times 10^8 / (t_{½}) \text{ (atomic weight)} \quad \text{or}$$

$$[3.577 \times 10^5 \times \text{mass(g)}] / [t_{½} \times \text{atomic weight}]$$

where $t_{½}$ = the radiological half-life in days.

In the case of radioactive materials contained in living organisms, an additional consideration is made for the reduction in observed activity due to regular processes of elimination of the respective chemical or biochemical substance from the organism. This introduces a rate constant called the biological half-life (t_b) which is the time required for biological processes to eliminate one-half of the activity. This time is virtually the same for both stable and radioactive isotopes of any given element.

Under such conditions the time required for a radioactive element to be halved as a result of the combined action of radioactive decay and biological elimination is the effective clearance half-time:

$$t_{eff} = (t_b \times t_{½}) / (t_b + t_{½}).$$

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

Table D-2. Half-Lives of Some Radionuclides in Adult Body Organs

		Half-life[a]		
Radionuclide	Critical organ	Physical	Biological	Effective
Uranium 238	Kidney	4,460,000,000 y	4 d	4 d
Hydrogen 3[b] (Tritium)	Whole body	12.3 y	10 d	10 d
Iodine 131	Thyroid	8 d	80 d	7.3 d
Strontium 90	Bone	28 y	50 y	18 y
Plutonium 239	Bone surface	24,400 y	50 y	50 y
	Lung	24,400 y	500 d	500 d
Cobalt 60	Whole body	5.3 y	99.5 d	95 d
Iron 55	Spleen	2.7 y	600 d	388 d
Iron 59	Spleen	45.1 d	600 d	42 d
Manganese 54	Liver	303 d	25 d	23 d
Cesium 137	Whole body	30 y	70 d	70 d

[a]d = days, y = years
[b]Mixed in body water as tritiated water

D.2.3 Interaction of Radiation with Matter

Both ionizing and nonionizing radiation will interact with materials; that is, radiation will lose kinetic energy to any solid, liquid or gas through which it passes by a variety of mechanisms. The transfer of energy to a medium by either electromagnetic or particulate radiation may be sufficient to cause formation of ions. This process is called ionization. Compared to other types of radiation that may be absorbed, such as radio waves or microwave 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) and neutral particles (neutrons) are indirectly ionizing; that is, they give up their energy in various interactions with cellular molecules, and the energy is then utilized to produce a fast-moving charged particle such as an electron. It is the electron that then may react with and transfer energy to a target molecule. This particle is called a “primary ionizing particle. Charged particles, in contrast, strike the tissue or medium and directly react with target molecules, such as oxygen or water. These particulate radiations are directly ionizing radiations. Examples of directly ionizing particles include alpha and beta particles. Indirectly ionizing radiations are always more penetrating than directly ionizing particulate radiations.

Mass, charge, and velocity of a particle, as well as the electron density of the material with which it interacts, all affect the rate at which ionization occurs. The higher the charge of the particle and the lower the velocity, the greater the propensity to cause ionization. Heavy, highly charged particles, such as alpha particles, lose energy rapidly with distance and, therefore, do not penetrate deeply. The result of these interaction processes is a gradual slowing down of any incident particle until it is brought to rest or "stopped" at the end of its range.

D.2.4 Characteristics of Emitted Radiation

D.2.4.1 Alpha Emission. In alpha emission, an alpha particle consisting of two protons and two neutrons is emitted with a resulting decrease in the atomic mass number by four and reduction of the atomic number of two, thereby changing the parent to a different element. The alpha particle is identical to a helium nucleus consisting of two neutrons and two protons. It results from the radioactive decay of some heavy elements such as uranium, plutonium, radium, thorium, and radon. All alpha particles emitted by a given radioisotope have the same energy.

Most of the alpha particles that are likely to be found have energies in the range of about 4 to 8 MeV, depending on the isotope from which they came.

The alpha particle has an electrical charge of +2. Because of this double positive charge and their size, alpha particles have great ionizing power and, thus, lose their kinetic energy quickly. This results in very little penetrating power. In fact, an alpha particle cannot penetrate a sheet of paper. The range of an alpha particle (the distance the charged particle travels from the point of origin to its resting point) is about 4 cm in air, which decreases considerably to a few micrometers in tissue. These properties cause alpha emitters to be hazardous only if there is internal contamination (i.e., if the radionuclide is inside the body).

D.2.4.2 Beta Emission. A beta particle (β) is a high-velocity electron ejected from a disintegrating nucleus. The particle may be either a negatively charged electron, termed a negatron (β^Z) or a positively charged electron, termed a positron (β^E). Although the precise definition of "beta emission" refers to both β^Z and β^E, common usage of the term generally applies only to the negative particle, as distinguished from the positron emission, which refers to the β^E particle.

D.2.4.2.1 Beta Negative Emission. Beta particle (β^Z) emission is another process by which a radionuclide, with a neutron excess achieves stability. Beta particle emission decreases the number of neutrons by one and increases the number of protons by one, while the atomic mass number remains unchanged.[1] This transformation results in the formation of a different element. The energy spectrum of beta particle emission ranges from a certain maximum down to zero with the mean energy of the spectrum being about one-third of the maximum. The range 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.

D.2.4.2.2 Positron Emission. In cases in which there are too many protons in the nucleus, positron emission may occur. In this case a proton may be thought of as being converted into a neutron, and a positron (β^E) is emitted.[1] This increases the number of neutrons by one, decreases the number of protons by one, and again leaves the atomic mass number unchanged. The gamma radiation resulting from the annihilation (see glossary) of the positron makes all positron emitting isotopes more of an external radiation hazard than pure β emitters of equal energy.

D.2.4.2.3 Gamma Emission. Radioactive decay by alpha, beta, or positron emission, or electron capture often leaves some of the energy resulting from these changes in the nucleus. As a result, the nucleus is raised to an excited level. None of these excited nuclei can remain in this high-energy state. Nuclei release this energy returning to ground state or to the lowest possible stable energy level. The energy released is in the form of gamma radiation (high energy photons) and has an energy equal to the change in the energy state of the nucleus. Gamma and x rays behave similarly but differ in their origin; gamma emissions originate in the nucleus while x rays originate in the orbital electron structure or from rapidly changing the velocity of an electron (e.g., as occurs when shielding high energy beta particles or stopping the electron beam in an x ray tube).

D.3 ESTIMATION OF ENERGY DEPOSITION IN HUMAN TISSUES

Two forms of potential radiation exposures can result: internal and external. The term exposure denotes physical interaction of the radiation emitted from the radioactive material with cells and tissues of the human body. An exposure can be "acute" or "chronic" depending on how long an individual or organ is exposed to the radiation. Internal exposures occur when radionuclides, which have entered the body (e.g., through the inhalation, ingestion, or dermal pathways), undergo radioactive decay resulting in the deposition of energy to internal organs. External exposures occur when radiation enters the body directly from sources located outside the body, such as radiation emitters from radionuclides on ground surfaces, dissolved in water, or dispersed in the air. In general, external exposures are from material emitting gamma radiation, which readily penetrate the skin and internal organs. Beta and alpha radiation from external sources are far less penetrating and deposit their energy primarily on the skin's outer layer. Consequently, their contribution to the absorbed dose of the total body dose, compared to that deposited by gamma rays, may be negligible.

[1] Neutrinos accompany negative beta particle emissions; anti-neutrinos accompany positron emissions

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. Radiation exposure (a measure of ionization density in air) is sometimes used as a surrogate for radiation dose in tissue from external radiation. Both exposure and dose are described below.

D.3.1 Exposure (Roentgen). The roentgen (R) is a unit of x or gamma-ray exposure and is a measured by the amount of ionization caused in air by gamma or x radiation. One roentgen produces 2.58×10^{-4} coulomb per kilogram of air. In the case of gamma radiation, over the commonly encountered range of photon energy, the energy deposition in tissue for an exposure of 1 R is about 0.0096 joules (J)/kg of tissue. Exposure is only defined for x and gamma radiation ionization in air, and is often incorrectly interchanged with the term dose.

D.3.2 Absorbed Dose (Gy, rad) and Absorbed Dose Rate (Gy/hr, rad/hr). The absorbed dose is defined as the energy absorbed from the incident radiation by a unit mass of the tissue or organ (dm). The differential equation for absorbed dose is:

$$D = de/dm$$

where: D = absorbed dose
e = mean energy deposited
m = mass in which the energy was deposited.

The SI unit of absorbed dose in any medium is the J/kg with the special name of Gray (Gy), where 1 J/kg = 10,000 ergs/gram = 1 Gy. In the historical system, 0.01 J/kg = 100 ergs/g = 1 rad, so 1 Gy = 100 rad.. For neutrons, the absorbed dose may be estimated using the similar metric, kinetic energy released in matter (kerma). Kerma is the sum of initial kinetic energies of all charged ionizing particles liberated in a unit mass.

Absorbed dose is a measurable quantity, so there are primary national and international standards for its determination. In practice, absorbed dose is averaged over organ or tissue volumes. This allows the absorbed dose from both external and internal sources of radiation to be added. For low doses, the acceptance of the linear no threshold (LNT) theory allows the correlation of dose with degree of adverse deterministic health effects. Radiation that does not penetrate tissue well (low energy x-rays, beta particles, and alpha particles) can produce a nonuniform distribution of absorbed dose resulting in differential health effects across an organ or tissue. An example is using shielding in radiation therapy so that a kidney tumor receives a lethal dose while sparing as much health tissue as practical, thus maximizing the remaining kidney function.

Internal and external absorbed doses delivered by 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, which has units of Gy/unit time or rad/unit time.

As a rough conversion, an exposure of 1 R in air results in an absorbed dose to soft tissue of approximately 0.01 J/kg.

See text below on other units of measure.

D.4 UNITS IN RADIATION PROTECTION AND REGULATION

D.4.1 Equivalent Dose (or Dose Equivalent)

Equivalent dose (international term) and dose equivalent (US term)are a radiation protection quantity used for setting limits that help ensure that deterministic effects (e.g. damage to a particular tissue) are kept within acceptable levels. The SI unit of equivalent dose is the J/kg, has the special name of Sievert (Sv) or rem, and is abbreviated H_T. It is a special radiation protection quantity that is used, for administrative and radiation safety purposes only, to

express the absorbed dose in a manner which considers the difference in biological effectiveness of various kinds of ionizing radiation. The equivalent dose concept is applicable only to doses that are not great enough to produce biomedical effects.

The equivalent dose in an organ or tissue (H_T) is determined by multiplying the absorbed dose by a radiation weighting factor and any modifying factors at the location of interest. The absorbed dose in an organ or tissue from radiation of type R ($D_{T,R}$) is a measurable or estimable quantity, while the radiation weighting factor (ω_R) for each primary radiation type (ω_R) has been studied and recommendations made for their values. The formula for calculating equivalent dose is:

$$H_T = \sum_R \omega_R D_{T,R}, \text{ or } \sum_R Q_R D_{T,R}.$$

Where ω_R = radiation weighting factor,
$D_{T,R}$ = absorbed dose to tissue T from radiation type R, and
Q_R = quality factor.

The radiation weighting factor (ω) or quality factor (Q) is a dimensionless quantity that depends in part on the stopping power for charged particles, and it accounts for the differences in biological effectiveness found among the types of radiation. Originally, relative biological effectiveness (RBE) was used rather than ω or Q to define the quantity, rem, which is of use in risk assessment. The NRC and DOE in the US, and the ICRU and ICRP in most of the remaining international community havepublished values for quality factors and radiation weighting factors provided in Tables D-3 and D-4.

The equivalent dose rate (or dose equivalent rate in the US) is the time rate of change of the equivalent dose (or dose equivalent) to organs and tissues and is expressed as Sv/unit time (or rem/unit time).

Table D-3. Recommended Values of Quality Factors and Radiation Weighting Factors

Type of Radiation	Quality Factor (NRC 2011)	Radiation Weighting Factor (w_R) (ICRP 2007)
Photons (x and γ rays)	1	1
Electrons	1	
Electrons and muons		1
High energy protons	10	
Protons and charged pions		2
Alpha particles, multiple-charged particles, fission fragments and heavy particles of unknown charge	20	
Alpha particles, fission fragments, heavy ions		20
Neutrons of unknown energy	10	
Neutrons of known energy	See Table D-4	A continuous function of neutron energy (range 2.4-21; see equation)

Source:
USNRC. 2011. Standards for the protection against radiation, tables 1004(b).1 and 1004(b).2. 10 CFR 20.1004. U.S. Nuclear Regulatory Commission, Washington, D.C.
ICRP
Radiation weighting factors for neutrons are based on particle energy according to the following formulas (ICRP 2007):

$$\omega_R = \begin{cases} 2.5 + 18.2e^{-\frac{\ln(E_n^2)}{6}}, & E_n < 1\ \text{MeV} \\ 5.0 + 17.0e^{-\frac{\ln(2E_n^2)}{6}}, & 1\ MeV \leq E_n \leq 50\ \text{MeV} \\ 2.5 + 3.25e^{-\frac{\ln(0.04E_n^2)}{6}}, & E_n > 50\ \text{MeV} \end{cases}$$

Table D-4 Mean Quality Factors, Q, and Fluence per Unit Dose Equivalent for Monoenergetic Neutrons

	Neutron energy (MeV)	Quality factor[a](Q)	Fluence per unit dose equivalent[b](neutrons $cm^{-2}rem^{-1}$)
(thermal)	2.5×10^{-8}	2	980×10^6
	1×10^{-7}	2	980×10^6
	1×10^{-6}	2	810×10^6
	1×10^{-5}	2	810×10^6
	1×10^{-4}	2	840×10^6
	1×10^{-3}	2	980×10^6
	1×10^{-2}	2.5	1010×10^6
	1×10^{-1}	7.5	170×10^6
	5×10^{-1}	11	39×10^6
	1	11	27×10^6
	2.5	9	29×10^6
	5	8	23×10^6
	7	7	24×10^6
	10	6.5	24×10^6
	14	7.5	17×10^6
	20	8	16×10^6
	40	7	14×10^6
	60	5.5	16×10^6
	1×10^2	4	20×10^6

	2×10^2	3.5	19×10^6
	3×10^2	3.5	16×10^6
	4×10^2	3.5	14×10^6

D.4.2 Relative Biological Effectiveness

RBE is used to denote the experimentally determined ratio of the absorbed dose from one radiation type to the absorbed dose of a reference radiation required to produce an identical biological effect under the same conditions. Gamma rays from cobalt-60, cesium-137, and 200–250 keV x-rays have been used as reference standards. The term RBE has been widely used in experimental radiobiology, and the term radiation weighting factor used in calculations of dose equivalent for radiation safety purposes (ICRP 2007; NCRP 1971; UNSCEAR 1982). RBE applies only to a specific biological end point, in a specific exposure, under specific conditions to a specific species. There are no generally accepted values of RBE.

D.4.3 Effective Dose or Effective Dose Equivalent

In an attempt to compare stochastic (e.g., cancer) detriment from absorbed dose of radiation in a limited portion of the body with the detriment from total body dose, the ICRP (1977) derived a concept of effective dose equivalent. ICRP changed this term to effective dose in 1990 (ICRP 1990) and reintroduced the term "effective dose equivalent" in 2007 (ICRP 2007). The term "effective dose equivalent" allows for the addition or direct comparison of cancer and genetic risk from various partial or whole body doses. In the U.S., the term "effective dose equivalent" is presently used by the NRC (NRC 2011) and DOE.

The effective dose (or effective dose equivalent) approach was developed to overcome limitations in using absorbed dose as a metric of the stochastic impact of ionizing radiation. 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 non-uniformly irradiated. This required the development of a tissue 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).

The effective dose (or effective dose equivalent) (H_E) is weighted for both the type of radiation (R) and the type of tissue (T), and has the formula:

$$H_E = \sum_T \omega_T H_T = \sum_T \omega_T \sum_R \omega_R D_{T,R},$$

where H_E = the effective dose (or effective dose equivalent) in tissue T,
ω_T = the tissue weighting factor in tissue T,
H_T = the equivalent dose (or dose equivalent dose),
ω_R = the radiation weighting factor, and
$D_{T,R}$ = the absorbed dose from radiation R to tissue T.

Tissue weighting factors for selected tissues are listed in Table D-5.

Table D-5. Tissue Weighting Factors for Calculating Effective Dose (or Effective Dose Equivalent) for Selected Tissues

Tissue	Tissue Weighting factor		
	NRC (2011) /ICRP26	NCRP115 and ICRP60	ICRP103
Bladder		0.05	0.04
Bone marrow (red)	0.12	0.12	0.12
Bone surface	0.03	0.01	0.01
Brain			0.01
Breast	0.15	0.05	0.12
Colon	–	0.12	0.12
Esophagus	–	0.05	0.04
Gonads	0.25	0.20	0.08
Liver	–	0.05	0.04
Lung	0.12	0.12	0.12
Salivary glands			0.01
Skin	–	0.01	0.01
Stomach	–	0.12	0.12
Thyroid	0.03	0.05	0.04
Subtotal	0.70	0.95	0.88
Remainder	0.30	0.05	0.12[a]
Total	1.00	1.00	1.00

ICRP60 = International Commission on Radiological Protection, 1990 Recommendations of the ICRP
NCRP115 = National Council on Radiation Protection and Measurements. 1993. Risk Estimates for Radiation Protection, Report 115. Bethesda, Maryland
NRC = Nuclear Regulatory Commission, Title 10, Code of Federal Regulations, Part 20
[a]ICRP Publication 103 remainder tissues include adrenals, extrathoracic (ET) region, gall bladder, heart, kidneys, lymphatic nodes, muscle, oral mucosa, pancreas, prostate, small intestine, spleen, thymus, uterus/cervix

The ICRU (1980), ICRP (1984), and NCRP (1985) recommended that the terms 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 historical units and the international system of units (SI) for radiological quantities is shown in Table D-6.

Table D-6. Comparison of Common and SI Units for Radiation Quantities

Quantity (Abbreviation)	Historical Unit	Historical Definition	SI unit	SI Definition
Activity (A)	curie (Ci)	3.7×10^{10} transformations s^{-1}	becquerel (Bq)	s^{-1}
Absorbed dose (D)	rad (rad)	10^{-2} Jkg^{-1}	gray (Gy)	Jkg^{-1}
Absorbed dose rate ($\dot{D}$)	rad per second (rad s^{-1})	10^{-2} $Jkg^{-1}s^{-1}$	gray per second (Gy s^{-1})	Jkg^{-1} s^{-1}
Equivalent Dose (or Dose equivalent) (H_T)	rem	10^{-2} Jkg^{-1}	sievert (Sv)	Jkg^{-1}

Equivalent Dose Rate (or Dose equivalent rate)	rem per second (rem s^{-1})	10^{-2} $Jkg^{-1}s^{-1}$	sievert per second (Sv s^{-1})	Jkg^{-1} s^{-1}
Effective dose (or Effective Dose Equivalent) (H_E)	rem	10^{-2} Jkg^{-1}	sievert (Sv)	Jkg^{-1}
Linear energy transfer (LET)	kiloelectron volts per micrometer (keV μm^{-1})	$1.602x10^{-10}$ Jm^{-1}	kiloelectron volts per micrometer (keV μm^{-1})	$1.602x10^{-10}$ Jm^{-1}

Jkg^{-1} = Joules per kilogram; $Jkg^{-1}s^{-1}$ = Joules per kilogram per second; Jm^{-1} = Joules per meter; s^{-1} = per second

D.4.4 Working Levels and Working Level Months (for Radon Dosimetry). Working level (WL) is a measure of the atmospheric concentration of radon and its short-lived progeny. One WL is defined as any combination of short-lived radon progeny (through polonium-214 [^{214}Po]), per liter of air, that will result in the emission of $1.3x10^5$ MeV of alpha energy. An activity concentration of 100 pCi ^{222}Rn/L of air, in equilibrium with its progeny, corresponds approximately to a potential alpha-energy concentration of 1 WL. The WL unit can also be used for thoron or ^{220}Rn. In this case, $1.3x10^5$ MeV of alpha energy (1 WL) is released by 7.5 pCi ^{220}Rn/L in equilibrium with its progeny. The potential alpha energy exposure of miners is commonly expressed in the unit Working Level Month (WLM). One WLM corresponds to inhalinga concentration of 1 WL for the reference period of 170 hours, or more generally

WLM = concentration (WL) x exposure time (months) / (one “month” = 170 working hours).

D.5 Dosimetry Models

Dosimetry models are used to estimate the dose from internally deposited radioactive substances. The models for internal dosimetry consider the amount of radionuclides entering the body, the factors affecting their movement or transport through the body, distribution and retention of radionuclides in the body, and the energy deposited in organs and tissues from the radiation that is emitted during spontaneous decay processes. The dose pattern for radioactive materials in the body may be strongly influenced by the route of entry of the material. For industrial workers, inhalation of radioactive particles with pulmonary deposition and puncture wounds with subcutaneous deposition have been the most frequent. The general population has been exposed via ingestion, inhalation, and external exposure to low levels of naturally occurring radionuclides as well as artificial radionuclides used in nuclear medicine procedures and released from isotope generation facilities, nuclear weapons testing, and nuclear reactor operations and accidents.

The models for external dosimetry consider only the photon doses (and neutron doses, where applicable) to organs of individuals who are immersed in air or are exposed to a contaminated object.

D.5.1 Ingestion. Ingestion of radioactive materials is most likely to occur from eating food or drinking water containing naturally occurring radioactive material and possibly also contaminated with artificial radionuclides. Also, a portion of inhaled radionuclides initially deposited in the lung will relocate to the throat and be swallowed. Ingestion of a sufficient amount of radioactive material may result in toxic effects as a result of either absorption of the radionuclide or irradiation of the gastrointestinal tract during passage through the tract, or a combination of both. The fraction of a radioactive material absorbed from the gastrointestinal tract is variable, depending on the specific element, the physical and chemical form of the material ingested, and the diet, as well as some other metabolic and physiological factors. The absorption of some elements is influenced by age, usually with higher absorption in the very young.

D.5.2 Inhalation. The nose and mouth have long been recognized as being a major portal of entry for both nonradioactive and radioactive materials. The deposition of particles within the lung is largely dependent upon the size and shape of the particles being inhaled (sometimes termed the atmospheric mean aerodynamic diameter or AMAD). After a particle is deposited, its retention will depend upon the physical and chemical properties of the dust and the physiological status of the lung. The retention of the particle in the lung depends on the location of

deposition, in addition to the physical and chemical properties of the particles. The converse of pulmonary retention is pulmonary clearance. There are three distinct mechanisms of clearance which operate simultaneously. Ciliary clearance acts only in the upper respiratory tract. The second and third mechanisms act mainly in the deep respiratory tract. These are phagocytosis and absorption. Phagocytosis is the engulfing of foreign bodies by alveolar macrophages and their subsequent removal either up the ciliary "escalator" or by entrance into the lymphatic system. Some inhaled soluble particles are absorbed into the blood and translocated to other organs and tissues.

D.5.3 Internal Emitters

An internal emitter is a radionuclide that is inside the body. The absorbed dose from internally deposited radioisotopes depends on the energy absorbed per unit tissue by the irradiated 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 of gamma energy may not be absorbed in tissue. The dose to an organ or tissue is a function of the effective retention half-time, the energy released in the tissue, the amount of radioactivity initially introduced, and the mass of the organ or tissue.

D.6 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 (e.g., protracted or fractionated exposures). Biological considerations include factors such as species, age, sex, and the portion of the body exposed. Several excellent reviews of the biological effects of radiation have been published, and the reader is referred to these for a more in-depth discussion (Brodsky 1996; Klaassen 2001; Hobbs and McClellan 1986; ICRP 1984; Mettler and Moseley 1985; Rubin and Casarett 1968).

D.6.1 Radiation Effects at the Cellular Level

breaks in DNA may be produced. These single strand breaks may be repaired rapidly. With doses in the range of 0.5-5 Gy (50–500 rad), 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 5 Gy (500 rad), 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 Bergonie-Tribondeau law, the sensitivity of cell lines is directly proportional to their mitotic rate and inversely proportional to the degree of differentiation (Mettler and Moseley 1985). Rubin and Casarett (1968) devised a classification system that categorized cells according to type, function, and mitotic activity. The categories range from the most sensitive type, "vegetative intermitotic cells," found in the stem cells of the bone marrow and the gastrointestinal tract, to the least sensitive cell type, "fixed postmitotic cells," found in striated muscles or long-lived neural tissues.

Cellular changes may result in cell death, which if extensive, may produce irreversible damage to an organ or tissue or may result in the death of the individual. If the cell recovers, altered metabolism and function may still occur, which may be repaired or may result in the manifestation of clinical symptoms. These changes may also be expressed at a later time as tumors, cellular mutations, or transformed tissue (scar tissue) which may result in abnormal tissue or compromised function.

D.6.2 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.

D.6.3 Low Level Radiation Effects

Cancer is the major latent harmful effect produced by ionizing radiation and the one that most people exposed to radiation are concerned about. The ability of alpha, beta, and gamma radiation to produce cancer in virtually every tissue and organ in laboratory animals has been well-demonstrated, while radiogenic cancer has not been observed in some human tissues and organs. The development of cancer is not an immediate effect. In humans, radiation-induced leukemia has the shortest latent period at 2 years, thyroid cancer after Chernobyl showed up in children about four years after the accident, while other radiation induced cancers have latent periods >20 years. For the non-radiogenic cancers, it has been hypothesized either that repair mechanisms effectively protect the individual or that the latency period exceeds the current human life span (Raabe 2010). The mechanism by which cancer is induced in living cells is complex and is a topic of intense study. Exposure to ionizing radiation can produce cancer; however, some sites appear to be more common than others, such as the breast, lung, stomach, and thyroid.

DNA is a major target molecule during exposure to ionizing radiation. Other macromolecules, such as lipids and proteins, are also at risk of damage when exposed to ionizing radiation. The genotoxicity of ionizing radiation is an area of intense study, as damage to the DNA is ultimately responsible for many of the adverse toxicological effects ascribed to ionizing radiation, including cancer. Damage to genetic material is basic to developmental or teratogenic effects, as well.

There is limited evidence of non-cancer human effects at low radiation doses. Non-cancer effects that have been reported are associated with the Japanese atomic bomb survivor population and include neurological and cardiovascular effects. Neurological effects were observed in fetuses exposed to prompt radiation during the detonations while they were in gestation weeks 8–15, less so for weeks 16–25, and were not observed for other developmental time frames. Cardiovascular effects have been reported for atomic bomb survivors following 60 years of follow-up. These include a statistically significant increase in heart disease (% elevated relative risk per Gy with 95% confidence interval = 14 [6–23] %/Gy, $p<0.001$) and a non-statistically significant increase in stroke (9 [1–17]%/Gy, $p=0.02$) above a dose of 0.5 Gy. These radiation-induced circulatory effects may be increased by other factors such as smoking, microvascular damage in the kidney and associated hypertension, high serum cholerterol, diabetes, and infection.

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APPENDIX E. INDEX

absorbed dose 91
adenocarcinoma 37
adipose tissue 56, 58, 59
adsorbed 119, 150
adsorption 150, 151
ambient air 115, 121, 122, 128, 129, 130, 144
bioaccumulation 144
biokinetics 56, 58, 59, 63, 64, 82
biomarkers 91, 92, 103, 147, 158
body weight effects 32
breast milk 141
cancer 5, 9, 10, 11, 12, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 35, 36, 37, 38, 39, 41, 42, 43, 44, 50, 77, 84, 87, 88, 90, 92, 93, 94, 95, 96, 97, 100, 101, 102, 103, 104, 117, 139, 159, 161
carcinogen 10, 20, 23, 28, 31, 44, 164
carcinogenic 19, 39, 87, 164
carcinoma 37
cardiovascular 32, 33, 43
cardiovascular effects 33
chromosomal aberrations 45, 48, 49, 93
clearance 18, 50, 51, 53, 54, 63, 64, 66, 69, 71, 72, 73, 75, 77, 79, 84, 94
death 10, 18, 19, 23, 32, 33, 39, 94, 100
developmental effects 35, 42, 43, 102, 105
DNA 45, 46, 48, 85, 87, 91, 96, 104
endocrine 43, 88, 89
fetus 89
general population 137, 159
genotoxic 19, 45, 93
genotoxicity 45, 49, 93, 101
groundwater 3, 4, 9, 116, 117, 118, 121, 122, 123, 125, 126, 127, 130, 133, 134, 135, 138, 142
half-life 2, 15, 18, 50, 71, 82, 91, 116, 122, 130, 145, 147, 149, 152, 153
hematological effects 33
immune system 102
immunological 18, 34
immunological effects 34
leukemia 22, 38, 77, 101, 102
lymphatic 65
metabolic effects 43
micronuclei 45, 48, 93
mucociliary 51, 53, 72, 94
neurobehavioral 89
neurological effects 34, 42, 43
nuclear 1, 38, 116, 140, 148, 151, 154
ocular effects 34, 43
odds ratio 26, 27, 29, 87, 96
partition coefficients 56, 57, 58, 64, 77, 79, 82
pharmacodynamic 60
pharmacokinetic 60, 61, 62, 84, 90

pulmonary fibrosis 32, 101, 102
rate constant 52, 54, 56, 79
renal effects 33, 34
reproductive effects 34, 35, 42, 43, 102
respiratory effects 32, 33, 96
retention 60, 69, 71, 72, 82, 111
sequestered 75
solubility 51, 53, 54, 56, 57, 58, 65, 69, 84, 122, 130
systemic effects 32, 42, 43
thyroid 77
toxicokinetic 15, 50, 102, 103, 104
tumors 12, 22, 42, 88, 94, 95, 104, 117
volatility 131
volatilization 125