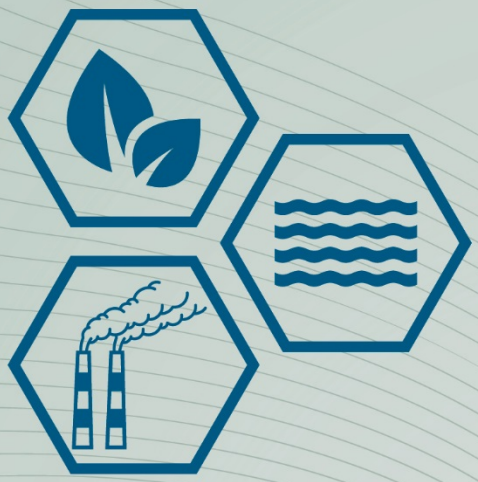


Toxicological Profile for Thorium

September 2019

ATSDR
U.S. Department of Health and Human Services
Agency for Toxic Substances and Disease Registry

CS274127-A

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.

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 these toxic substances described therein. 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 focus of the profiles is on health and toxicologic information; therefore, each toxicological profile begins with a relevance to public health discussion which would allow a public health professional to make a real-time determination of whether the presence of a particular substance in the environment poses a potential threat to human health. The adequacy of information to determine a substance's health effects is described in a health effects summary. Data needs that are of significance to the protection of public health are identified by ATSDR.

Each profile includes the following:

(A) The examination, summary, and interpretation of available toxicologic information and epidemiologic evaluations on a toxic substance to ascertain the levels of significant human exposure for the substance due to associated acute, intermediate, and chronic exposures;

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

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

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

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

Patrick N. Breysse, Ph.D., CIH
Director, National Center for Environmental Health and
Agency for Toxic Substances and Disease Registry
Centers for Disease Control and Prevention

*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 (NPL) 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 NPL, 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.

VERSION HISTORY

Date	Description
September 2019	Update of data in Chapters 2, 3, and 7
October 2014	Addendum to the toxicological profile
October 1990	Final toxicological profile released

CONTRIBUTORS & REVIEWERS

CHEMICAL MANAGER TEAM

Sam Keith, M.S., C.H.P.
ATSDR, Division of Toxicology and Human Health Sciences, Atlanta, GA

David W. Wohlers, Ph.D.
Lisa Ingerman, Ph.D., DABT
SRC, Inc., North Syracuse, NY

REVIEWERS

Interagency Minimal Risk Level Workgroup:

Includes ATSDR; National Center for Environmental Health (NCEH); National Institute of Occupational Health and Safety (NIOSH); U.S. Environmental Protection Agency (EPA); National Toxicology Program (NTP).

Additional reviews for science and/or policy:

ATSDR, Division of Community Health Investigations; ATSDR, Office of Science; NCEH, Division of Laboratory Science; NCEH, Division of Environmental Health Science and Practice.

CONTENTS

LIST OF FIGURES

LIST OF TABLES

CHAPTER 1. RELEVANCE TO PUBLIC HEALTH

1.1 OVERVIEW AND U.S. EXPOSURES

ATSDR's *Toxicological Profile for Thorium* was released in 1990. In order to update the literature in this profile, ATSDR conducted a literature search focused on health effects information as described in Appendix B. Chapters 2 and 3 were revised to reflect the most current health effects data. In some cases, other sections of the profile were updated as needed or for consistency with the updated health effects data. However, the focus of the update to this profile is on health effects information.

Thorium is a radioactive element that occurs naturally in the environment; thus, background levels occur in air, water, and soil. Atmospheric thorium levels above natural background levels occur mainly from mining, milling, and processing operations; phosphate rock processing and phosphate fertilizer production; and coal-fired utilities and industrial boilers. No recent data are available on estimated releases of thorium to the atmosphere, water, or soil from the only domestic manufacturing and processing facility required to report to the Toxics Release Inventory (TRI16 2017).

The most likely sources of exposure of the general population to thorium are from inhalation of air and ingestion of food and drinking water containing thorium. Workers are exposed to higher levels of thorium and other radionuclides in certain thorium industries, as indicated by the measured exhaled breath and tissue levels of these chemicals. However, concentrations of thorium in air, food, and/or drinking water are normally very low and thorium-containing substances are not generally readily absorbed by the body.

1.2 SUMMARY OF HEALTH EFFECTS

- Respiratory disease has been associated with occupational exposure to thorium; workers were also exposed to other radioactive and nonradioactive compounds and other radionuclides.
- Cancer of the lung and blood-producing tissues has been associated with occupational exposure to thorium and other radionuclides.
- Hematological effects and pulmonary effects (cirrhosis and cancer of the lung) were observed in animals following inhalation exposure to thorium.
- Adverse effects on the skin, the testes, and sperm morphology were reported in animals after thorium nitrate was applied on the scrotum.

- Among patients receiving a radioactive colloidal suspension of thorium dioxide ($^{232}ThO_2$) by intravascular injection to visualize selected veins or arteries, adverse effects on the liver and associated organs and tissues, and the reticuloendothelial system were common.

Very little data exist on health effects due to inhalation, oral, or dermal exposure of thorium in humans or animals. It has not been determined whether the adverse health effects associated with exposure to thorium are the result of the ionizing radiation, the chemical toxicity of thorium, or a combination of radiation and chemical toxicity. The small number of epidemiology studies have primarily focused on the potential increases in the risk of cancer deaths in workers exposed to airborne thorium and its progeny radionuclides. Inhalation, oral, and dermal studies in laboratory animals have identified several potential targets of toxicity including the respiratory tract, hematological system, skin, and testes. However, most studies did not find adverse effects.

Some evidence of respiratory disease, liver disease, and increased incidence of pancreatic, lung, and hematopoietic cancers in humans was reported following occupational exposure (Archer et al. 1973; Farid and Conibear 1983; Polednak et al. 1983; Stehney et al. 1980). These effects were seen in thorium workers exposed to many toxic agents; therefore, the effects cannot be positively attributed directly to thorium exposure. Although the studies found some associations, co-exposure to other compounds such as silica (silicon dioxide) and the lack of control for smoking limit the interpretation of these data.

Intermediate-duration animal studies have shown pneumocirrhosis (cirrhosis of the lung), adverse hematological effects, and increased incidences of lung cancer following inhalation exposure to thorium (Hall et al. 1951; Likhachev 1976; Likhachev et al. 1973a, 1973b). Chronic inhalation exposure to low levels of thorium dioxide did not result in adverse effects in rats, rabbits, or dogs (Hodge et al. 1960). Oral studies in animals showed death at high exposure levels, but no other systemic effects were observed (Patrick and Cross 1948). Dermally-administered thorium nitrate in animals showed effects on the skin, the testes, and sperm morphology when administered directly on the scrotum, but no other systemic effects were observed (Tandon et al. 1975).

In addition to these studies, there are a number of studies evaluating the health effects of thorium involved the intravascular injection of a colloidal suspension form of $^{232}ThO_2$, which was produced under the trade name, Thorotrast. Thorotrast exhibited unique physico-chemical characteristics that enabled it to distribute to, and remain within, bone marrow and selected other tissues. These physico-chemical characteristics and the intravascular injection route of exposure to Thorotrast are in contrast to the physico-chemical characteristics of thorium in the natural environment and natural routes of human

exposure to thorium (inhalation, oral, dermal). Therefore, results from Thorotrast-injected patients are not considered an appropriate basis for assessing thorium toxicity apart from colloidal Thorotrast. Thorotrast was used globally during the period 1928–1954. Although the colloid contained various sized particles, some manufacturers eliminated larger particles and retained smaller particles (average size 10 nm) in the range of nanomaterials (Dalheimer et al. 1988). The manufacture and use of Thorotrast ceased when delayed adverse health effects were recognized and attributed to its use. Several cohorts of Thorotrast-injected patients were followed for up to several decades and results were summarized in published reports; the most recent follow-up studies include Becker et al. (2008), dos Santos Silva et al. (2003), Mori et al. (1999b), and Travis et al. (2003). Early reports and follow-up studies identified the liver (and associated organs and tissues) and the reticuloendothelial system as critical targets of Thorotrast toxicity.

1.3 MINIMAL RISK LEVELS (MRLs)

No acute-, intermediate-, or chronic-duration inhalation or oral MRLs were derived for thorium due to a lack of suitable human or animal data regarding health effects following inhalation or oral exposure to thorium and its progeny. Inhalation and oral MRL values are summarized in Table 1-1 and discussed in greater detail in Appendix A.

Table 1-1. Minimal Risk Levels (MRLs) for Thorium[a]

Exposure duration	MRL	Critical effect	Point of departure	Uncertainty factor	Reference
Inhalation exposure					
Acute	Insufficient data for MRL derivation				
Intermediate	Insufficient data for MRL derivation				
Chronic	Insufficient data for MRL derivation				
Oral exposure					
Acute	Insufficient data for MRL derivation				
Intermediate	Insufficient data for MRL derivation				
Chronic	Insufficient data for MRL derivation				

[a]See Appendix A for additional information.

CHAPTER 2. HEALTH EFFECTS

2.1 INTRODUCTION

The primary purpose of this chapter is to provide public health officials, physicians, toxicologists, and other interested individuals and groups with an overall perspective on the toxicology of thorium. 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. When available, mechanisms of action are discussed along with the health effects data; toxicokinetic mechanistic data are discussed in Section 3.1.

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

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 by health effect. These data are discussed in terms of route of exposure (inhalation, oral, and dermal) and three exposure periods: acute (≤14 days), intermediate (15–364 days), and chronic (≥365 days).

As discussed in Appendix B, a literature search was conducted to identify relevant studies examining health effect endpoints. Figure 2-1 provides an overview of the database of studies in humans or experimental animals included in this chapter of the profile. These studies evaluate the potential health effects associated with inhalation, oral, or dermal exposure to thorium, but may not be inclusive of the entire body of literature.

Summaries of animal inhalation studies are presented in Table 2-1 and Figure 2-2. Summaries of animal oral studies are presented in Table 2-2 and Figure 2-3. Summaries of animal dermal studies are presented in Table 2-3.

Levels of significant exposure (LSEs) for each route and duration are presented in tables and illustrated in figures. The points in the figures showing no-observed-adverse-effect levels (NOAELs) or lowest-observed-adverse-effect levels (LOAELs) reflect the actual doses (levels of exposure) used in the studies. LOAELs have been classified into "less serious" or "serious" effects. "Serious" effects are those that evoke failure in a biological system and can lead to morbidity or mortality (e.g., acute respiratory distress or death). "Less serious" effects are those that are not expected to cause significant dysfunction or death, or those whose significance to the organism is not entirely clear. ATSDR acknowledges that a considerable amount of judgment may be required in establishing whether an endpoint should be

classified as a NOAEL, "less serious" LOAEL, or "serious" LOAEL, and that in some cases, there will be insufficient data to decide whether the effect is indicative of significant dysfunction. However, the Agency has established guidelines and policies that are used to classify these endpoints. ATSDR believes that there is sufficient merit in this approach to warrant an attempt at distinguishing between "less serious" and "serious" effects. The distinction between "less serious" effects and "serious" effects is considered to be important because it helps the users of the profiles to identify levels of exposure at which major health effects start to appear. LOAELs or NOAELs should also help in determining whether or not the effects vary with dose and/or duration, and place into perspective the possible significance of these effects to human health.

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

There are limited data available on the toxicity of thorium following inhalation, oral, or dermal exposure. A few studies examined thorium workers, presumably exposed via inhalation; however, the studies poorly controlled for cigarette smoking and exposure to other toxic compounds. The available laboratory animal data provide some suggestive evidence of gastrointestinal, hematological, and reproductive effects. Signs of gastrointestinal irritation (retching, gagging, and vomiting) were observed in dogs exposed to airborne thorium tetranitrate. Alterations in erythrocytes and/or leukocytes were observed in dogs following exposure to airborne thorium nitrate, thorium oxalate, or thorium tetrafluoride. Edema of the seminiferous tubules were observed in rats following dermal applications to scrotal skin.

There is considerable information on the toxicity of Thorotrast, a colloidal solution of thorium dioxide which was administered intravascularly to visualize vascular structures. A number of these patients have been followed for decades. Observed effects include liver disease, blood disorders, hematopoietic cancers, and bile duct and gall bladder cancers.

Thorium is a metallic element that exists only as radioactive isotopes. A total of 31 thorium isotopes are recognized by physicists ($^{208–238}$Th). Most are manmade, but six isotopes ($^{227, 228, 230, 231, 132, 234}$Th) occur naturally as components of the ^{238}U series, ^{232}Th series, and ^{235}U series (see Figure 4-1). Isotopes in the ^{232}Th series (^{228}Th, ^{232}Th) comprise 99.9% of the naturally-occurring thorium in the environment; isotopes in the ^{238}U series (^{230}Th, ^{234}Th) comprise the remainder of naturally-occurring thorium. All thorium isotopes emit alpha or beta particles with or without gamma radiation (NNDC 2018; Weast 1983) as they decay primarily toward isotopes of lead (Pb). Thorium isotopes vary with respect to decay rates (e.g.,

specific activities) and the various decay chain isotopes produced (see Chapter 4). This toxicological profile for thorium includes chemical, radiological, and physical information for elemental thorium (Th), thorium dioxide (ThO_2), thorium nitrate tetrahydrate ($Th(NO_3)_4 \cdot 4H_2O$), thorium fluoride tetrahydrate ($ThF_4 \cdot 4H_2O$), and thorium carbonate ($Th(CO_3)_2$). Health effects data are available for thorium dioxide, thorium nitrate, and thorium fluoride. Uptake and disposition of thorium in the body (and, hence, the potential for specific health effects from internalized thorium) depend upon the chemical properties of the particular thorium compound to which one may be exposed, as well as the route of exposure (see Section 3.1 for more information regarding uptake and disposition of thorium). Available toxicokinetic, radiological, and health effects data for thorium have not been useful in determining whether thorium toxicity is attributable to radiological, chemical, or combined radiological and chemical properties. Exposure to thorium compounds in amounts large enough to pose a serious chemical health risk would be expected to pose a radiation health risk as well, particularly within lungs where insoluble thorium compounds may be retained and in other tissues where absorbed thorium is retained (e.g., liver, bone).

Alpha particle radiation is the type of radiation from thorium in nature that is of greatest health concern. The equilibrium rate of emission of alpha particles and gamma rays from thorium is very low because the decay rates are limited by the decay rates of the parent radionuclides, which range from 7.1×10^8 to 1.4×10^{10} years. Alpha particles are unable to deeply penetrate skin, but can travel short distances in the body (about 4–6 cell diameters) if they are emitted from within the body. The intensity and energy of alpha particles emitted depends on the particular isotope of thorium in question (see Chapter 4). The decay rate or activity of radioactive elements has traditionally been specified in curies (Ci). One curie is the quantity of radioactive material in which approximately 37 billion atoms disintegrate (decay) per second (3.7×10^{10} dps). In international usage, the S.I. unit (the International System of Units) for activity is the Becquerel (Bq), which is the quantity of radioactive material in which 1 atom disintegrates per second (1 Bq = 27 pCi). In animal studies, thorium exposure levels (typically expressed in units of mg thorium/m^3 in air for inhalation studies or mg thorium/kg body weight/day for oral studies) have been converted to activity units (nCi/m^3 or nCi/kg/day; based on the specific activity of a given thorium compound) for presentation in Chapter 2. The specific activity of ^{230}Th is 7.4×10^8 Bq/g (0.02 Ci/g); the specific activity of ^{232}Th is 4,080 Bq/g (1.1×10^{-7} Ci/g).

Once thorium is internalized, it is distributed and excreted at a rate of transfer that is dependent on age. The internal radiation dose from thorium is actually a measure of the amount of energy that the alpha, beta, and gamma emissions deposit in tissue. The short-range alpha and beta radiation produce higher localized doses than longer-range gamma radiation that deposits smaller amounts of energy throughout

the body. Molecular damage results from the direct ionization of atoms that are encountered by alpha radiation, from the indirect ionization of atoms by gamma- and x-rays, and by interactions of resulting free radicals with nearby atoms (free radicals are atoms or groups of atoms containing at least one unpaired electron and existing for a brief period of time before reacting to produce a stable molecule). Tissue damage results when molecular damage is extensive and not sufficiently repaired in a timely manner.

Three primary terms used in assessing radiation dose and health effects are absorbed dose, equivalent dose, and effective dose. In radiation biology, the term absorbed dose refers to the amount of energy deposited by radiation per unit mass of tissue, expressed in units of rad or gray (Gy). An energy deposition of 1 joule/kg = 1 Gy = 100 rad (see Appendix D for a detailed description of principles of ionizing radiation). The equivalent dose (in unit of Sievert or Sv) is the biologically effective dose; it is the absorbed dose multiplied by a radiation weighting factor that is specific to the radiation type. The equivalent dose (H) from internalized thorium radionuclides is estimated using the quantity of material entering the body (via ingestion or inhalation), the biokinetic parameters for thorium (retention, distribution, and excretion), the energies and intensities of the alpha, beta, and gamma radiations emitted, and the parameters describing the profile of absorbed radiation energy within the body. If, for example, a person ingests a given activity of ^{232}Th, the tissues of the body will absorb some or all of the energy of the emitted alpha, beta, and gamma radiation in a pattern reflecting the kinetics of distribution and elimination of the ingested ^{232}Th, the rate at which the radioactive isotope decays to a stable form, and age and other individual parameters for the person during the period in which the radionuclide remains in the body (which affects both the biokinetics of the thorium as well as the potential length of time over which the tissues can be exposed to the radiation). Each tissue and organ, therefore, can receive a different equivalent dose. The effective dose (also measured in units of Sv) is an assessment of the risk of cancer induction from an equivalent dose. Effective dose is estimated by multiplying the equivalent dose by the tissue-specific weighting factor for that organ or tissue, and then adding the various components. This makes effective dose an estimate of the uniform, entire-body risk of developing cancer. It places non-uniform body exposure on the same scale as uniform irradiation with respect to overall cancer induction risk.

The U.S. Environmental Protection Agency (EPA) has published a set of internal dose conversion factors for reference persons of various ages (newborn; 1, 5, 10, or 15 years of age; and adult) in its Federal Guidance Report No. 13 supplemental CD (EPA 1999). These values were updated by Oak Ridge National Laboratory in 2014 (DOE 2014a, 2014b). Age-specific dose coefficients for inhalation and

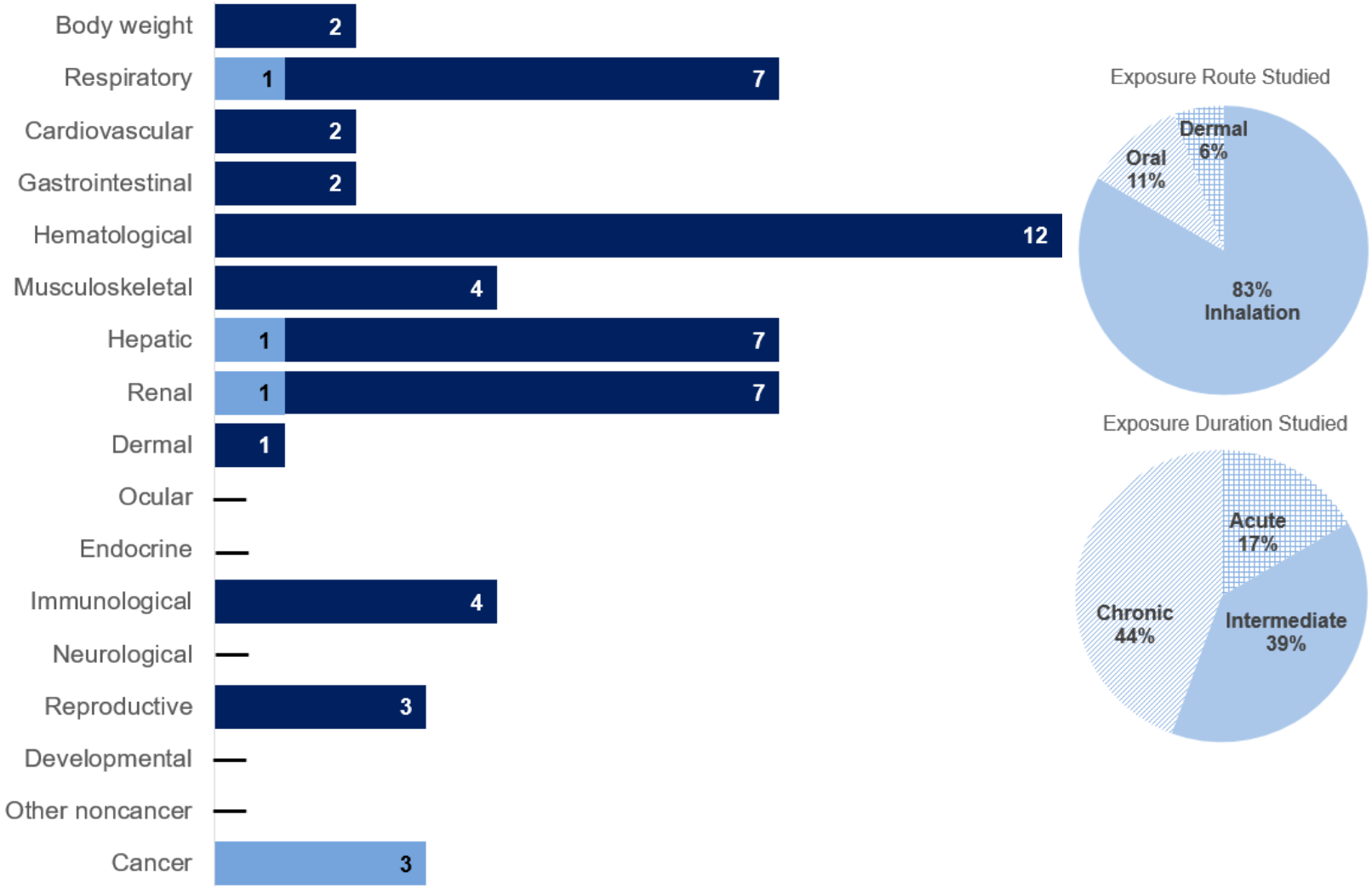
ingestion of any of the radioactive isotopes of thorium by the general public also can be found in International Commission on Radiological Protection (ICRP) publications 67 (ICRP 1994a), 71 (ICRP 1995), and 72 (ICRP 1996) and compiled in Publication 119 (ICRP 2012). Dose coefficients for inhalation, ingestion, and submersion in a cloud of thorium radionuclides can be found in EPA Federal Guidance Report No. 11 (EPA 1988b). Dose coefficients for external exposure to radioisotopes of thorium in air, surface water, or soil contaminated to various depths can be found in EPA Federal Guidance Report No. 12 (EPA 1993) as well as ICRP Publication 116 (2010).

Either a large or small amount of radiation can be damaging to health. Current scientific consensus is that radiation can also increase the probability of cancer, and the current assumption is that no threshold level exists below which there is no additional risk of cancer. There is considerable debate about how great the cancer risks are when people are chronically exposed to very low levels of radiation. Since everyone is environmentally exposed to low levels of radiation, and since the average individual is exposed to significantly more diagnostic medical radiation than environmental radiation without obvious adverse health impact, the minimum amount of additional radiation that may constitute a health hazard is not well known.

Sections 2.2–2.19 summarize the health effects associated with thorium. Section 2.21 summarizes information regarding health effects of Thorotrast, a colloidal suspension of $^{232}ThO_2$ that was medically injected into patients' veins or arteries worldwide from the late 1920s until the early 1950s as a contrast medium for radiographic procedures, particularly to visualize vascular structures following its intravascular injection. This information is not summarized in Sections 2.2–2.19 because Thorotrast was not a substance found in the environment, was administered via an unnatural route not relevant to environmental exposure of human toxicity concern, and Thorotrast distributed within the body unlike the other thorium compounds to which individuals would be exposed. However, the health effects associated with Thorotrast demonstrate the hazard of alpha radiation to tissues where Thorotrast was retained.

Figure 2-1. Overview of the Number of Studies Examining Thorium Health Effects

Most studies examined the potential hematological, respiratory, hepatic and renal effects of thorium
Fewer studies evaluated health effects in **humans** than **animals** (counts represent studies examining endpoint)



*Includes studies discussed in Chapter 2. A total of 57 studies (including those finding no effect) have examined toxicity; most animal studies examined multiple endpoints.

Table 2-1. Levels of Significant Exposure to Thorium – Inhalation

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (nCi/m^3)	Parameters monitored	Endpoint	NOAEL (nCi/m^3)	Less serious LOAEL (nCi/m^3)	Serious LOAEL (nCi/m^3)	Effect
ACUTE EXPOSURE									
1	Dog (NS) 4 F	10 exposures 5 days/week 6 hours/day	4.0	BW, GN, HP, BC, UR	Death				No deaths reported
					Hemato		4.0		Leukocytosis, abnormal lymphocytes, and hypersegmented polymorphonuclear granulocytes; no changes in RBC counts
Thorium nitrate tetrahydrate									
Hall et al. 1951									
2	Dog (NS) 4 F	10 exposures 5 days/week 6 hours/day	4.8	BW, GN, HP, BC, UR	Death				No deaths reported
					Hemato		4.8		Decreased RBC, increased percentage of lymphocytes and nonfilamented polymorphonuclear neutrophils
Thorium dioxide									
Hall et al. 1951									
3	Rabbit (NS) 3 M, 3 F	10–11 exposures 5 days/week 6 hours/day	M: 3.8, F: 3.5	BW, GN, HP, BC, UR	Death				No deaths reported
					Hemato	3.8 M 3.5 F			No change in RBC counts
Thorium nitrate tetrahydrate									
Hall et al. 1951									
INTERMEDIATE EXPOSURE									
4	Dog (NS) 4 F	51 exposures 5 days/week 6 hours/day	0.9	BW, GN, HP, BC, UR	Death				No deaths reported
					Hemato		0.9		Decreased RBC and filamented neutrophils and increased nonfilamented neutrophils
Thorium tetrafluoride									
Hall et al. 1951									

Table 2-1. Levels of Significant Exposure to Thorium – Inhalation

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (nCi/m^3)	Parameters monitored	Endpoint	NOAEL (nCi/m^3)	Less serious LOAEL (nCi/m^3)	Serious LOAEL (nCi/m^3)	Effect
5	Dog (NS) 2 M, 2 F	45 exposures 5 days/week 6 hours/day	1.4	BW, GN, HP, BC, UR	Death				No deaths reported
					Hemato		1.4		Decreased RBC counts
Thorium oxalate									
Hall et al. 1951									
6	Rabbit (NS) 6 M	21 exposures 5 days/week 6 hours/day	1.6	BW, GN, HP, BC, UR	Death				No deaths reported
					Hemato	1.6			
Thorium oxalate									
Hall et al. 1951									
CHRONIC EXPOSURE									
7	Rat (NS) 125 F	1 year 5 days/week 6 hours/day	0.55	BW, HP, BC, CS	Death				No deaths were observed
					Resp	0.55			
					Hemato	0.55			
					Musc/skel	0.55			
					Hepatic	0.55			
					Renal	0.55			
					Immuno	0.55			No histological alterations in lymph nodes
Thorium dioxide									
Hodge et al. 1960									

Table 2-1. Levels of Significant Exposure to Thorium – Inhalation

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (nCi/m^3)	Parameters monitored	Endpoint	NOAEL (nCi/m^3)	Less serious LOAEL (nCi/m^3)	Serious LOAEL (nCi/m^3)	Effect
8	Guinea pig (NS) 20 F	14 months 5 days/week 6 hours/day	0.55	BW, HP, BC, CS	Death				No deaths were observed
					Resp	0.55			
					Hemato	0.55			
					Musc/skel	0.55			
					Hepatic	0.55			
					Renal	0.55			
					Immuno	0.55			No histological alterations in lymph nodes
Thorium dioxide Hodge et al. 1960									
9	Dog (NS) 13 M, 13 F	14 months 5 days/week 6 hours/day	0.55	BW, HP, BC, CS	Death				No deaths were observed
					Resp	0.55			
					Hemato	0.55			
					Musc/skel	0.55			
					Hepatic	0.55			
					Renal	0.55			
					Immuno	0.55			No histological alterations in lymph nodes
Thorium dioxide Hodge et al. 1960									

Table 2-1. Levels of Significant Exposure to Thorium – Inhalation

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (nCi/m^3)	Parameters monitored	Endpoint	NOAEL (nCi/m^3)	Less serious LOAEL (nCi/m^3)	Serious LOAEL (nCi/m^3)	Effect
10	Rabbit (NS) 10 M	14 months 5 days/week 6 hours/day	0.55	BW, HP, BC, CS	Death				No deaths were observed
					Resp	0.55			
					Hemato	0.55			
					Musc/skel	0.55			
					Hepatic	0.55			
					Renal	0.55			
					Immuno	0.55			No histological alterations in lymph nodes
Thorium dioxide									
Hodge et al. 1960									

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

BC = serum (blood) chemistry; BW = body weight; CS = clinical signs; F = female(s); GN = gross necropsy; Hemato = hematological; HP = histopathology; Immuno = immunological; LOAEL = lowest-observed-adverse-effect level; M = male(s); mo = month(s); Musc/skel = muscular/skeletal; nCi = nanocuries; NOAEL = no-observed-adverse-effect level; NS = not specified; RBC = red blood cell; Resp = respiratory; UR = urinalysis

Figure 2-2. Levels of Significant Exposure to Thorium – Inhalation
Acute (≤14 days)

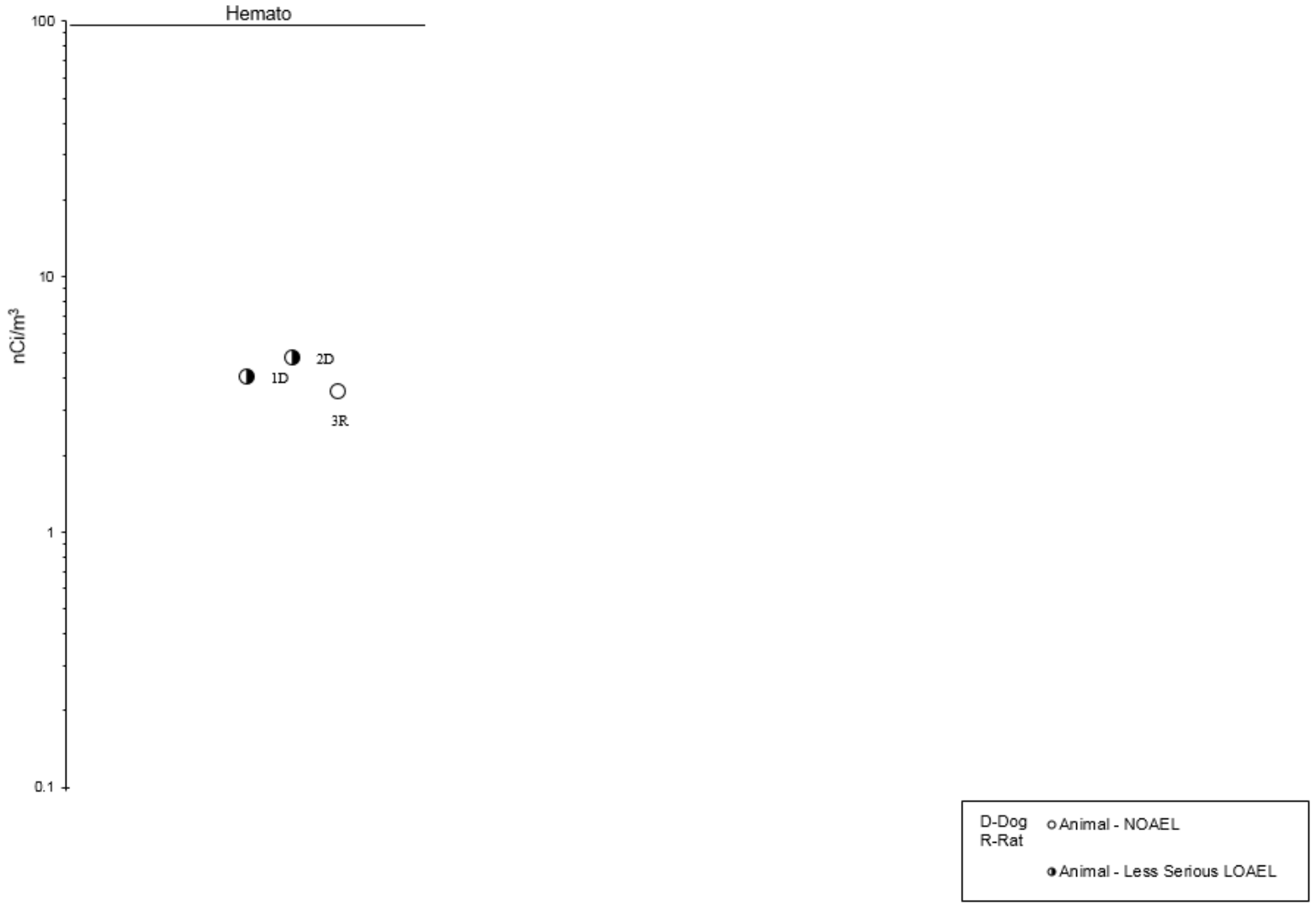


Figure 2-2. Levels of Significant Exposure to Thorium – Inhalation
Intermediate (15-364)

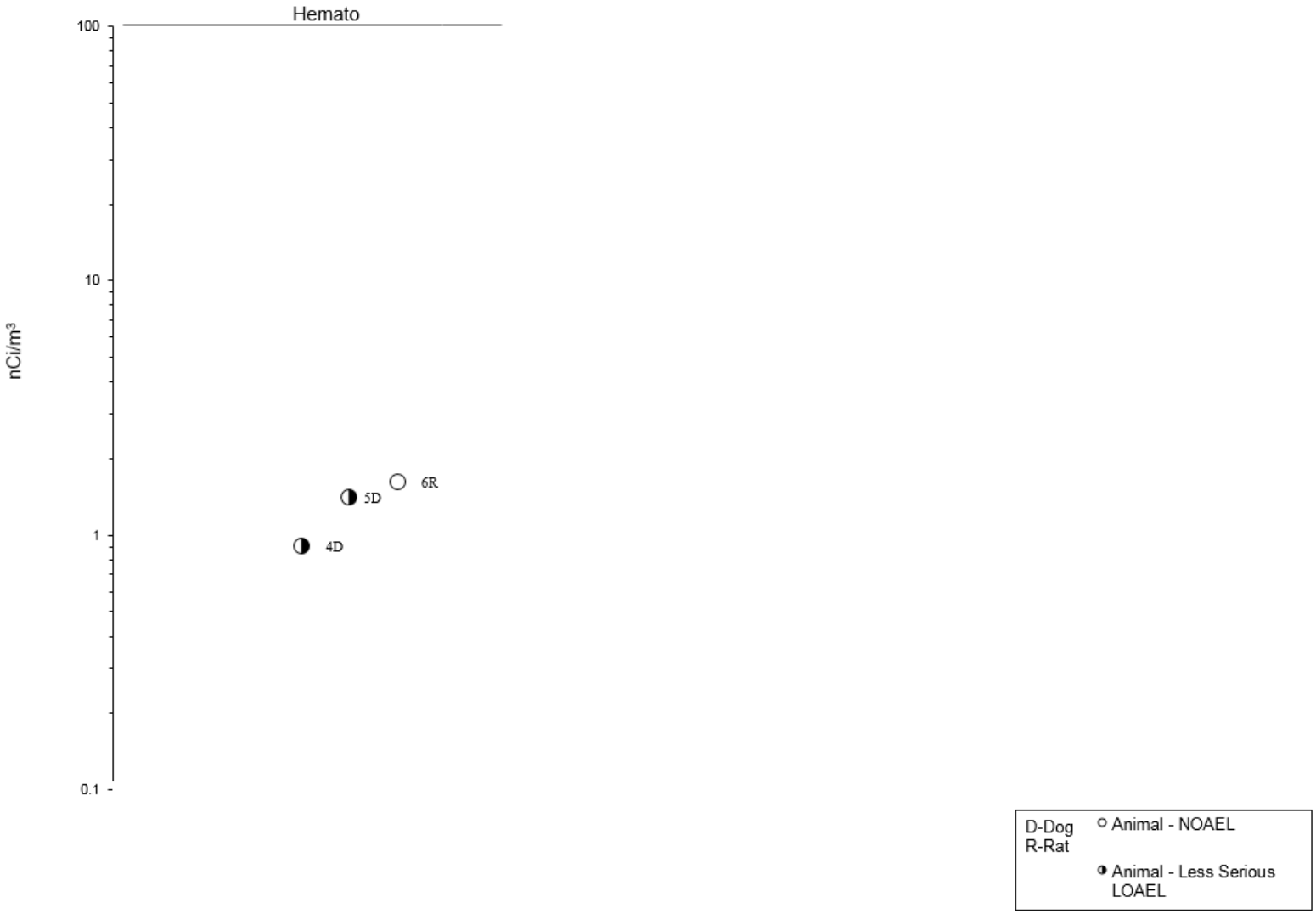


Figure 2-2. Levels of Significant Exposure to Thorium – Inhalation

Chronic (≥365 days)

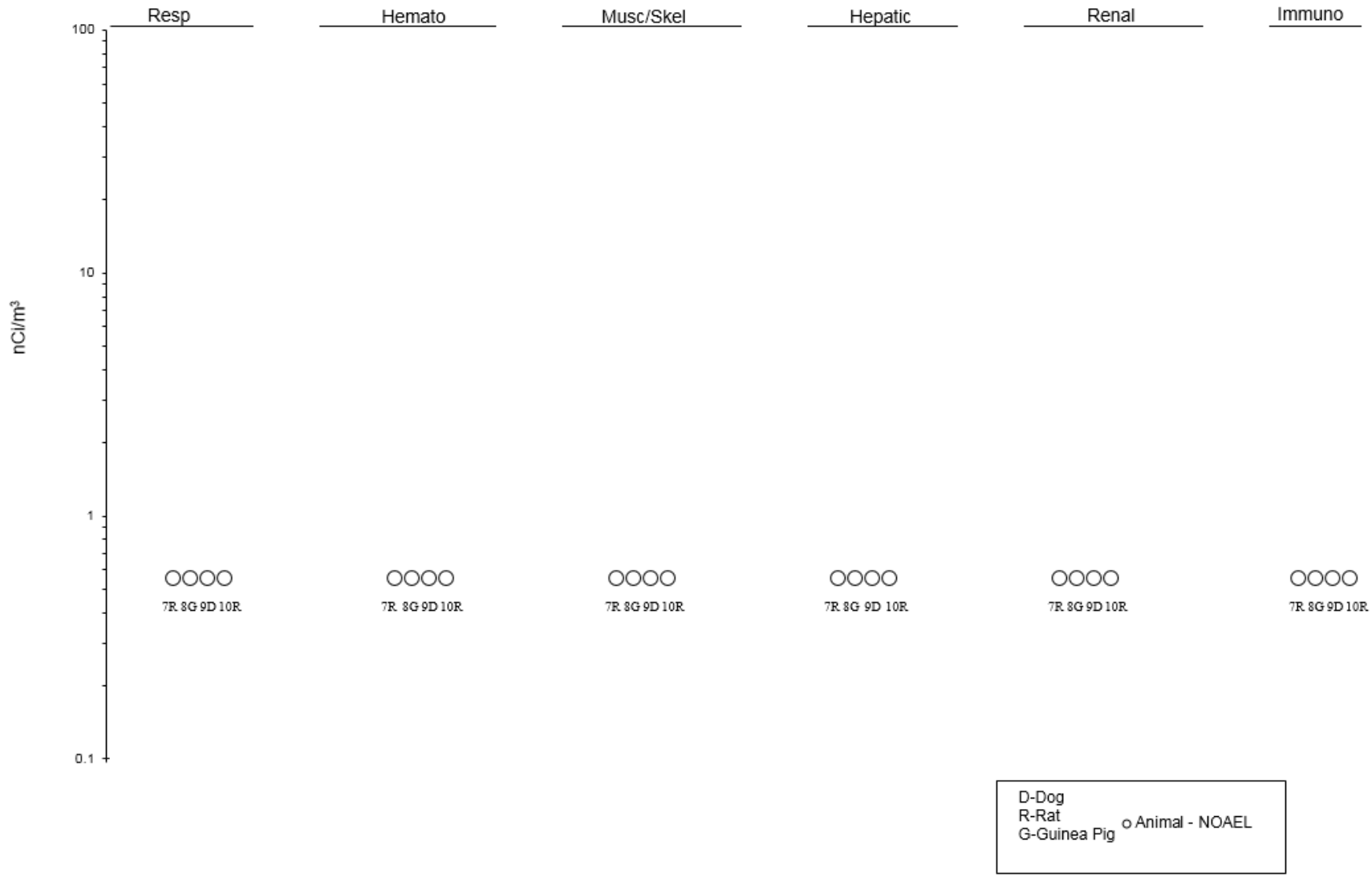


Table 2-2. Levels of Significant Exposure to Thorium – Oral

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (nCi/kg/day)	Parameters monitored	Endpoint	NOAEL (nCi/kg/day)	Less serious LOAEL (nCi/kg/day)	Serious LOAEL (nCi/kg/day)	Effect
ACUTE EXPOSURE									
1	Mouse (NS) 10–20 F	1 days (G)	84–110	GN, CS	Death	84	110		4/20 died
Thorium nitrate									
Patrick and Cross 1948									
INTERMEDIATE EXPOSURE									
2	Rat (Wistar) 20 M, 20 F	105–131 days (F)	0, 1.3, 2.1, 3.4% Th in diet; 1.3%= 130 nCi/kg/day	BW, CS, GN, HE, HP	Death				Deaths were observed at ≥2.1% dietary levels
					Bd wt			130 M	24.6% decrease in body weight gain in males
					Resp	130			
					Cardio	130			
					Gastro	130			
					Hemato	130			
					Hepatic	130			
					Renal	130			
					Repro	130			
Thorium nitrate tetrahydrate									
Downs et al. 1959									

Table 2-2. Levels of Significant Exposure to Thorium – Oral

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (nCi/kg/day)	Parameters monitored	Endpoint	NOAEL (nCi/kg/day)	Less serious LOAEL (nCi/kg/day)	Serious LOAEL (nCi/kg/day)	Effect
3	Mouse (NS) 20F	4 months (W)	12	GN, CS	Death		12		10/20 died
Thorium nitrate									
Patrick and Cross 1948									

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

Bd wt or BW = body weight; Cardio = cardiovascular; CS = clinical signs; (F) = food; F = female(s); (G) = gavage; Gastro = gastrointestinal; GN = gross necropsy; Hemato = hematological; HP = histopathology; LOAEL = lowest-observed-adverse-effect level; M = male(s); NOAEL = no-observed-adverse-effect level; NS = not specified; Repro = reproductive; Resp = respiratory; (W) = water

Figure 2-3. Levels of Significant Exposure to Thorium – Oral
Acute (≤14 days)

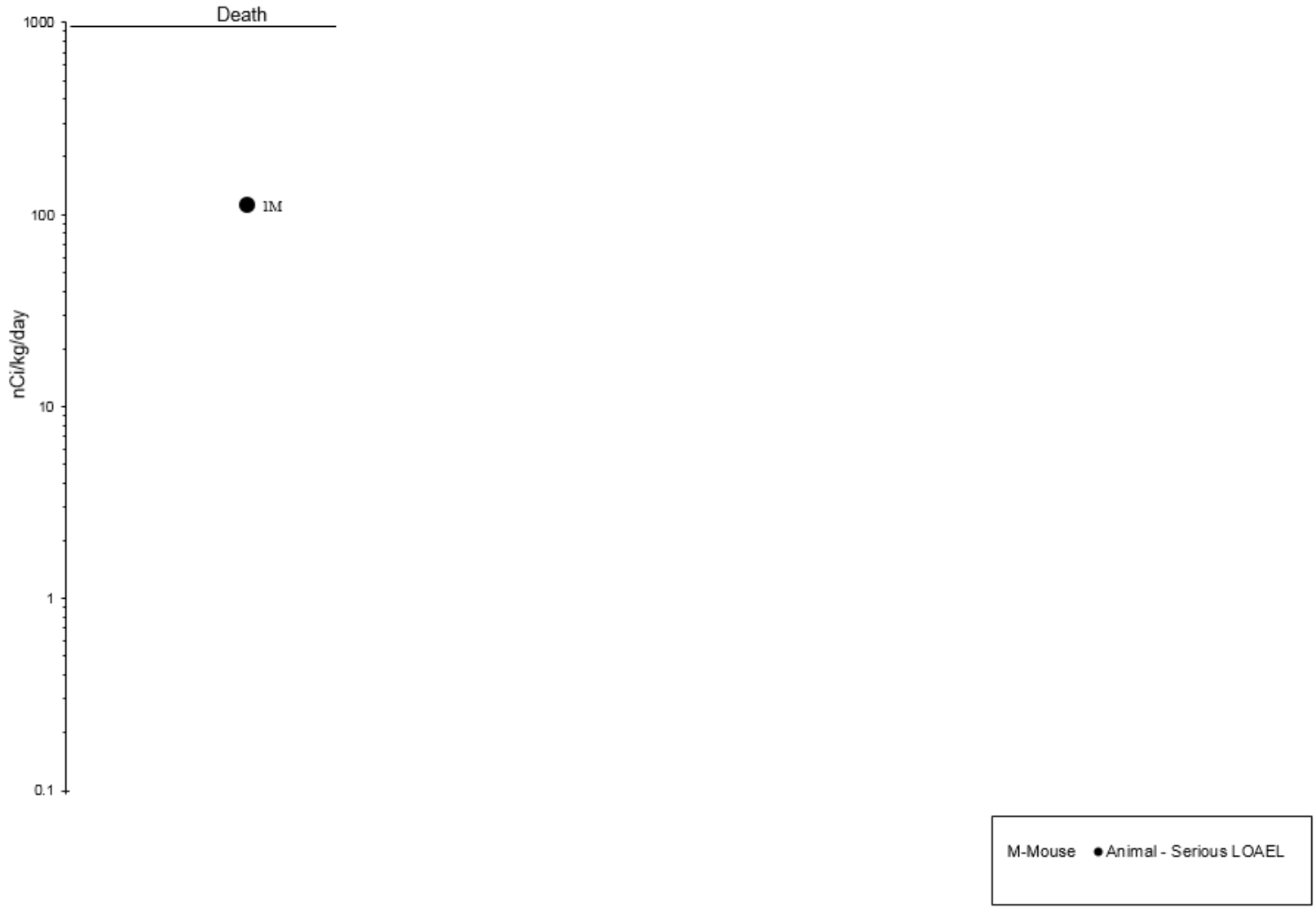


Figure 2-3. Levels of Significant Exposure to Thorium – Oral

Intermediate (15-364 days)

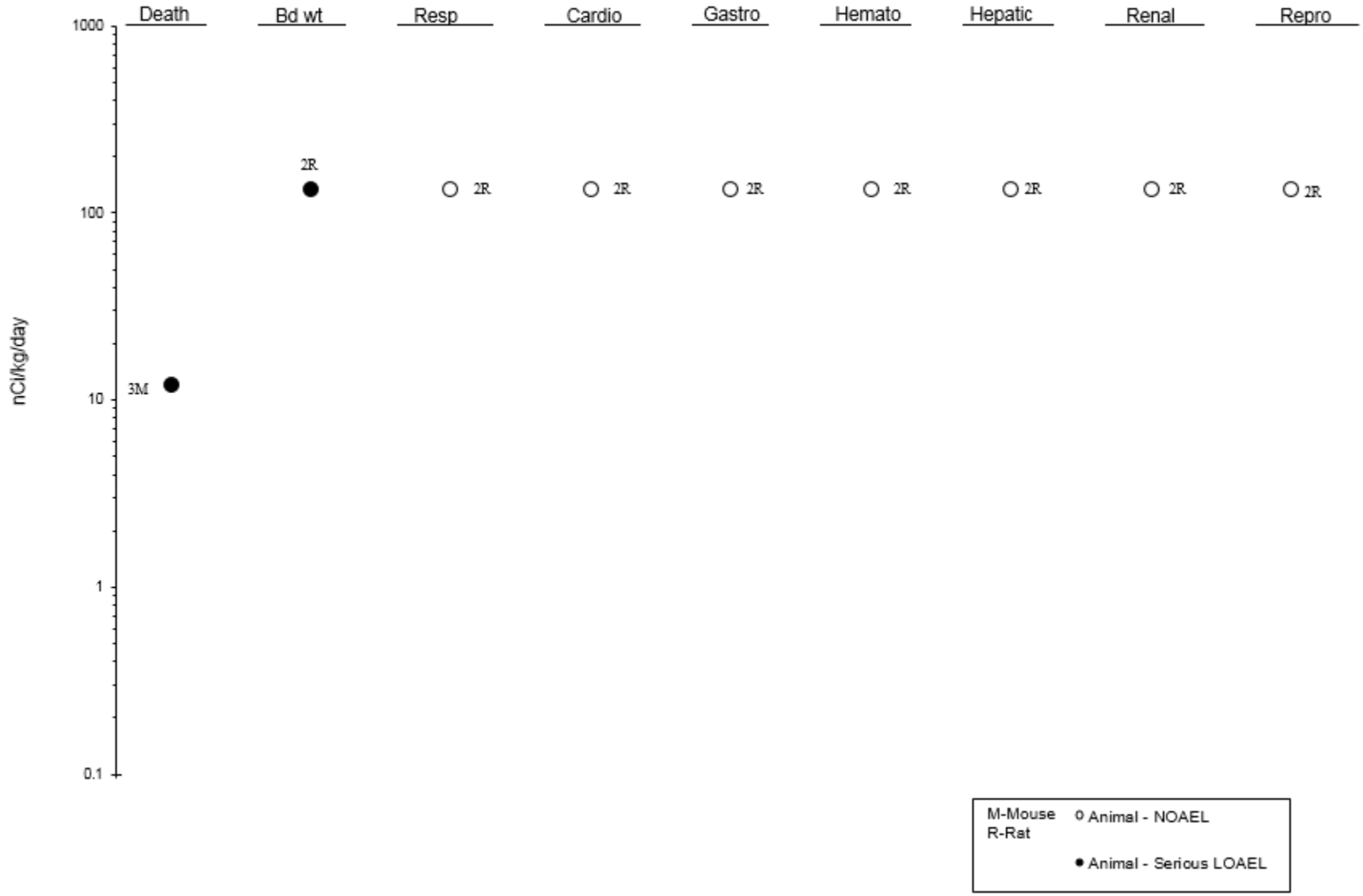


Table 2-3. Levels of Significant Exposure to Thorium – Dermal

Species (strain) No./group	Exposure parameters	Doses (nCi/kg)	Parameters monitored	Endpoint	NOAEL (nCi/kg)	Less serious LOAEL (nCi/kg)	Serious LOAEL (nCi/kg)	Effect
INTERMEDIATE EXPOSURE								
Rat (NS) 4 M	15 days	15, 29, 58	GN HP CS	Death				No deaths were observed
				Hepatic	58			
				Renal	58			
				Dermal		15		Hyperkeratinization at ≥15 nCi/kg/day; mild acanthosis at 58 nCi/kg/day
				Repro		15		Mild edema of seminiferous tubules at ≥15 nCi/kg/day; desquamation of sperm at 58 nCi/kg/day
Thorium nitrate								
Tandon et al. 1975								

CS = clinical signs; GN = gross necropsy; HP = histopathology; LOAEL = lowest-observed-adverse-effect level; M = male(s); NOAEL = no-observed-adverse-effect level; NS = not specified; Repro = reproductive

2.2 DEATH

In a study of male workers at a thorium processing facility, no increases in deaths from all causes were found; the standardized mortality ratio (SMR) was 1.05 (95% confidence interval [CI] 0.96–1.15), in comparison to U.S. white males (Polednak et al. 1983; Stehney et al. 1980); the workers were primarily employed as laborers and operators in the thorium extraction process. The estimated thorium concentrations ranged from 0.003 to 0.192 nCi/m^3 for a period of 1–33 years. In a follow-up study that also examined female workers primarily involved in the production of incandescent gas mantles, the SMRs for all causes were 1.12 (95% CI 1.05–1.21) among 3,119 male workers and 0.74 (95% CI 0.63–0.86) among 677 female workers (Liu et al. 1992).

In a series of acute- and intermediate-duration inhalation exposures to thorium nitrate, thorium dioxide, thorium fluoride, or thorium oxalate, no deaths were observed in dogs or rabbits exposed to 0.9–4.8 nCi/m^3 10–51 times (Hall et al. 1951). Similarly, no deaths were reported in rats, guinea pigs, dogs, or rabbits exposed to 0.55 nCi/m^3 as thorium dioxide for 14 months (Hodge et al. 1960). A single gavage administration of 110 nCi/kg as thorium nitrate resulted in the death of 4/20 mice (Patrick and Cross 1948); no deaths were observed at 84 nCi/kg. Repeated exposure (4 months) to thorium nitrate in drinking water resulted in 50% mortality in mice exposed to 12 nCi/kg/day (Patrick and Cross 1948). Downs et al. (1959) reported increases in mortality in weanling and mature rats exposed to dietary concentrations of thorium nitrate ≥2.1% for intermediate durations; the investigators attributed the deaths to the poor nutritional status of the rats (marked decreases in food intake and body weight gain) rather than a direct effect of thorium nitrate. With the exception of one group of animals, doses could not be calculated for this study; no deaths were observed in rats exposed to 130 nCi/kg/day. No deaths were reported in a 15-day dermal exposure rat study in which 58 nCi/kg/day as thorium nitrate was applied to the lateroabdominal and scrotal skin (Tandon et al. 1975).

Syao-Shan et al. (1970b) compared the acute lethality of thorium nitrate, thorium chloride, and thorium dioxide in mice receiving a single intraperitoneal injection. The estimated LD_{50} doses were 370.8 mg thorium/kg for thorium nitrate and 589.1 mg thorium/kg for thorium chloride; no significant increases in mortality were observed at 2,000 mg thorium/kg as thorium dioxide, which was the highest dose tested. The investigators suggested that solubility determined the relative toxicity of the three compounds. Downs et al. (1959) reported 1- and 2-day LD_{50} values of 648 and 513 mg thorium/kg, respectively, for thorium nitrate administered via intraperitoneal injection to mature female rats. When administered to

weanling rats, the LD_{50} value ranged between 852 and 1,065 mg thorium/kg, suggesting that weanlings were less sensitive than mature animals.

2.3 BODY WEIGHT

Weight loss was reported in mature rats exposed to thorium nitrate in the diet at 4.3% thorium for 90–114 days (Downs et al. 1959). However, marked decreases in food intake were also observed at this dietary concentration. In weanling rats treated with thorium nitrate in the diet for 98–137 days at concentrations ≥0.43% thorium, decreases in body weight gain were observed (Downs et al. 1959); decreases in food intake were also reported in the weanling rats. Due to inadequate reporting of food intake, doses cannot be calculated for this study, with the exception of one group for which the investigators provided dose information. A 24.6% decrease in body weight gain was observed in male rats exposed to 130 nCi/kg/day (dietary concentration of 1.3% thorium). Weight loss was also observed in rats administered a single intraperitoneal dose of 60.8 mg thorium/kg as thorium nitrate dissolved in trisodium citrate (M^{c}Clinton and Schubert 1948).

2.4 RESPIRATORY

No increase in the risk of deaths from respiratory disease (SMR 1.31, 95% CI 0.92–1.83) was observed in a study of 3,039 thorium refinery workers (Polednak et al. 1983). It is noted that the analysis did not control for smoking or exposure to other compounds, such as cerium, uranium, and other rare earth elements, which may have contributed to the overall risk. Exposure level estimates for inhalation intakes ranged from 0.003 to 0.192 nCi/m^3 for a period of 1–33 years.

In a poorly reported study, hypertrophic rhinitis and progressive pneumosclerosis (interstitial pneumonia) of the lungs were observed in rats exposed intermittently (5 hours/day, 5 days/week) for 6–9 months to an inert aerosol (loparite dust) enriched with 10 or 49% insoluble thorium dioxide, or to thorium dioxide (100%) alone (Likhachev et al. 1973a); no information on exposure levels or specific activity of the aerosol was provided. It is noted exposure to the loparite dust vehicle also resulted in lung damage, including chronic “broncho-bronchiolitis” and foci of desquamative pneumosclerosis. The investigators reported that the severity of the lung sclerosis was directly related to the radiation dose and the amount of thorium dioxide. Sclerosis of the lungs became evident in 3–6 months in the 100% thorium dioxide group, in 9–12 months in the 49% thorium dioxide group, in 12–15 months in the 10% thorium dioxide group, and in 18–24 months in the inert aerosol control group. Since the exact amount of thorium administered was not clear from the report, the results of the study do not appear in Table 2-1.

No histopathological alterations were observed in the lungs of rats, guinea pigs, rabbits, or dogs exposed to 0.55 nCi/m^3 as thorium dioxide 6 hours/day, 5 days/week for 14 months (Hodge et al. 1960). No histological alterations were observed in the lungs of rats exposed to dietary thorium nitrate for 90–137 days at concentrations as high as 4.3% thorium (Downs et al. 1959); the lack of food consumption data precludes calculating doses for all but one group. No lung lesions were observed in the rats exposed at 1.3% thorium (130 nCi/kg/day).

Pneumonia, suppurative lesions of the bronchi with sclerotic changes of peribronchial tissue, and bronchiectasis were observed in rats receiving a single intratracheal dose of 0.192 nCi/kg of thorium dioxide (Gaidova and Syao-Shan 1970). McClinton and Schubert (1948) reported nasal hemorrhages in rats administered 60.8 mg/kg as thorium nitrate dissolved in trisodium citrate via intraperitoneal injection; the dose also resulted in lethality.

2.5 CARDIOVASCULAR

In a study of thorium process workers, no increases in deaths from circulatory diseases were found among male workers (Liu et al. 1992). However, in female workers primarily involved in the production of incandescent gas mantles, there was an inverse association between deaths from circulatory disease and thorium exposure (Liu et al. 1992). Dietary exposure to thorium (as thorium nitrate) at 130 nCi/kg/day did not result in histopathological changes in the heart of rats exposed for 105–131 days (Downs et al. 1959); no lesions were observed at higher dietary concentrations (up to 4.3% thorium).

In contrast, 11 months after a single intratracheal and intraperitoneal injection of thorium dioxide in rats, a sharp and persistent fall in blood pressure was found (Syao-Shan 1970d); however, the magnitude of the decrease in blood pressure was not dose-related.

2.6 GASTROINTESTINAL

Hall et al. (1951) reported retching, gagging, and occasional vomiting in dogs exposed to 4.0 nCi/m^3 as thorium tetranitrate 6 hours/day, 5 days/week for 10 exposures; no information on the incidence or frequency of the effect was provided. The study did not appear to use a control group, which would provide insight into whether the effect was compound specific or due to dust exposure. Occasional intestinal hemorrhages were reported in mice that died following a single gavage exposure to thorium nitrate (Patrick and Cross 1948). It was not reported whether the intestinal hemorrhage was the cause of

death in the mice. The level at which this occurred was not reported. The possibility that intestinal damage resulted from improper gavage technique cannot be ruled out; therefore, these data are not presented in Table 2-2. No histopathological changes in the stomach or intestines were found in rats exposed to thorium (as thorium nitrate) for 105–131 days at 130 nCi/kg/day (Downs et al. 1959). Similarly, no gastrointestinal lesions were observed in rats exposed to higher dietary concentrations (up to 4.3% thorium) for intermediate durations; doses could not be calculated for these groups.

2.7 HEMATOLOGICAL

Information on the potential of thorium to adversely affect the hematological system comes from an occupational exposure study and several experimental animal studies. A complete blood count was done on a cohort of 273 male monazite sand refinery workers to determine the effect of thorium on the hematological system. The estimated body burden (calculated from *in vivo* detection of external gamma rays emitted by daughter products of thorium still in the subject's body and from thoron [^{220}Rn] in expired air) of thorium was higher in those workers exposed for a longer time period, but the blood count did not correlate with the body burden of thorium (Conibear 1983). A correlation was found, however, between the blood count and cigarette smoking habits. Exposure level estimates for inhalation intakes of nicotine or thorium were not reported, and the external gamma-ray exposure rate was between 0.5 and 5.0 milliroetgren/hour. Because the workers were exposed to other toxic compounds (silica, yttrium, acid and alkali fumes) as well as other radioactive materials, toxic effects cannot necessarily be attributed to thorium.

A series of inhalation studies in dogs (6 hours/day, 5 days/week) reported decreases in erythrocyte counts after 10 exposures to 4.8 nCi/m^3 thorium dioxide, 45 exposures to 1.4 nCi/m^3 thorium oxalate, or 51 exposures to 0.9 nCi/m^3 thorium tetrafluoride (Hall et al. 1951). This study also found alterations in leukocytes including leukocytosis, distorted monocytes, abnormal forms of lymphocytes, and hypersegmented polymorphonuclear granulocytes in dogs exposed to 4.0 nCi/m^3 thorium nitrate; increased filamented neutrophils in dogs exposed to thorium tetrafluoride; and increased number of polymorphonuclear neutrophils in dogs exposed to thorium dioxide. No hematological alterations were observed in male and female rabbits exposed to 3.8 or 3.5 nCi/m^3 thorium dioxide, respectively, for 10–11 exposures (Hall et al. 1951). It is noted that in the Hall et al. (1951) study, no control group was used; pre-exposure blood counts were used as reference values. No effects on hematological parameters or the histopathology of the spleen were found in rats, guinea pigs, rabbits, or dogs exposed to 0.55 nCi/m^3 as thorium dioxide 6 hours/day, 5 days/week for 1 year (Hodge et al. 1960).

Dietary intake of thorium nitrate at 130 nCi/kg/day by rats treated for 105–131 days did not result in histopathological changes in the spleen or alterations in erythrocyte, leukocyte (total and differential), or platelet counts (Downs et al. 1959). Higher dietary concentrations (up to 4.3% thorium, doses could not be calculated due to lack of food consumption data) also did not result in hematological alterations in mature or weanling rats exposed for intermediate durations.

An *in vitro* study found that thorium nitrate induces aggregation and hemolysis in human erythrocytes (Kumar et al. 2010); it is not known if this would also occur *in vivo*.

2.8 MUSCULOSKELETAL

No histological alterations were observed in the femur of rats, guinea pigs, rabbits, or dogs exposed for 1 year to 0.55 nCi/m^3 as thorium dioxide for 1 year (6 hours/day, 5 days/week) (Hodge et al. 1960).

2.9 HEPATIC

The levels of aspartate aminotransferase (AST), globulin, and total bilirubin in sera of a cohort of 275 former workers in a thorium refinery were correlated with body burdens of radioactive material (Farid and Conibear 1983). The levels of AST and total bilirubin were significantly higher in thorium-exposed workers, as compared to U.S. white males. Globulin levels also increased with increasing levels of body burden, but not significantly. Although the enzymatic levels tested were elevated, they were still within the normal range. No exposure concentrations were reported.

Hepatic effects have not been observed in studies of laboratory animals. Inhalation exposure to 0.55 nCi/m^3 thorium dioxide for 1 year did not result in histopathological alterations in the livers of rats, guinea pigs, rabbits, or dogs (Hodge et al. 1960). Similarly, no histopathological changes in the liver were found in rats exposed to thorium (as thorium nitrate) in the food for 105–131 days at 1.3% (130 nCi/kg/day) or in other rats exposed at dietary concentrations as high as 4.3% thorium (Downs et al. 1959). Dermal exposure to 58 nCi/kg/day as thorium nitrate applied for 15 days to latero-abdominal and scrotal areas did not result in histopathological alterations in the liver of rats (Tandon et al. 1975).

2.10 RENAL

There are limited data on the renal toxicity of thorium in humans following inhalation, oral, or dermal exposure. In a study of former thorium refinery workers (Farid and Conibear 1983; see Section 2.9 for details), no alterations in serum albumin, total protein, or alkaline phosphatase levels were observed.

No histopathological effects on the kidneys were found in rats, guinea pigs, rabbits, or dogs exposed via inhalation to 0.55 nCi/m^3 as thorium dioxide 6 hours/day, 5 days/week for 1 year (Hodge et al. 1960) in weanling rats exposed to 130 nCi/kg/day as thorium nitrate in the diet for 105–131 days (Downs et al. 1959), weanling or mature rats exposed to dietary thorium nitrate concentrations as high as 4.3% thorium (doses could not be calculated due to lack of food intake data) for 90–137 days (Downs et al. 1959), or in rats exposed via dermal application of 58 nCi/kg/day as thorium nitrate for 15 days (Tandon et al. 1975).

2.11 DERMAL

Information on the dermal toxicity of thorium is limited to a study in which rats received daily dermal applications of thorium nitrate to the lateroabdominal and scrotal areas of rats for 15 days (Tandon et al. 1975). Mild hyperkeratinization of the lateroabdominal skin was found at ≥15 nCi/kg/day. At 58 nCi/kg/day, mild acanthosis and thickening of the epithelial lining of the lateroabdominal skin were seen. At this level, mild acanthosis, swollen collagen fibers, and foamy dermis were found in the scrotal skin.

2.12 OCULAR

No studies examining ocular toxicity were identified in humans or animals.

2.13 ENDOCRINE

No studies examining endocrine effects were identified in humans or animals.

2.14 IMMUNOLOGICAL

Information on the immunotoxicity of thorium is limited to inhalation studies examining the lymph nodes. Progressive lymph node atrophy was observed in rats exposed to dust containing 46 or 100% thorium dioxide for 6–9 months (Likhachev et al. 1973a). A second inhalation study did not find histopathological effects in the lymph nodes of rats, guinea pigs, rabbits, or dogs exposed to 0.55 nCi/m^3

as thorium dioxide for 6 hours/day, 5 days/week for 1 year (Hodge et al. 1960); no parameters of immune function were examined.

2.15 NEUROLOGICAL

No inhalation, oral, or dermal studies evaluating neurological endpoints were identified.

A 30-day exposure to 1.09 µCi/kg/day as thorium nitrate administered via intraperitoneal injection resulted in marked edema and neuronal degeneration in the cerebellum of mice (Kumar et al. 2009). Increases in acetylcholinesterase (AChE) specific activity were observed in the cerebellum, cortex, hippocampus, and striatum regions of the brain; the increases in AChE activity were significantly correlated with increases in thorium levels in those regions of the brain. Thorium nitrate exposure also resulted in impaired learning and memory-based neurobehavior in the mice (Kumar et al. 2009).

2.16 REPRODUCTIVE

No histopathological changes in the gonads were found in male and female rats exposed for 105–131 days to 1.3% thorium as thorium nitrate in the diet (130 nCi/kg/day) (Downs et al. 1959). Dietary exposure to thorium nitrate at higher levels (up to 4.3% thorium; doses could not be calculated due to lack of food intake data) for 90–137 days did not result in histopathological changes in the gonads of mature or weanling rats (Downs et al. 1959).

Daily dermal applications of thorium nitrate to the lateroabdominal and scrotal skin of rats for 15 days resulted in mild edema of the seminiferous tubules and the interstitium at ≥15 nCi/kg/day (Tandon et al. 1975). At 58 nCi/kg/day, some desquamation of sperm and giant spermatid-type cells was found. The percentage of sperm affected by thorium treatment was not reported. Based on the rapid onset of effects, the investigators suggested that the effects were due to chemical toxicity rather than a radiological effect.

Several parenteral exposure studies examined potential testicular effects. Intratesticular injection of 1.5 mg thorium/kg as thorium nitrate resulted in decreases in testicular weight, severe testicular necrosis, which resulted in degeneration of almost all of the seminiferous tubules and a total lack of spermatozoa in rats within 2 days of injection (Kamboj and Kar 1964). Decreases in relative testes weight, deformation of seminiferous tubules with extensive degeneration of spermatogenic stages and reductions in the number of Leydig cells were observed in mice administered intraperitoneal injections of 0.5 mmol/mL/kg of thorium nitrate for 7 days (Jadon and Mathur 1983). In contrast, subcutaneous administration of

1.5 mg thorium/kg as thorium nitrate did not result in testicular alterations or alteration of residual spermatozoa in the ductus deferens in rats (Kamboj and Kar 1964) and an intravenous injection of 0.3 µCi/kg ^{238}Th (thorium compound not specified) did not result in testicular lesions in dogs (Ellis and Berlinger 1967).

2.17 DEVELOPMENTAL

No developmental toxicity studies were identified for thorium.

2.18 OTHER NONCANCER

No studies examining other noncancer endpoints were identified.

2.19 CANCER

Investigators have evaluated the carcinogenicity of thorium in two cohorts of thorium workers. The first cohort consisted of 3,039 male workers at a thorium processing facility in Illinois who began work in 1940 or later (Polednak et al. 1983; Stehney et al. 1980); most of the workers were labors and operators involved in thorium extraction. The workers were exposed to thorium and its progeny radionuclides, including ^{220}Rn (thoron). Thorium exposure was estimated using job classification and exposure duration; however, individual exposure levels were not estimated. The concentration of α-emitting radionuclides was estimated in a subset of 592 workers in various job categories; the exposure levels ranged from 0.003 to 0.192 nCi/m^3. No associations between thorium exposure and deaths from all cancers (SMR 1.21, 95% CI 0.99–1.48) or specific types of cancer were found, as compared to the mortality rates for U.S. white males. SMRs for lung cancer and pancreatic cancer were 1.44 (95% CI 0.98, 2.02) and 2.01 (95% CI 0.92, 3.82), respectively (Polednak et al. 1983). Among the subset of 592 workers with exposure to thorium dust and employment of ≥1 year, an elevated risk of death from all cancer was found (SMR 1.75, 95% CI 1.26–2.39). An association was also found for deaths from pancreatic cancer (SMR 4.13; 95% CI 1.34–9.63). The authors indicated that smoking may be a confounding factor in the increased rates of cancer; however, the smoking histories were not available for the subjects. A follow-up study of this cohort (Liu et al. 1992) was expanded to include female workers primarily working in the incandescent gas mantle area where there were low levels of thorium; the total number of examined workers was 3,796 (3,119 males and 677 females). Increases in deaths from all cancers (SMR 1.23, 95% CI 1.04–1.43) and lung cancer (SMR 1.36, 95% CI 1.02–1.78) were found among male workers; as noted for the Polednak et al. (1983) study, the study did not control for smoking,

which may have contributed to the increased risk. No increase in pancreatic cancer (SMR 1.47, 95% CI 0.70–2.71) was found. An inverse association between thorium exposure and cancer deaths were found among the female workers (all cancers SMR 0.53, 95% CI 0.36–0.78). Dividing the male workers into subgroups based on job classification, duration of employment, time since first employment, year of first employment, or age at first employment did not result in substantial variations in deaths from all cancers or lung cancer; see Table 2-4 for a summary of mortality ratios. However, it demonstrates that the increased risk was generally seen in shorter-term workers (≤1 month for lung cancer only), in workers more recently hired (<15 years since first employment), and in workers first employed at an older age (≥30 years old).

Table 2-4. Standardized Mortality Ratios for All Cancers and Lung Cancers Among Male Thorium Workers

	All cancers			Lung cancer		
	Number of deaths	SMR	95% CI	Number of deaths	SMR	95% CI
Job classification						
Laborers and operators in the thorium extraction process	113	1.23	1.01–1.47	39	1.38	0.98–1.89
Other laborers, foremen, maintenance and repair men, superintendents	19	1.44	0.86–2.24	6	1.37	0.50–2.99
Personnel in receiving, shipping, control laboratory, office, and others	21	1.28	0.79–1.96	5	1.12	0.36–2.62
Duration of employment						
≤1 month	55	1.38	1.04–1.80	22	1.80	1.13–2.73
2-12 months	44	0.99	0.72–1.33	15	1.10	0.62–1.81
≥13 months	54	1.44	1.08–1.88	13	1.16	0.62–1.99
Time since first employment						
<15 years	57	1.40	1.06–1.82	17	1.73	1.01–2.77
15–29 years	67	1.21	0.94–1.54	21	1.17	0.73–1.80
≥30 years	29	1.12	0.75–1.51	12	1.29	0.67–2.25
Year at first employment						
1915–1954	115	1.27	1.05–1.53	33	1.24	0.85–1.74
1955–1973	38	1.21	0.85–1.65	17	1.65	0.96–2.64

Table 2-4. Standardized Mortality Ratios for All Cancers and Lung Cancers Among Male Thorium Workers

	All cancers			Lung cancer		
	Number of deaths	SMR	95% CI	Number of deaths	SMR	95% CI
Age at first employment						
<20 years	7	0.85	0.34–1.75	3	1.16	0.23–3.39
20–29 years	25	0.97	0.63–1.43	7	0.81	0.33–1.67
≥30 years	121	1.38	1.15–1.65	40	1.55	1.11–2.11

CI = confidence interval; SMR = standardized mortality ratio

Source: Liu et al. 1992

The second cohort consisted of workers in the Baiyan Obo rare earth and iron mine in China. Early studies of this cohort were summarized in IARC (2001). Chen et al. (2005) noted that the ore from this mine contained 10% silicon dioxide and 0.04% thorium by weight. An elevated risk of lung cancer was found among 2,903 miners (2,390 males, 513 females) exposed to ore dust containing thorium and progeny nuclides (SMR 5.15, 95% CI 3.36–7.89). An increased lung cancer risk was also found among approximately 2,000 control miners inhaling dust free air (SMR 2.30, 95% CI 1.17–4.51). IARC (2001) notes that the ratio of the two SMRs was not significantly increased. IARC (2001) noted that the high lung cancer mortality rates in the two groups were likely due to high smoking rates (80%), as compared to the Chinese male population. A 20-year follow-up of this cohort calculated SMRs for lung cancer of 6.13 (95% CI 4.41–8.52) among the thorium dust miners and 1.90 (95% CI 0.94–3.84) in the control miners (Chen et al. 2003). The investigators (Chen et al. 2003, 2005) noted that the high cancer rate among the thorium miners was due to exposure to thorium dioxide, silica dioxide, and thoron progeny. It is noted that none of the analyses of cancer deaths adjusted for smoking or silica dioxide exposure.

The carcinogenicity of thorium has not been evaluated in laboratory animals following inhalation, oral, or dermal exposure. Parenteral studies have found increases in tumors had several sites including lungs, liver, bone, and mammary glands of rats, mice, and dogs (Bruenger et al. 1991; Dougherty et al. 1962; Gaidova and Syao-Shan 1970; Gilman and Ruckerbauer 1962; Gonzalez-Vasconcellos et al. 2011; Gossner 1982; Grampa 1967; Gridgeman 1971; Guimaraes et al. 1955; Lloyd et al. 1995; Luz et al. 1979, 1985; Mays et al. 1987; Müller et al. 1978, 1983; Spiers and Beddoe 1983; Stover 1981; Thurman et al. 1971).

The U.S. Department of Health and Human Services categorized thorium dioxide as reasonably anticipated to be a human carcinogen (NTP 2016) based on human and laboratory animal evidence of carcinogenicity following parenteral exposure to Thorotrast or colloidal thorium dioxide. IARC (2012) categorized internalized radionuclides that emit α-particles as carcinogenic to humans (Group 1). IARC (2012) also categorized ^{232}Th (as Thorotrast) as carcinogenic to humans (Group 1). IARC (2012) conclusions were based on the finding that there is sufficient evidence in humans for the carcinogenicity of ^{232}Th as stabilized ^{232}thorium dioxide in colloidal form (Thorotrast). It also considers that there is sufficient evidence in experimental animals for the carcinogenicity of ^{228}Th, ^{230}Th, and ^{232}Th. See Section 2.21 for discussion of the health effects of Thorotrast.

2.20 GENOTOXICITY

Limited information was located regarding the genotoxicity of thorium. Hoegerman and Cummins (1983) assessed the frequency of chromosome aberrations in the lymphocytes of 47 male workers in a thorium processing plant. The workers were divided into three groups based on their body burdens of radioactivity: low (0 nCi/kg), moderate (0.003 nCi/kg), and high (0.015 nCi/kg). An increased frequency of chromosomal aberrations (dicentric ring chromosomes) was found in the combined high and moderate burden groups compared to the low-burden group and historical controls. No significant differences were found in the frequency of two-break chromosomal aberrations. A positive correlation was not established between the frequency of chromosomal aberrations and duration of employment. Costa-Ribeiro et al. (1975) also reported a statistically significant ($p<0.05$) increase in the number of chromosomal aberrations (dicentrics) in 240 monazite sand millers, as compared to controls. No significant differences in the incidence of translocations were observed. No exposure concentrations were reported in either study. Based on the limited human data, thorium appears to be a genotoxic agent.

A mixture of thorium and lanthanum in the ratio found in Brazilian monazite sand was evaluated *in vitro* for cytotoxicity and genotoxicity to human T-lymphocyte leukemia cells. The mixture was found to be cytotoxic, but not genotoxic (Oliveira et al. 2014).

A study by Nishioka (1975) screened thorium chloride (0.05 M) as a potential mutagen by determining whether it inhibited bacterial growth in *Bacillus subtilis* strains H17 (Rec$^+$, *arg*$^-$, and *trp*$^-$) and M45 (Rec$^-$, *arg*$^-$, and *trp*$^-$). Since bacterial growth was not inhibited, thorium was not further tested for mutagenicity. Thorium chloride (10%) was shown to have no effect on the survival of *Klebsiella oxvtoca* or *Klebsiella pneumoniae* (Wong 1988).

Refer to Section 2.21 for information regarding the genotoxicity of Thorotrast.

2.21 THOROTRAST

Thorotrast (a colloidal solution of thorium dioxide [$^{232}ThO_2$]) is an α-particle emitting contrast medium that was injected intravascularly into patients (estimates in the millions) throughout the world (mostly in the 1930s and 1940s), particularly to visualize vascular structures. However, thorium became sequestered mainly in the reticuloendothelial system (mostly liver, spleen, and red bone marrow) where thorium and its progeny caused a variety of adverse health effects.

Distribution, Retention, and Dosimetry of Thorotrast. Approximately 97% of intravenously-injected Thorotrast is taken up by the reticuloendothelial system (RES) and distributed to the liver (59%), spleen (29%), and bone marrow (9%) (BEIR IV 1988; Kaul and Muth 1978; Kaul and Noffz 1978; Parr et al. 1968; Wegener et al. 1976). Thorium is also deposited in the lymph nodes throughout the body after being transported from the liver and the spleen via the lymph ducts (Wegener et al. 1976). The distribution is inhomogeneous in all tissues and organs since thorium, which is complexed with transferrin in the serum (Peter and Lehmann 1981), is taken up by the macrophages of the RES (Hallegot and Galle 1988; Odegaard et al. 1978). Thorotrast tends to remain in the RES, but some of the ^{228}Ra and ^{224}Ra, produced by decay of their parent nuclides, escapes from Thorotrast deposits and migrates to bone (Kaul and Noffz 1978; Parr et al. 1968). The dose rate to the organs of the RES is dependent upon the nonuniform deposition of Thorotrast aggregates (clumping of the colloid within the organ), the self-absorption of alpha particles in the aggregate itself (alpha particles are absorbed by the aggregate and not by the surrounding tissue), and the characteristic metabolic behavior of thorium daughters (Kato et al. 1979; Kaul and Noffz 1978).

Estimated average dose rates from the intravenous injection of 30 mL of Thorotrast were 30 rad/year in liver, 80 rad/year in spleen, 10 rad/year in red bone marrow, 4.5 rad/year in lungs, and 15 rad/year in the cells on the bone surface. The dose to compact bone was 3.3 rad/year and the dose to cancellous bone was 4.8 rad/year (Kaul and Muth 1978). Due to the uneven distribution of thorium within the colloid, however, these mean annual doses must be considered estimates. The fact that toxic effects rarely appeared in the spleen following Thorotrast injection regardless of the high radiation dose implies that the liver is more susceptible than the spleen to the effects of radiation and/or Thorotrast. Mays (1978) determined the dose rate to the endosteum (the sensitive cells for the induction of bone sarcoma may lie

within 10 μm of bone surfaces) to be about 16 rad/year (7 rad/year from ^{224}Ra [5.1], ^{228}Th [1.5], and ^{228}Ra [0.4] translocated from Thorotrast to calcified bone and 9 rad/year from Thorotrast on bone surfaces [5.9] and in red marrow [3.1]). Kaul and Noffz (1978) estimated that the alpha doses 30 years after injection of 25 mL of Thorotrast would be 750 rad in liver, 2,100 rad in spleen, 270 rad in red bone marrow, 18 rad in total calcified bone, 13 rad in the kidneys, and 60–620 rad in various parts of the lungs.

The distribution of Thorotrast-derived thorium activity in organs from a female subject who had been injected with Thorotrast 36 years earlier was evaluated using autopsy tissues from the U.S. Transuranium and Uranium Registry (Kathren and Hill 1992; McInroy et al. 1992; Priest et al. 1992). More than 90% of the thorium was found in the RES, which includes liver (approximately 44–47% of the total), skeleton (32–35%), spleen (11–13%), and lymph nodes (0.28–0.65%). Radiation absorbed doses to the female subject were estimated to have been 121 Gy (12,100 rad) in the spleen (resulting in hyposplenism), 15 Gy (1,500 rad) in the liver, 4 Gy (400 rad) in the skeleton, and 16 Gy (1,600 rad) in the injection site granuloma or Thorotrastoma (Kathren and Hill 1992; McInroy et al. 1992).

Priest et al. (1992) reported that Thorotrast does not distribute uniformly in liver and bone. ^{232}Th radioactivity in bone marrow was largely restricted to areas of cellular bone marrow where it was found throughout the red marrow tissue and concentrated within cells that were commonly aggregated within focalized areas of the marrow. Total bone concentrations of ^{232}Th from highest to lowest were in the pelvis and vertebrae, ribs, upper leg, shoulder and skull, and other extremities. However, disequilibrium in the ^{228}Th:^{230}Th ratio demonstrates some mobility of the more soluble ^{228}Ra intermediary isotope, allowing the ^{228}Th progeny to deposit on distal bone surfaces, such as the fibula that has little red marrow. This is consistent with thorium being a bone surface seeker (Lloyd et al. 1984), while colloidal Thorotrast enters the marrow cavities. Significant deposits were not found in fatty yellow marrow (Kathren and Hill 1992).

The distribution pattern of intravenously-injected Thorotrast in animals is similar to the pattern in humans; most of the Thorotrast is taken up by the RES (Guimaraes et al. 1955; McNeill et al. 1973; Riedel et al. 1979). Riedel et al. (1979) evaluated the distribution of injected thorium dioxide colloids (Thorotrast) in rats, mice, and a single dog, and compared distribution patterns with results obtained for mice, rabbits, and humans by other investigators. Of the injected Thorotrast dose, the liver accounted for 37–75% (rat), 51.8 and 57.8% (mouse), 54.1% (rabbit), 66.2% (dog), and 59% (human). The spleen accounted for 3.5–15.9% (rat), 18.8–18.9% (mouse), 3.2% (rabbit), 4.1% (dog), and 26.5% (human). The study concluded that the biological behavior of colloids was generally similar in humans and animals.

Humphreys et al. (1998) injected four monkeys with Thorotrast to assess any inhomogeneities in bone marrow distribution. Thorotrast was found to evenly distribute in the red marrow at 1 week post-injection. However, Priest et al. (1992) found that after 3–4 years, Thorotrast was deposited as conglomerates within macrophages, similar to the aggregations observed in the red bone marrow of the human autopsy case.

The biological half-time for Thorotrast is estimated to be >400 years, based on measuring thorium and progeny in excreta from Thorotrast patients, determining that <1% of the thorium was excreted during the early period following injection, and analyses of thorium in their autopsy tissues (Hursh et al. 1957). Therefore, most intravascularly-injected Thorotrast was retained in the RES for a lifetime once it was deposited in tissue; those atoms that decayed and became more soluble progeny could redistribute, but very little of the thorium itself was excreted.

Toxic Effects of Thorotrast. The health effects of Thorotrast has been studied for many decades following its use as a contrast medium in patients worldwide. Table 2-5 summarizes selected results from recent follow up studies of intravascularly-injected Thorotrast cohorts in Germany (Becker et al. 2008), Portugal (dos Santos Silva et al. 2003), Denmark and Sweden (Travis et al. 2003), the United States (Travis et al. 2003), and Japan (Mori et al. 1999b). Common to these follow up studies was extremely high rates of liver cancer. Other commonly-reported effects associated with Thorotrast included nonneoplastic liver disease, blood disorders, hematopoietic cancers, and cancer of the bile duct and gall bladder.

Localized fibrosis infiltrated with macrophages was often found surrounding deposits of Thorotrast at the point of intravenous injection. These granulomas were termed Thorotrastoma and resulted from fibroblastic proliferation due to the extravascular deposition of Thorotrast (Coorey 1983; Stanley and Calcaterra 1981; Stougaard et al. 1984; Wustrow et al. 1988). Histologically, the Thorotrastoma consisted of dense, hyalinized connective tissue with Thorotrast found both free and in the cytoplasm of macrophages (Grampa 1971). The Thorotrastoma most commonly occurred in the neck after a cerebral angiography and appeared 4–6 years after intravenous injection (Frank 1980).

Table 2-5. Selected Thorotrast Treatment-Related Health Effects in Humans

Becker et al. 2008 (Germany)

Study design: Cohort study of 2,326 Thorotrast-injected patients and 1,890 unexposed control patients from the same hospitals in West Germany and Vienna, Austria. Study groups were identified in 1967 with follow up through 2004 (9 Thorotrast-injected patients and 151 control patients still alive). SMRs (reference=100) were calculated for Thorotrast-injected subjects and control subjects using mortality rates of West Germany from 1952 to 2002 as reference. RRs were calculated as the ratio between SMR for Thorotrast-injected subjects and SMR for unexposed control subjects.

Results: Thorotrast treatment was positively associated with death from multiple causes, particularly malignancies of the liver and hematopoietic system; life expectancy was shortened by 14 years; and mortality was increased with cumulative time since first exposure.

Cause of death	Thorotrast-exposed SMR (95% CI)	Unexposed SMR (95% CI)	Exposed/unexposed RR (95% CI)
Males			
Total mortality	287 (273–301)	153 (145–162)	1.9 (1.7–2.0)
Diseases of nervous system, eye, ear	1,169 (956–1,430)	493 (380–641)	2.4 (1.7–3.4)
Diseases of the circulatory system	150 (135–166)	104 (95–115)	1.4 (1.2–1.7)
Diseases of the digestive system	641 (568–724)	127 (99–163)	5.0 (3.8–6.8)
Neoplasms (benign/unknown characteristics)	1,116 (873–1,426)	300 (198–456)	3.7 (2.3–6.4)
Malignant neoplasms	398 (366–433)	109 (95–125)	3.7 (3.1–2.0)
Digestive organs and peritoneum	616 (554–687)	116 (94–143)	5.3 (4.2–6.8)
Liver and intrahepatic bile ducts	16,695 (14,703–18,957)	238 (107–529)	71 (32–195)
Gall bladder and extrahepatic bile ducts	1,656 (1,183–2,318)	200 (90–446)	8.1 (3.4–23.6)
Pancreas	288 (174–478)	53 (19.9–141)	5.5 1.7–22.7)
Male genital organs	269 (187–387)	119 (82–173)	2.2 (1.3–3.8)
Brain, unspecified parts of nervous system	933 (595–1,463)	296 (141–620)	3.3 (1.3–9.2)
Multiple myeloma, immunoproliferative	464 (208–1,032)	50 (7–352)	9.2 (1.1–425)
Myeloid leukemia	675 (374–1,219)	89 (22–357)	7.6 (1.7–70)
Leukemia (unspecified cell type)	1,330 (802–2,207)	129 (32–517)	10.2 (2.4–92)

Table 2-5. Selected Thorotrast Treatment-Related Health Effects in Humans

Females			
Total mortality	387 (357–419)	212 (192–233)	1.8 (1.6-2.1)
Diseases of the digestive system	784 (623–986)	229 (153–341)	3.4 (2.1–5.7)
Neoplasms (benign/unknown characteristics)	2,579 (1,971-3376)	281 (126–626)	8.8 (3.8–25)
Malignant neoplasms	395 (339–460)	174 (140–217)	2.3 (1.7–3.0)
Digestive organs and peritoneum	480 (382–601)	136 (92–201)	3.5 (2.2–5.8)
Liver and intrahepatic bile ducts	12,680 (9,337–17,221)	439 (110–1,753)	34 (8.9–292)
Brain, unspecified parts of nervous system	3,320 2,064–5,340)	185 (26–1,312)	17.0 (2.7–711)

dos Santos Silva et al. 2003 (Portugal)

Study design: Cohort study of 1,096 Thorotrast-injected patients and 1,014 nonradioactive contrast-injected patients (controls) from hospitals in Portugal. Study groups were identified in 1961 with follow up through 1996. SMRs (reference=1) were calculated for Thorotrast-injected subjects and control subjects using national mortality rates for Portugal for the years 1930 to 1996 as reference. RRs were calculated as the ratio between SMR for Thorotrast-injected subjects and SMR for unexposed control subjects.

Results: Thorotrast treatment was positively associated with death from multiple causes, particularly chronic liver disease, liver cancer, neoplastic and nonneoplastic hematological disorders, and nonneoplastic diseases of the respiratory system; risks for these conditions remained high for >40 years following Thorotrast treatment.

Cause of death	Thorotrast-exposed SMR	Unexposed SMR	Exposed/unexposed RR (95% CI)
All causes	3.26[a]	1.24[a]	2.63 (2.28–3.04)
All malignant and benign neoplasms	7.02[a]	1.04	6.72 (4.83–9.51)
Hematological diseases	21.7[a]	3.62	6.00 (1.14–59.2)
Diseases of nervous system	16.8[a]	1.33	12.7 (3.89–65.2)
Diseases of the respiratory system	2.42[a]	0.56	4.31 (2.15–9.22)
Chronic liver disease	5.74[a]	1.12	5.12 (2.62–10.7)
Other diseases of the digestive system	4.33[a]	0.89	12.0 (2.75–108)
Neoplastic/nonneoplastic hematological diseases	11.6[a]	1.02	11.4 (3.36–60.2)
Cancer of lymphatic and hematopoietic tissues	9.17[a]	0.42	21.9 (3.24–935)
Leukemia	8.17[a]	0.80	10.2 (1.24–471)
Liver cancer	338[a]	7.98[b]	42.4 (13.90–210)
Liver cancer and chronic liver disease	15.2[a]	1.35	11.2 (6.49–20.7)
All Thorotrast-related causes	6.88[a]	1.08	6.35 (4.75–8.59)

Table 2-5. Selected Thorotrast Treatment-Related Health Effects in Humans

Travis et al. 2003 (Denmark and Sweden)

Study design: Cohort study of 773 and 431 Thorotrast-injected patients in Denmark and Sweden, respectively, and 1,180 nonradioactive contrast-injected patients (controls) in Denmark. Thorotrast treatment was undertaken during 1935–1947 in Denmark and 1932–1950 in Sweden. Registry-based patient follow up began 2 years after angiography and continued until January 20, 1992 in Denmark and December 31, 1992 in Sweden. For site-specific cancer incidence, SIRs (reference=1) were calculated as the ratio of observed to expected cases in the general population. RRs were calculated as the ratio between the SIR for Thorotrast-injected subjects and the SIR for unexposed control subjects.

Results: Thorotrast treatment was positively associated with all cancers and selected site-specific cancer, particularly cancer of the liver, bile duct, and gall bladder, and leukemia. Risk of cancer increased with time since Thorotrast treatment and persisted for 50 years. Increasing cumulative radiation dose was associated with increasing risk of cancer.

Cancer cause of death	Thorotrast-exposed SIR	Unexposed SIR	Exposed/unexposed RR (95% CI)
All cancers	3.3[b]	1.0	3.4 (2.9–4.1)
All cancer except brain and nervous system	3.2[b]	1.0	3.5 (2.9–4.2)
Stomach	1.2	0.5	2.7 (1.1–7.9)
Liver (primary)	108.9[b]	0 (1.5 expected)	Infinity (44.2–infinity)
Liver (not specified as primary)	33.0[b]	0 (1.0 expected)	Infinity (8.2–infinity)
Bile ducts	17.1[b]	0.6	26.4 (4.3–1,133.9)
Gall bladder	9.9[b]	1.1	11.0 (1.3–391.0)
Pancreas	2.0	0.8	3.8 (1.3–12.3)
Ovary, fallopian tube, broad ligament	2.0	0.5	4.3 (1.1–24.3)
All male genital	1.5	0.5	4.7 (1.8–15)
Prostate	1.4	0.5	4.5 (1.6–16.3)
Kidney	2.7[b]	0.8	5.7 (1.9–21.0)
Metastases	8.3[b]	0.4	12.2 (3.3-989.7)
Leukemia, all non-chronic lymphocytic leukemia	15.2[b]	0.9	15.2 (4.4–149.6)
Thorotrast-related cancers	37.5[b]	0.6	76.2 (32.2-247.8)

Table 2-5. Selected Thorotrast Treatment-Related Health Effects in Humans

Travis et al. 2003 (United States)

Study design: Cohort study of 446 Thorotrast-injected patients and 212 nonradioactive contrast-injected patients (controls) in the United States. Thorotrast treatment was undertaken during 1935–1955. Registry-based patient follow-up began 2 years after angiography and continued until December 31, 1992. For site-specific cancer mortality, SMRs (reference=1) were calculated as the ratio of observed to expected cases in the general population. RRs were calculated as the ratio between the SMR for Thorotrast-injected subjects and the SMR for unexposed control subjects.

Results: Thorotrast treatment was positively associated with all cancers and particularly with liver cancer.

Cancer cause of death	Thorotrast-exposed SIR	Unexposed SIR	Exposed/unexposed RR (95% CI)
All cancers	3.8[b]	1.4	4.0 (2.5–6.7)
All cancer except brain and nervous system	3.1[b]	1.0	5.3 (3.1–9.7)
All digestive organs and peritoneum	3.4[b]	0.8	8.9 (3.0–38.1)
Liver	25.1[b]	2.2	22.5(1.8–464.3)
Thorotrast-related cancers	15.3[b]	1.8	20.1 (2.2–73.4)

Table 2-5. Selected Thorotrast Treatment-Related Health Effects in Humans

Mori et al. 1999b (Japan)

Study design: Cohort study of 412 Thorotrast-injected war-wounded veterans and 1,649 war-wounded veterans not injected with Thorotrast (controls) in Japan. For 262 Thorotrast-injected patients, follow-up was initiated at the time of injection; for the other 150 Thorotrast-injected patients, follow-up began January 1, 1979. Follow-up of controls was initiated on the date of injury. Follow-up was terminated on July 15, 1998. Registry-based patient follow up began 2 years after angiography and continued until December 31, 1992. Rate ratios were calculated for major causes of death.

Results: Thorotrast treatment was positively associated with several causes of death, particularly for liver cancer, leukemia, and liver cirrhosis. Rate ratios for all deaths of Thorotrast patients began to increase after a 20-year latent period.

Cause of death	Rate ratio (95% CI)
All causes	2.5 (2.2–2.8)
Liver cancer	35.9 (24.2–53.4
Liver cirrhosis	6.9 (4.0–12.0)
Lung cancer	2.0 (1.0–3.9)
Leukemia	12.5 (4.5–34.7)

[a]p<0.001
[b]p<0.05

CI = confidence interval; RR = relative risk; SIR = standardized incidence ratio; SMR = standardized mortality ratio

Genotoxicity of Thorotrast. The intravenous injection of Thorotrast resulted in radiation-induced chromosomal aberrations in patients (Fischer et al. 1967; Kemmer 1979; Kemmer et al. 1971, 1979; Sadamori et al. 1987; Sasaki et al. 1987). A positive correlation was found between the chromosomal aberration rate and the administered amount of Thorotrast (Buckton and Langlands 1973; Fischer et al. 1967; Kemmer et al. 1971, 1973).

Kyoizumi et al. (1992) and Umeki et al. (1991) reported significantly increased frequencies of mutant T lymphocytes defective in T-cell receptor gene expression in the peripheral blood of patients injected with Thorotrast or ^{131}I, but not in atomic bomb survivors in Japan. The authors suggested that mutation frequency might be used as a radiation dosimeter to identify individuals who recently had been exposed to high doses of radiation, and noted that the analysis required only 1 mL of blood, commercially-available antibodies, and equipment available in many laboratories.

Radiation-induced increased frequencies of chromosomal aberrations (multicentrics and centric and acentric rings), but not mutations, have been reported in peripheral blood lymphocytes at the hypoxanthine phosphoribosyltransferase locus (Littlefield et al. 1997; Platz et al. 2000) or in bone marrow hemopoietic stem cells (Tanosaki et al. 1999) of Thorotrast patients.

Andersson et al. (1995b) evaluated the potential for alpha radiation to increase the rate of p53 point mutations in Thorotrast patients. Tissues containing 18 hepatocellular carcinomas, 9 cholangio-carcinomas, and 9 hepatic angiosarcomas were evaluated, with attention being paid to codon 249 of the p53 gene. No high scores were observed for p53 protein expression, and the scores appeared to be lower than those reported for European hepatocellular carcinomas.

CHAPTER 3. TOXICOKINETICS, SUSCEPTIBLE POPULATIONS, BIOMARKERS, CHEMICAL INTERACTIONS

3.1 TOXICOKINETICS

- Thorium is not readily absorbed from the lungs or gastrointestinal tract; absorption depends on compound solubility and particle size.
- Thorium distributes primarily to lymph nodes and bone surface, and can be retained in the lungs following inhalation exposure.
- Elemental thorium cannot be metabolized.
- Most inhaled thorium is excreted in the feces following ciliary clearance from the lungs to the gastrointestinal tract. Most ingested thorium is unabsorbed and excreted in the feces.

3.1.1 Absorption

Inhalation Exposure. The absorption of thorium from the lungs is dependent upon the chemical nature of the isotope and the size of the aerosol particle (Boecker 1963; Boecker et al. 1963; Moores et al. 1980; Newton et al. 1981; Sunta et al. 1987; Syao-Shan 1970a). Increasing the particle size (>2 μm) increases deposition in the respiratory tract of mice, but decreases deposition in the alveolar region. A linear relationship was found between aerosol dosage of ^{232}Th and the amount deposited in the alveolar region (Moores et al. 1980). Approximately twice as much ^{234}Th is absorbed from the lungs of rats exposed to soluble thorium citrate (33%) compared to soluble thorium chloride (19%) (Boecker et al. 1963). However, following the initial difference in absorption, thorium shows the same distribution and excretion pattern, regardless of absorbed compound. Syao-Shan (1970a) determined that 1.5–5.0% of the administered amount to rats is absorbed from the lungs 1 day after intratracheal administration of insoluble $^{232}ThO_2$. Deposited ThO_2 tends to remain in the lungs for long periods of time; 68–73% of $^{232}ThO_2$ remained in the lungs after 1 day, while 15–30% remained after 21 months. Thorium is removed primarily by ciliary clearance and is excreted in the feces (Wrenn et al. 1981). ICRP (ICRP 1979) assumes that a total of 5% absorption of inhaled thorium is transferred to the blood. However, the solubilities of the thorium compounds appear to be an important biological factor, as evidenced by differences in toxicity: LD_{50} values after 30 days following intraperitoneal injection in mice were 370.8 mg thorium/kg for soluble ^{232}Th (as thorium nitrate) and 589.1 mg thorium/kg for soluble ^{232}Th (as thorium chloride), while the highest dose (2,000 mg thorium/kg) for insoluble $^{232}ThO_2$ resulted in 10% mortality (1/10), the same rate of death observed among control mice (Syao-Shan 1970b).

Lung levels of ^{230}Th and ^{232}Th in workers occupationally exposed to thorium (miners and millers) are significantly higher than those not occupationally exposed (Gilbert et al. 1985; Singh et al. 1981; Vocaturo et al. 1983; Wrenn et al. 1985). In a review of the epidemiological evidence, Wrenn et al. (1981) concluded that the major route of exposure was inhalation. Although intake of thorium through the air may account for <1% of the total intake, absorption through the lungs accounts for approximately 2/3 of the ultimate uptake in the body. This is due primarily to the low gastrointestinal absorption rate (0.02%) in humans (Maletskos et al. 1969; Sullivan et al. 1983).

Oral Exposure. ICRP has recommended a human gastrointestinal absorption value of 0.02% for all forms of thorium (ICRP 1979). In a review of the literature by Johnson and Lamothe (1989), a human gastrointestinal absorption value of 0.1–1% was calculated. Absorption of thorium (as thorium nitrate) is 40-fold higher in neonatal rats (1.1–1.2%) (Sullivan 1980b; Sullivan et al. 1983) than in adult rats (0.028–0.5%) (Sullivan 1980a; Traikovich 1970).

Absorption of thorium in adult mice was 0.065% (Sullivan et al. 1983). These data suggest that infants may be a susceptible population for exposure. In other studies of actinide elements (including thorium), little variation in gastrointestinal absorption was found between rats, guinea pigs, and dogs. Chemical form, solubility, and particle size were found to be the determinants of absorption (Sullivan 1980a). The absorption of various forms and isotopes of thorium in rats was compared by Pavlovskaia (1973). It was found that the rate of absorption of thorium-ethylenediaminetetraacetic acid (EDTA) by the gastrointestinal tract was 60 times greater than that of thorium dioxide. Thorium nitrate had an absorption rate 4 times greater than thorium dioxide, and the absorption rate of thorium chloride was 10 or 20 times greater than thorium dioxide, depending on concentration. The absorption differences are attributable to different solubilities of the various chemical forms.

Dermal Exposure. No studies were located regarding the rate and extent of absorption of thorium following dermal exposure of humans or animals. Absorption of thorium through the skin of animals can be inferred, however, because testicular effects were seen in rats following application of thorium nitrate directly to the lateroabdominal and scrotal skin (Tandon et al. 1975).

3.1.2 Distribution

Glover et al. (2001) reported on the distribution of ^{232}Th activity in the tissues of a whole-body donor (with no known occupational exposure to thorium) to the U.S. Transuranium and Uranium Registries. The whole-body activity (310 mBq [8.38 pCi] or 76 μg based on a specific activity of 4,080 Bq/g [110.27 nCi/g]) was distributed among the respiratory system (39.1%), skeleton (34.2%), muscle (16.6%), skin (8.39%), tracheobronchial lymph nodes (4.13%), central nervous system (0.329%), liver (0.22%), kidneys (0.11%), spleen (0.065%), and other soft tissues combined (1.1%). The percentages total 104%, perhaps indicating that the thorium content of tracheobronchial lymph nodes was included with the respiratory system entry.

Iyengar et al. (2004) estimated contents of several elements, including thorium, in selected organs of the adult Asian population using measured data from road accident victims in China, India, the Philippines, and Republic of Korea who had been healthy prior to accidental death. Reported thorium contents were 3.96–22.1 μg (median 14.45 μg) in the skeleton, 0.89–7.79 μg (median 3.21 μg) in the lung, and 0.12–0.53 μg (median 0.23 μg) in the liver. The thorium content in the skeleton and liver was considered to have resulted from the ingestion of thorium, whereas inhalation of ambient thorium dust was thought to have been the major route of exposure for the thorium content in the lungs.

Harley and Fisenne (1990) assessed the distribution of uranium and thorium in vertebra (highly trabecular bone), rib (a mixture of trabecular and cortical bone), and long bone shafts (highly cortical bone) from skeletal remains of three human donors. Respective mean activity concentrations in vertebra, rib, and long bone shaft were 0.063, 0.083, and 0.044 Bq/kg (1.70, 2.24, and 1.19 pCi/kg) for ^{230}Th, and 0.048, 0.045, and 0.030 Bq/kg (1.30, 1.22, and 0.81 pCi/kg) for ^{232}Th.

Kumar et al. (2009) studied the distribution of thorium in the brains of female Swiss albino mice following intraperitoneal exposure of eight animals for 30 days to 4.1 mg thorium/kg/day as thorium nitrate pentahydrate. Thorium distributed nonuniformly within the brain following the order: cerebellum (1.2%) > cortex (0.8%) > hippocampus (0.66%) > striatum (0.4%).

Inhalation Exposure. The median concentrations of ^{232}Th, ^{230}Th, and ^{228}Th in bone and various soft tissues of autopsy samples of a control population from Grand Junction, Colorado, and Washington, DC are presented in Table 3-1 (Ibrahim et al. 1983; Wrenn et al. 1981; Singh et al. 1983). The maximum concentration of all three thorium isotopes was found in the tracheobronchial lymph nodes, with lungs

Table 3-1. The Median Concentrations of Thorium Isotopes in Autopsy Samples from Grand Junction, Colorado, and Washington, DC (in pCi/kg Wet Weight)

Organ	Number of samples analyzed	Grand Junction, Colorado			Number of samples analyzed	Washington, DC		
		^{228}Th	^{230}Th	^{232}Th		^{228}Th	^{230}Th	^{232}Th
Lung	19	0.28	0.84	0.58	10	0.24	0.31	0.32
Lymph node	14	5.1	11.0	7.8	10	2.6	4.6	2.8
Liver	16	0.07	0.15	0.03	10	0.09	0.15	0.05
Kidney	17	0.07	0.29	0.07	8	0.09	0.17	0.03
Bone	16	0.54	0.92	0.16	7	0.66	0.32	0.1
Testicles	44	0.02	0.06	0.05	–	–	–	–
Spleen	14	0.06	0.13	0.09	–	–	–	–
Thyroid	1	0.33	0.82	0.65	–	–	–	–

Sources: Ibrahim et al. 1983; Singh et al. 1983; Wrenn et al. 1981

and bones containing the next highest activity of thorium isotopes. The high activity in the lymph nodes implies that some of the thorium is cleared from the lungs by the lymphatic system and deposited in the lymph nodes (Mausner 1982; Wrenn et al. 1981).

One possible explanation for the higher activity of ^{228}Th than ^{232}Th in bone is that a major portion of the ^{228}Th may be from intake of ^{228}Ra (radium appears to be absorbed from the gastrointestinal tract to a greater extent than thorium); ^{228}Ra concentrates in bones and decays to ^{228}Th (Wrenn et al. 1981).

The dose rates to various organs in humans from environmental thorium were estimated to be 2.2–4.5, 0.41–0.44, 0.19–0.23, 0.057–0.071, and 0.071–0.072 mrad/year in the lymph nodes, bone, lungs, liver, and kidneys, respectively (Wrenn et al. 1981). The dose rates to organs tended to be higher in subjects living in the vicinity of uranium mine tailings, and the dose rates to the organs in miners were even higher (4.8–10.5 mrad/year in the lymph nodes and 1.2–1.5 mrad/year in the lungs) (Wrenn et al. 1981).

Chen et al. (2003) estimated average thorium lung burdens of 1.60 Bq (43.24 pCi) in a group of 638 rare-earth miners in China who were considered to have experienced occupational exposure to thorium dust; an average thorium lung burden of 0.30 Bq (8.11 pCi) was estimated for a group of 143 workers at the same mine who were classified as not exposed to thorium dust. The estimates of lung burdens were based on measurements of exhaled thoron (^{220}Rn) activity.

Jaiswal et al. (2004) assessed thorium lung burden and total body thorium content in five workers employed for 10–32 years in a plant that processed thorium concentrate. Average thorium activity measured in various departments of the plant was generally <0.12 Bq/m^3 (3.24 pCi/m^3). Lung and whole-body thorium contents were estimated from results of *in vivo* gamma counting of actinium-228 (^{228}Ac) and thallium-208 (^{208}Tl); limits of detection for thorium in the thoracic area and whole body were 12 and 52 Bq (324.32 and 1,405.41 pCi), respectively. Measured thorium lung burden ranged from 15 to 67 Bq (405.41–1,810.81 pCi); total body thorium content ranged from <52 to 168 Bq (<1,405.41–4,540.54 pCi).

Hewson and Fardy (1993) reported blood and urine thorium concentrations ranging from 170 to 2,000 ng/L (geometric mean 480 ng/L; geometric standard deviation [GSD] 1.7, n=25) in the serum and 3–210 ng/L (geometric mean 31 ng/L, n=32) in the urine of mineral sands workers in Western Australia. The geometric means of unexposed workers were 320 ng/L for serum and 5 ng/L for urine. Based on periodically-recorded data regarding alpha radioactivity in the workplace air and historical worker data, the study authors calculated a geometric mean ^{232}Th intake of 0.4 Bq/day (10.81 pCi/day) and geometric

mean exposure time period of 1,597 days for the 25 workers. Neither serum nor urine concentrations correlated with cumulative exposures, but serum levels were less variable and considered to be a more reliable indicator of exposure.

Stehney (1999) measured ^{232}Th concentrations in human autopsy tissue samples from four thorium mill workers, including a millwright and three laborers. Those values were used to compare two predictive dosimetry models (one based on ICRP Report No. 30, the other based on ICRP Report No. 68 and 69), and the latter was found to be more accurate. Stehney and Lucas (2000) later reported additional analytical results for the same four workers and an additional laborer. The ^{232}Th concentrations (in mBq per g wet tissue) were 0.009–0.068 for kidneys, 0.015–0.68 for liver, 0.14–1.19 for bones, 0.97–5.8 for spleen, 0.17–79 for lungs, and 3.9–1,210 for pulmonary lymph nodes (0.24–1.84 pCi/g for kidneys, 0.405–18.38 pCi/g for liver, 3.78–32.16 pCi/g for bones, 26.22–156.76 pCi/g for spleen, 4.59–21.35 pCi/g for lungs, and 105.41–32,702.70 pCi/g for pulmonary lymph nodes). Distribution was higher in lower portions of the lung (possibly due to settling) and higher in vertebrae than in other bones. Lung levels remained high for decades after exposure ended, indicating that actinides were retained with a much longer half-time than the 500 days recommended by ICRP Publication No. 30, but results were not sufficient to recommend a new value. After extended periods, the fractions of thorium remaining in bone, liver, and lungs were comparable between workers and the general population.

Hall et al. (1951) exposed rats and rabbits by inhalation to various thorium compounds for 6 hours/day, 5 days/week. For rats, a trend was noted for increasing deposition with length of exposure, with 11.4 mg/m^3 of thorium tetrafluoride producing femur concentrations of 3.1, 6.1, 4.3, and 8.9 µg thorium/g femur at 1, 2, 3, and 4 weeks of exposure, respectively. Rats exposed to 28 mg/m^3 of thorium oxalate for 4 weeks resulted lung, femur, spleen, and liver concentrations of 126, 5.2, <1.5, and 0.64 µg thorium/g tissue, respectively. This deposition trend held for rabbits, but with a 4-fold smaller relative lung burden.

Hodge et al. (1960) repeatedly exposed dogs to thorium dioxide dust at 5 mg/m^3 (0.55 nCi/m^3) for 1 year. At 6–7 years following cessation of exposures, thorium was found in lung and pulmonary lymph nodes at wet tissue concentrations of 0.84 and 37 mg/g, respectively (ratio of thorium levels in lung:pulmonary lymph nodes = 1:44). These results demonstrate distribution of insoluble thorium dioxide to pulmonary lymph nodes and long-term retention in both lung and pulmonary lymph nodes.

Oral Exposure. Autopsy data of persons environmentally exposed to thorium indicated that pulmonary lymph nodes contained the highest levels of thorium (mean 53.4 µg/kg), followed by the lungs (mean of

5.4 µg/kg, ranging from 1.5 to 16 µg/kg) and bones (mean of 0.55 µg/kg, ranging from 0.2 to 9.0 µg/kg) (Sunta et al. 1987). This study estimated that the daily intake of thorium through food, water, and inhalation was 2.29 µg/day, with the majority from food and water ingestion (2.27 µg/kg). However, it was determined that, since absorption through the gastrointestinal tract is low (0.02%), two-thirds of the body burden of thorium results from inhalation exposure.

Neonatal rats retained 50% of the absorbed amount of thorium (1.1% of the administered amount) in the skeleton (Sullivan et al. 1983). In the same study, adult mice retained 75% of the absorbed amount of thorium (0.065% of the administered amount) in the skeleton. Traikovich (1970) found that about 75% of the absorbed amount (0.5% of the administered amount) of ^{232}Th (as thorium nitrate) was located in the bones of rats.

Dermal Exposure. No studies were located regarding the rate and extent of distribution of thorium following dermal exposure of humans or animals.

Other Routes of Exposure. Maletskos et al. (1969) found that, following intravenous injection in humans, ^{234}Th from thorium citrate generally was retained in the skeleton and soft tissues rather than in the RES, as found with Thorotrast. Studies in mice also demonstrated that intraperitoneally-injected ^{227}Th distributes directly to bone (Müller et al. 1978). A similar distribution pattern was found in dogs injected intravenously with ^{228}Th as thorium citrate (Stover et al. 1960). Intravenous exposure studies in rats and guinea pigs, however, showed a distribution of ^{234}Th (from thorium sulfate) similar to Thorotrast: 60–68% in the liver, 3–7% in the spleen, 0.4–l% in the kidneys, and about 10% in the remaining carcass, including bone (Scott et al. 1952). Peter-Witt and Volf (1985) determined that the mass of ^{234}Th intravenously injected (carrier-free) in rats dictated the pattern of distribution. A "critical" concentration of thorium in the extracellular space was found to be between 10^{-7} and 10^{-6} M; above this concentration, thorium hydrolyzes, becomes colloidal, and distributes primarily to organs of the reticuloendothelial system; below this concentration, thorium is distributed primarily to bone. The exposure levels in the human and animal studies cannot be compared since the concentration injected was not reported in the human study.

Kumar et al. (2012) assessed the distribution of thorium in liver and blood of rats injected intramuscularly with 0.6 mg thorium/kg as thorium nitrate. After 24 hours, 42% of the thorium was in retained the liver and 11% was in the blood.

3.1.3 Metabolism

Transferrin plays a major role in the transport and cellular uptake of thorium (Peter and Lehmann 1981). Thorium can be displaced from transferrin by an excess of iron, but it is not known whether thorium and iron bind to the same sites on the transferrin molecule.

Jeanson et al. (2010) assessed the pH-dependence of thorium binding to transferrin *in vitro*. They reported that Th(IV) (unlike tetravalent plutonium and neptunium) was never completely complexed to transferrin over the pH range studied, and especially below pH 7. They suggested that a relatively large ionic size, coupled with a relatively weak hydrolysis constant, allows thorium to be easily displaced from transferrin or blocked from interaction. This is consistent with the transferrin pH cycle.

3.1.4 Excretion

Inhalation Exposure. After inhalation exposure, the primary route of excretion is in the feces following ciliary clearance from the lungs to the gastrointestinal tract (Wrenn et al. 1981). Fecal excretion may account for as much as 97% of total excretion (Fisher et al. 1983). Higher levels of ^{230}Th were excreted in the feces by active crushermen (uranium mill workers exposed to uranium ore dust in the crusher building) compared to retired workers or controls (Fisher et al. 1983). Levels of ^{230}Th in the urine were comparable to those of retired workers, and the levels in both were significantly greater than controls.

The biological half-lives of ^{232}Th and ^{230}Th in the lungs of subjects living in the vicinity of uranium mine tailings (Grand Junction, Colorado) were 5.3 and 1.4 years, respectively. The biological half-lives for subjects in a non-mine area (Washington, DC) were 2.6 and 1.0 years for ^{232}Th and ^{230}Th, respectively (Wrenn et al. 1981). Since biological half-lives in humans should be the same regardless of where people live, the differences at the two locations may reflect the duration of exposure, the time between exposure and sampling, or the inhalation of larger particle size dust in Grand Junction compared to Washington, DC. The ^{232}Th from nature apparently is retained in the lungs longer than the ^{230}Th.

In a subject who had accidentally inhaled ^{228}Th (alpha emitter, radioactive half-life of 1.9 years) as thorium dioxide, the biological half-life for long-term clearance of ^{228}Th from the body was at least 14 years as a result of skeletal deposition (Newton et al. 1981). The early lung clearance of ^{228}Th was found to be on the order of approximately 50 days, thereby designating thorium dioxide a class W compound (biological half-life in weeks) as opposed to the class Y (biological half-life in years) designation recommended by ICRP (1979). Classes D, W, and Y (days, weeks, and years) have been

redesignated as classes F, M, and S (fast, medium, and slow). Davis (1985), however, concluded that both ^{232}Th (as thorium nitrate) and $^{232}ThO_2$ were class Y compounds by determining the solubility in simulated lung fluid. The near equilibrium of ^{230}Th, ^{234}U, and ^{238}U in the lungs of former uranium miners suggests that the elimination rates of these nuclides are similar (Singh et al. 1987; Wrenn et al. 1985). In dogs, the ^{230}Th/^{234}U ratio increases with time, suggesting that uranium is cleared faster than thorium from dog lungs (Singh et al. 1986). An effective half-life of about 10 days in the lungs of rats was reported for ^{227}Th inhaled as thorium nitrate (radioactive half-life of 18.7 days and biological half-life of about 20 days) (Müller et al. 1975). Pavlovskaia et al. (1974a) determined that the excretion of intratracheally-administered ^{228}Th (as thorium dioxide or thorium chloride) in the feces occurred in two phases in the rat: in the first phase, up to 60% of the ^{228}Th contained in the body was eliminated, and in the second phase, the rate of ^{228}Th excretion in the feces averaged 0.25% of the body burden daily.

Hewson and Fardy (1993) reported thorium concentrations ranging from 3 to 210 ng/L (geometric mean 31 ng/L; GSD 2.6) in the urine of 34 mineral sands workers in Western Australia. It was estimated that urinary excretion averaged 2.5% of the thorium body burden. Based on periodically-recorded data regarding alpha radioactivity in the workplace air and historical worker data, the study authors calculated a geometric mean ^{232}Th intake of 0.40 Bq/day (10.81 pCi/day) and geometric mean exposure time period of 1,383 days for these 34 workers. However, neither urine nor serum concentration related to either the period of employment or cumulative exposure.

Terry et al. (1995) assessed the fecal excretion of thorium in two workers exposed to thorium in the monazite section of a mineral sands dry separation plant over a 5-day work period followed by a 5-day work period without exposure to thorium dust. The workers had been isolated from airborne radioactive dust for at least 7 days prior to the monitoring period. For the 5-day exposure period, one worker wore an air sampler and the other a cascade impactor. Exposures totaled 26.4 Bq (713.51 pCi) of 14 μm atmospheric median aerodynamic diameter (AMAD) dust particles. For both workers, peak thorium fecal excretion occurred on day 6 (the day after the end of the 5-day exposure period). The rapid excretion following exposure indicated that fecal sampling can be used to assess acute exposures to thorium. During the 10-day monitoring period, fecal excretion was 970 μg thorium for one worker and 1,980 μg thorium for the other worker. The 2-fold difference was unexpected and speculated to be due to mouth breathing versus nose breathing.

Jaiswal et al. (2004) measured thorium activity in the lungs, total body, and daily urine of five workers employed for 10–32 years in a plant that processed thorium hydroxide concentrate and exposed primarily

by the inhalation route. The lung activity measured for each individual (15–67 Bq; 405.41–1,810.81 pCi) was used to estimate their total body content and daily urine excretion. Those values were compared with measured total body content (<52–168 Bq; <1,405.41–4,540.54 pCi) and daily urinary activity (0.46–1.84 mBq; 12.43–49.73 pCi). Measured and calculated results compared more favorably when using the combined ICRP human respiratory tract model (ICRP 1994b) and ICRP biokinetic model (ICRP 1995) than with the older biokinetic model (ICRP 1979).

Oral Exposure. It was determined in several species of animals (mice, rats, rabbits) that >95% of the ingested amount is excreted in the feces within several days (approximately 2–4 days) (Patrick and Cross 1948; Scott et al. 1952; Sollmann and Brown 1907). Sollmann and Brown (1907) concluded that, since very little thorium was excreted in the feces following intravenous or intramuscular injection, and since very little thorium was excreted in the urine following ingestion, appreciable amounts of thorium were neither absorbed nor excreted from the gastrointestinal tract.

Dermal Exposure. No studies were located regarding the rate and extent of excretion of thorium following dermal exposure of humans or animals.

Other Routes of Exposure. In contrast to the thorium from Thorotrast (a thorium dioxide and dextran suspension) after intravenous injection, a higher percentage of thorium from more soluble thorium compounds is excreted. Following intravenous injection of ^{234}Th (as thorium citrate) in humans, there is a relatively rapid but small (7%) amount of excretion within the first 20 days. A urine/feces ratio of 12 for male subjects and 24 for female subjects was determined. About 93% of the injected ^{234}Th was retained at 100 days after injection, with a biological half-time of >5 years (Maletskos et al. 1969).

Less than 5% of thorium was excreted in the urine up to 42 days after intravenous injection of ^{234}Th (as thorium sulfate) in rats and guinea pigs (Scott et al. 1952). After intravenous injection, the amount of thorium excreted in the feces was 0.7–24.5% of the level administered for 14–42 days in rats, 0.6 and 14.6% for 2 and 5 days in guinea pigs, and 0.9% for 7 days in rabbits. In dogs injected with ^{228}Th (as thorium citrate), urinary excretion dominated initially, but after 2.5 years, the fecal to urinary ratio approximated 1.0 (Stover 1981; Stover et al. 1960). Thomas et al. (1963) reported the excretion of thorium citrate administered as ^{234}Th tracer plus ^{232}Th carrier in rats. No differences were found in the rate or route of excretion following various routes of administration (intravenous, intraperitoneal, intratracheal, and intramuscular). In the first 2 days, 25–30% of the thorium was excreted. Most of the thorium was excreted in the feces and not in the urine. At a high exposure level, the feces/urine ratio was

45 and at a low level, it was 1.6. This indicates that at the high level, thorium was hydrolyzed, became insoluble, was taken up by the RES, and was quickly cleared from the blood. The higher fecal levels of thorium in the high exposure level animals suggest greater biliary excretion.

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

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 endpoints.

The ICRP developed a Human Respiratory Tract Model (HRTM) for Radiological Protection, which contains respiratory tract deposition and clearance compartmental models for inhalation exposure that may be applied to thorium (ICRP 1994b, 1996). The ICRP also developed a biokinetic model for human oral exposure that applies to thorium (ICRP 1995). Several more recent enhancements to the oral exposure model have been reported. A multicompartmental gastrointestinal tract model was developed to replace what was originally a single parameter model (Human Alimentary Tract Model, HATM) (ICRP 2006). A hair compartment was developed to support biomonitoring of ingestion intakes (e.g., drinking water exposures) (Li et al. 2009). Drinking water and dietary exposure models and Bayesian approaches have been developed to improve thorium dose assessments made with the ICRP model (Little et al. 2003, 2007). The National Council on Radiation Protection and Measurements (NCRP) has also developed a respiratory tract and biokinetics model for inhaled radionuclides (NCRP 1997).

Human Respiratory Tract Model for Radiological Protection (ICRP 1994b, 1996)

Deposition. The ICRP 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. ICRP provides inhalation dose coefficients that can be used to estimate the committed equivalent and effective doses to organs and tissues throughout the body based on a unit intake of radioactive material. The model applies to three levels of particle solubility and a wide

range of particle sizes (approximately 0.0005–100 μm in diameter), and parameter values can be adjusted for various segments of the population (e.g., sex, age, level of physical exertion). This model also allows one to evaluate the bounds of uncertainty in deposition estimates. Uncertainties arise from natural biological variability among individuals and the need to interpret some experimental evidence that remains inconclusive. It is applicable to particles containing uranium, but was developed for a wide variety of radionuclides and their chemical forms.

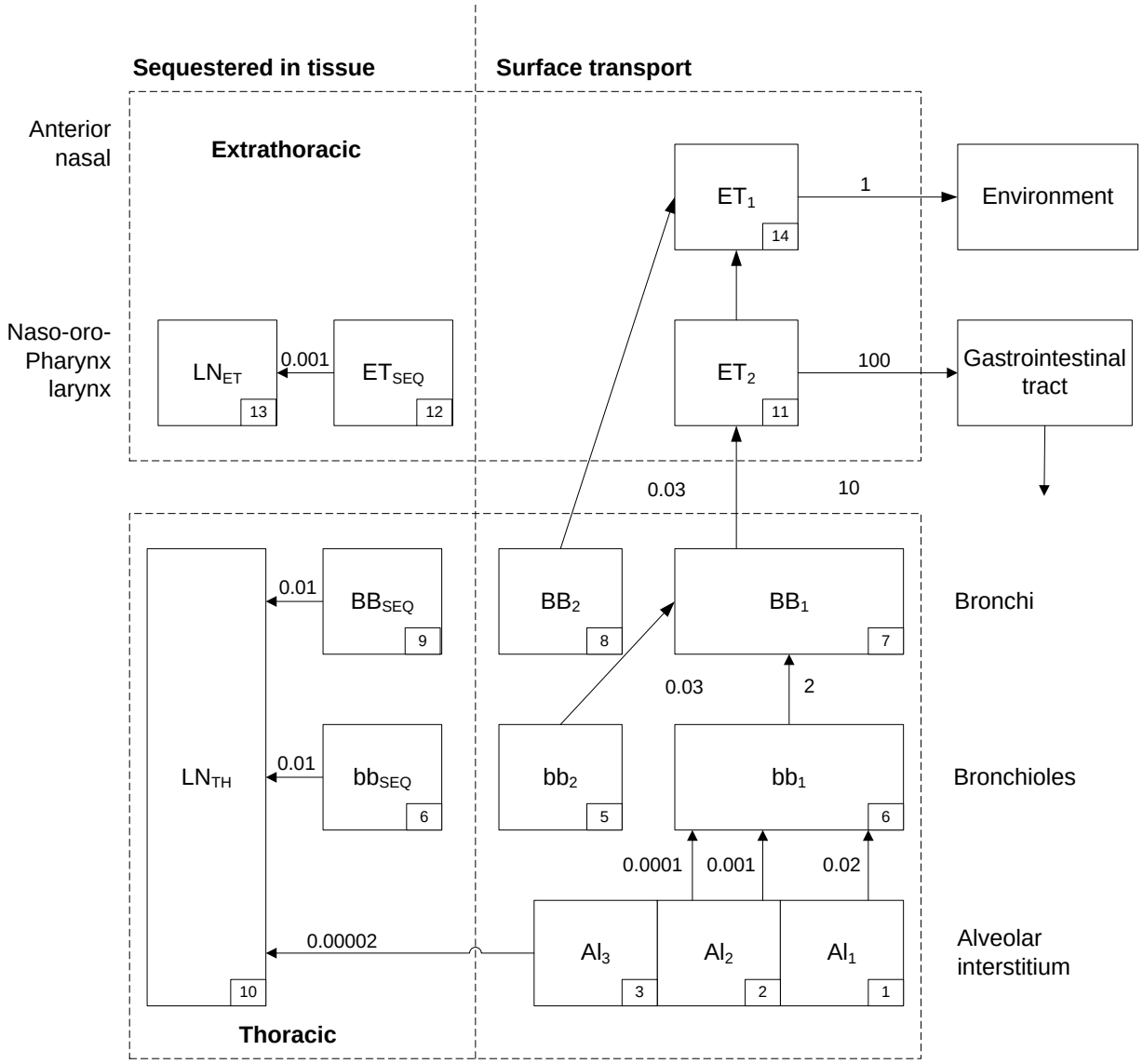
The ICRP deposition model estimates the amount of inhaled material that initially enters each compartment (see Figure 3-1). The model was developed with five compartments: (1) the anterior nasal passages (ET1); (2) all other extrathoracic airways (ET2) (posterior nasal passages, the nasopharynx and oropharynx, and the larynx); (3) the bronchi (BB); (4) the bronchioles (bb); and (5) the alveolar interstitium (AI). Particles deposited in each of the regions may be removed from each region and redistributed either upward into the respiratory tree or to the lymphatic system and blood by different particle removal mechanisms.

For extrathoracic deposition, the model uses experimental data, where deposition is related to particle size and airflow parameters, and scales deposition for women and children from adult male data. Similarly to the extrathoracic region, experimental data served as the basis for lung (bronchi, bronchioles, and alveoli) aerosol transport and deposition. A theoretical model of gas transport and particle deposition was used to interpret data and to predict deposition for compartments and subpopulations other than adult males. Table 3-2 provides reference respiratory values for the general Caucasian population under several levels of activity.

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.

Figure 3-2 presents the compartmental model and is linked to the deposition model (Figure 3-1) and to reference values presented in Table 3-3. Table 3-3 provides clearance rates and deposition fractions for each compartment for insoluble particles. The table provides rates of insoluble particle transport for each of the compartments, expressed as a fraction per day and also as half-time. ICRP 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.

Figure 3-1. Respiratory Tract Compartments in Which Particles May be Deposited*



*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

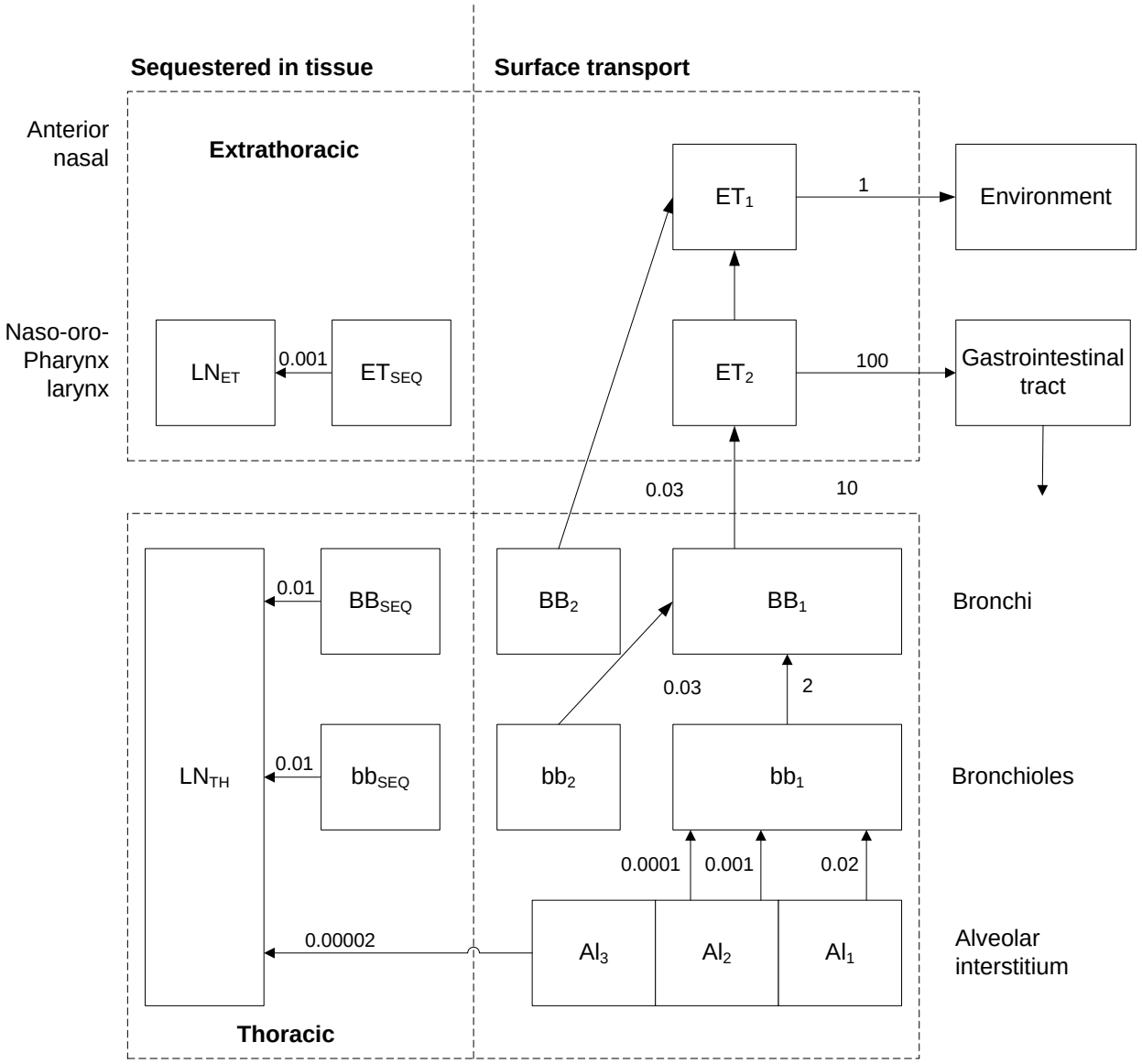
Table 3-2. Reference Respiratory Values for a General Caucasian Population at Different Levels of Activity

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	0.5	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	0.75	0.464
B ($m^3 hour^{-1}$)	NA	0.22	0.32	–	–	0.38	0.48	0.4	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	1.3	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 3-2. Environmental Pathways for Potential Human Health Effects from Thorium*



*See Table 3-3 for rates, half-lives, and fractions by compartment.

Source: ICRP 1994b

Table 3-3. 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

Table 3-3. 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 fs is size-dependent. For modeling purposes, f_s is taken to be:

$$f_s = 0.5 \text{ for } d_{ae} \leq 2.5\sqrt{(\rho/x)}\ \mu m \text{ and}$$

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

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

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., BB1, BB2, BBseq), 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 (ET1), nose blowing, sneezing, and wiping remove most of the deposited particles. Particles remain here for about a day. For particles with activity median aerodynamic diameters (AMADs) a few micrometers or greater, the ET1 compartment is probably the largest deposition site. A majority of particles deposited at the back of the nasal passages and in the larynx (ET2) 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 are cleared more slowly. Evidence for this is found in human studies. For humans, retention of particles deposited in the lungs (BB and bb) is apparently biphasic. The “slow” action of the cilia may remove as many as half of the bronchi- and bronchiole-deposited particles. In human bronchi and bronchiole regions, mucus moves more slowly the closer to the alveoli it is. 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 BB2 and bb2 and both with clearance half-times estimated at 20 days. Particle size is a primary determinant of the fraction deposited in this slow thoracic compartment. A small fraction of particles deposited in the BB and bb regions is retained in the airway wall for even longer periods (BBseq and bbseq).

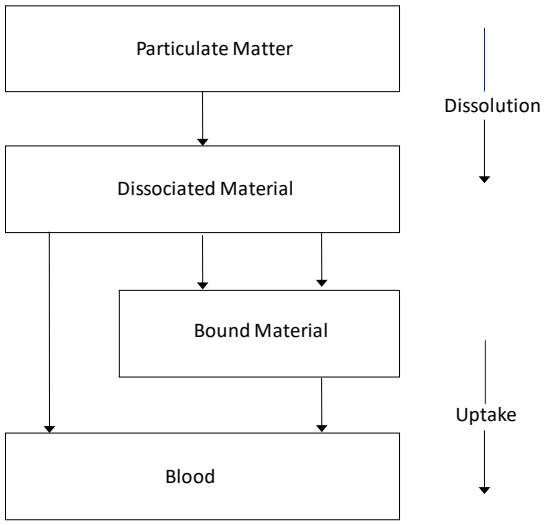
If particles reach and become deposited in the alveoli, they tend to stay imbedded in the fluid on the alveolar surface or move into the lymph nodes. The one mechanism by which particles are physically resuspended and removed from the AI region is coughing. For modeling purposes, the AI region is divided into three subcompartments to represent different clearance rates, all of which are slow. 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 given a half-time of several hundred days. Over time, AI particle transport falls and some compounds have been found in lungs 10–50 years after exposure.

Absorption into Blood. The ICRP model assumes that absorption into blood occurs at equivalent rates in all parts of the respiratory tract, except in the anterior nasal passages (ET1), where no absorption occurs. It is essentially a two-stage process, as shown in Figure 3-3. 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), and S (slow):

- 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 ET2. Thus, for nose breathing, there is rapid absorption of approximately 25% of the deposit in ET and 50% for mouth breathing. No thorium compounds are assigned as type F; however, thorium nitrate might behave in this manner under some circumstances.
- 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 ET2. Thus, there is rapid absorption of approximately 2.5% of the deposit in ET for nose breathing, and 5% for mouth breathing. Type M thorium compounds include nitrate and all other compounds than oxides, and hydroxides.
- 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. Type S thorium compounds include oxides and hydroxides.

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

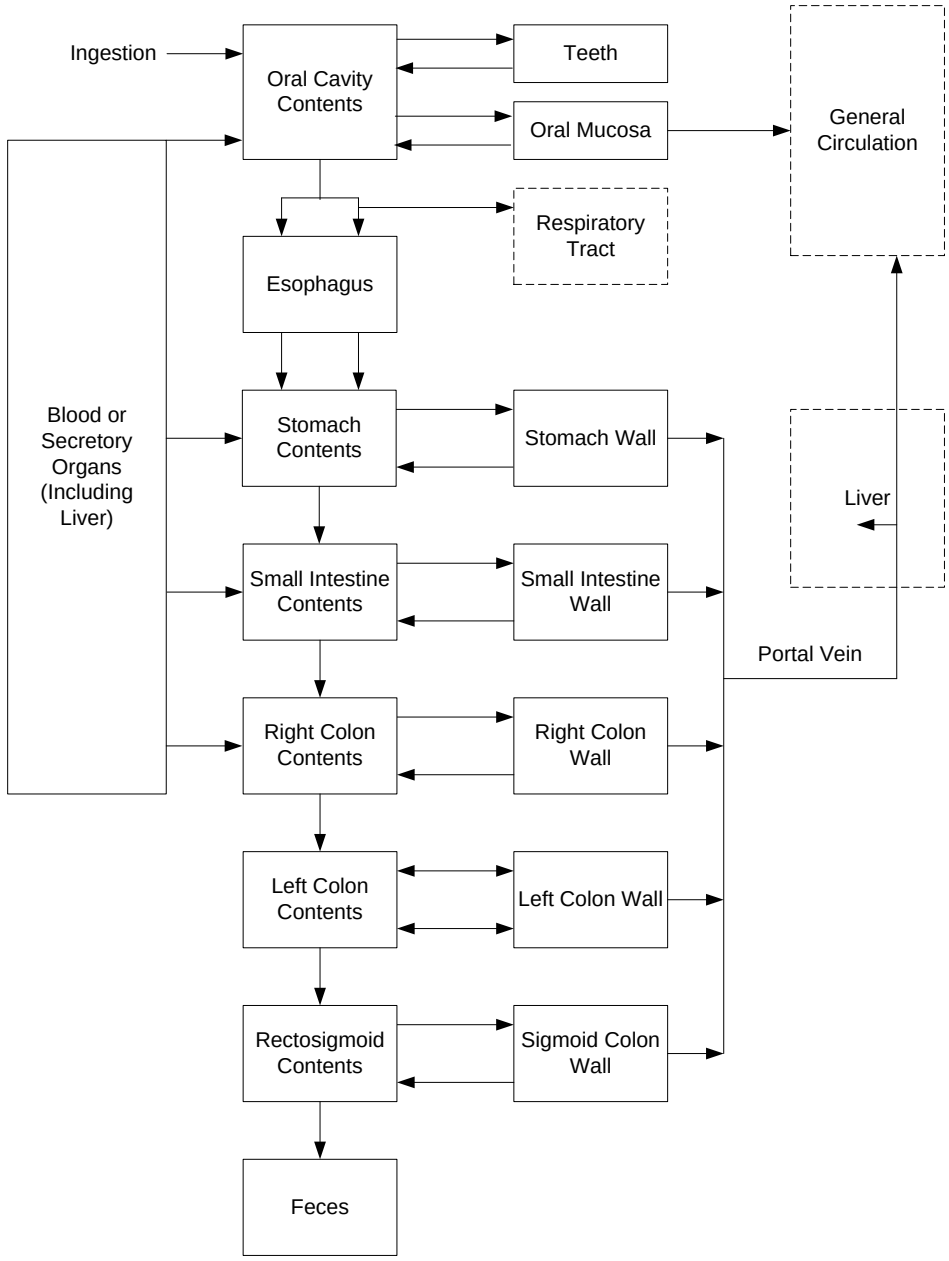


Human Alimentary Tract Model for Radiological Protection (ICRP 2006)

The ICRP HATM is a generic multicompartment gastrointestinal tract model that was developed for applications to radiation risk assessments of radionuclides. The model replaced an earlier gastrointestinal absorption model that consisted of single compartment and single parameter representation of absorption of radionuclides into the central plasma compartment from the small intestine. The structure of the multicompartment model is shown in Figure 3-4. The model simulates the following major processes that can contribute to absorption of radionuclides from the gastrointestinal tract as well as contact and retention of radionuclides in the gastrointestinal tract tissues (i.e., which could contribute to radiation dose to these tissues):

- Entry of a radionuclide into the mouth by ingestion, or into the esophagus after mechanical clearance from the respiratory tract; sequential transfer of the radionuclide through the contents of the oral cavity, esophagus, stomach, small intestine, and segments of the colon, followed by excretion in feces.
- Deposition and retention on or between the teeth and return to the oral cavity.
- Deposition and retention in the oral mucosa or walls of the stomach and intestines.
- Transfer from the oral mucosa or walls of the stomach and intestines back into the luminal contents or into blood (absorption).
- Transfer from various secretary organs or blood into the contents of certain segments of the alimentary tract (secretion).

Figure 3-4. Structure of the Human Alimentary Tract Model (HATM)



ICRP (1995) developed a compartmental model of the kinetics of ingested thorium in humans that is directly applicable to adults and contains conservative assumptions for applicability to 3-month-old infants; 1-, 5-, and 10-year-old children, and 15-year-old adolescents. The model is a revision of an earlier ICRP biokinetic model of thorium (ICRP 1979). Thorium in blood distributes to the skeleton, liver, kidneys, gonads, and gastrointestinal tract. Excretion pathways included in the model are kidney to urine and feces. The model has been evaluated with human data on thorium lung retention and urinary excretion and postmortem thorium tissue levels in workers exposed to airborne thorium or members of the general population without known occupational exposure to thorium (Jaiswal et al. 2004; Li et al. 2007; Roth et al. 2005; Stehney 1999; Terry and Hewson 1995; Terry et al. 1995). The model has also been evaluated using measured biokinetic data from rats following intratracheal instillation of thorium compounds (Hodgson et al. 2003; Stradling et al. 2001). The model has been used to establish the radiation dose (Sv) per unit of ingested or inhaled thorium (Bq) for intake ages 3 months to adult (ICRP 1995, 2001). The dose integration period is 50 years for acute intake at age 25 years. The model is designed to calculate radiation dose coefficients (Sv/Bq) corresponding to specific inhalation or ingestion exposures to thorium isotopes. Dose coefficients have been estimated for all major organs, including the bone surfaces, bone marrow, and liver, and other tissues (ICRP 1995, 1996). The model is based on both human and animal data for thorium; however, it might not reflect the distribution of injected Thorotrast due to its colloidal chemistry. However, it is intended for applications to human dosimetry. Applications to other species would require consideration of species-specific adjustments in model parameters.

3.1.6 Animal-to-Human Extrapolations

No data were located regarding species-specific differences in the toxicokinetics or toxicity of thorium compounds. The toxicity of thorium is generally considered to be radiological in nature, but may include chemical toxicity. Adverse health effects associated with relatively low-level thorium exposure for short durations might not be expected to be radiation induced.

3.2 CHILDREN AND OTHER POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

This section discusses potential health effects from exposures during the period from conception to maturity at 18 years of age in humans. 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. Children may be more or less susceptible than adults to health effects from exposure to hazardous substances and the relationship may change with developmental age.

This section also discusses unusually susceptible populations. A susceptible population may exhibit different or enhanced responses to certain chemicals than most persons exposed to the same level of these chemicals in the environment. Factors involved with increased susceptibility may include genetic makeup, age, health and nutritional status, and exposure to other toxic substances (e.g., cigarette smoke). These parameters can reduce detoxification or excretion or compromise organ function.

Populations at greater exposure risk to unusually high exposure levels to thorium are discussed in Section 5.7, Populations with Potentially High Exposures.

Limited information was located regarding populations with increased susceptibility to thorium.

Gonzalez-Vasconcellos et al. (2011) evaluated mice with Rb1 tumor suppressor gene and p16 germline defects to identify their impact on osteosarcomagenesis induced by thorium. Female mice (n=42–80) in each of three strains were injected with 185 Bq/g (~5,000 nCi/kg) of ^{227}Th, tumors were assessed over >400 days, and DNA of healthy and tumor tissues was assessed for the allelic ratio of Rb1 to p16 loci. Rb1 germline defects resulted in an increased predisposition for thorium-induced osteosarcoma. However, a p16 defect tends to shorten tumor latency, in the later stages of tumor promotion, rather than affecting susceptibility.

Neonatal animals have been found to absorb 20–40 times more thorium through the gastrointestinal tract than adult animals (Sullivan 1980a, 1980b; Sullivan et al. 1983), indicating that children may be more susceptible than adults to the effects of thorium. In contrast, LD_{50} values of 800–1,100 and 513 mg thorium/kg were reported for weanling and mature rats, respectively, exposed to thorium nitrate once via intraperitoneal injection, indicating that the mature rats were more susceptible than the weanlings to thorium lethality.

3.3 BIOMARKERS OF EXPOSURE AND EFFECT

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

A biomarker of exposure is a xenobiotic substance or its metabolite(s) or the product of an interaction between a xenobiotic agent and some target molecule(s) or cell(s) that is measured within a compartment

of an organism (NAS/NRC 1989). Biomarkers of exposure for a radionuclide can include radioactive decay products if they are measurable within a compartment. The preferred biomarkers of exposure are generally the substance itself, substance-specific metabolites in readily obtainable body fluid(s), or excreta. Biomarkers of exposure to thorium are discussed in Section 3.3.1. The National Report on Human Exposure to Environmental Chemicals provides an ongoing assessment of the exposure of a generalizable sample of the U.S. population to environmental chemicals using biomonitoring (see http://www.cdc.gov/exposurereport/). If available, biomonitoring data for thorium from this report are discussed in Section 5.6, General Population Exposure.

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 effect caused by thorium are discussed in Section 3.3.2.

A biomarker of susceptibility is an indicator of an inherent or acquired limitation of an organism's ability to respond to the challenge of exposure to a specific xenobiotic substance. It can be an intrinsic genetic or other characteristic or a preexisting disease that results in an increase in absorbed dose, a decrease in the biologically effective dose, or a target tissue response. If biomarkers of susceptibility exist, they are discussed in Section 3.2, Children and Other Populations that are Unusually Susceptible.

3.3.1 Biomarkers of Exposure

Exposure to thorium can be determined by measurement of radioactive thorium and/or daughters (e.g., ^{220}Rn, ^{222}Rn) in the feces, urine, and expired air. The primary route of excretion of thorium is in the feces following either inhalation or oral exposure. Fecal excretion is essentially complete in a matter of several days (Patrick and Cross 1948; Scott et al. 1952; Sollman and Brown 1907; Wrenn et al. 1981). The measurement of external gamma rays emitted from thorium daughters present in the subject's body and of thoron (^{222}Rn) in the expired air many years following exposure can be used to estimate the body burden of thorium (Conibear 1983).

No tissue concentrations in humans were found that correlated with health effects, but about 20 pCi was found in the lungs of an exposed worker suffering from lung fibrosis. However, it was not clear if the fibrosis was due to thorium, or to rare-earth-containing fumes and dusts (Vocaturo et al. 1983).

Blood levels of thorium following oral exposure of humans to simulated radium dial paint demonstrated that approximately 0.02% of the ingested amount was absorbed by the gastrointestinal tract (Maletskos et al. 1969). This study was the basis for the ICRP (1979) recommendation of an oral absorption factor of 0.02% for thorium.

3.3.2 Biomarkers of Effect

Occupational and experimental studies have shown that the lung, liver, and hematopoietic system are the target organ systems following inhalation exposure to thorium. No relationship was found, however, between the measured body burden of thorium in exposed workers and complete blood count parameters (e.g., hemoglobin, red and white blood cell) (Conibear 1983). Target organs systems have not been identified for oral or dermal exposure to thorium.

3.4 INTERACTIONS WITH OTHER CHEMICALS

Chromosomal aberrations have been reported in the lymphocytes of occupationally exposed workers and in *in vitro* studies. Oliveira et al. (2014) conducted *in vitro* analyses to evaluate whether occupational exposure to the multiple metals in Brazilian monazite sand might result in lymphocyte toxicity (cell viability, cell death, and DNA damage). The metals included thorium, cerium, and lanthanum, either individually or combined, with combinations in ratios typically found in monazite sand. Thorium and cerium individually and thorium+cesium+lanthanum did not cause toxicity in human T-lymphocyte leukemia cells during a 48-hour study. However, concentration-related decreasing cell viability was observed with increasing concentrations of thorium+lanthanum mixtures at concentrations ≥0.29 mM thorium + ≥1.17 mM lanthanum at 24 hours or ≥1.56 mM thorium + ≥0.39 mM lanthanum at 48 hours). At 24 hours, concentration-related increased incidence of necrosis was noted; increasing frequency of apoptotic cells was observed at concentrations up to 1.17 mM thorium + 0.29 mM lanthanum, with a decline in apoptosis at higher concentrations. The thorium+lanthanum mixture did not alter the DNA strand break profile. These results indicate that the thorium+lanthanum mixture was cytotoxic.

Some substances can interact with thorium by reducing deposition or increasing excretion of absorbed thorium. Tetracycline reduced the deposition of thorium in rat bone (Taylor et al. 1971). Studies with a

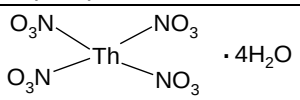
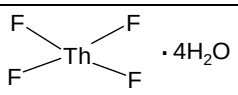
similar actinide element, plutonium, suggest that a thorium-tetracycline complex may be formed, which is excreted rapidly through the kidneys. Chelating agents such as EDTA and diethylenetriaminepentaacetic acid (DTPA) can remove some thorium from the body. Kumar et al. (2012) demonstrated that rats injected with thorium exhibited significantly increased serum levels of the liver enzymes alanine aminotransferase (ALT), AST, and alkaline phosphatase; however, thorium-treated rats that received DTPA treatment exhibited lower levels of these serum liver enzymes, suggestive of a reduction in the severity of thorium-induced liver effects. DTPA also appeared to mediate the effects of thorium on oxidative stress in the liver.

CHAPTER 4. CHEMICAL AND PHYSICAL INFORMATION

4.1 CHEMICAL IDENTITY

Data pertaining to the chemical identity (that is, the common terms or symbols used for the identification of the element) of thorium are listed in Table 4-1.

Table 4-1. Chemical Identity of Thorium and Compounds[a]

Characteristic	Thorium	Thorium dioxide	Thorium nitrate (tetrahydrate)	Thorium fluoride (tetrahydrate)
Synonym(s)[b] and registered trade name(s)	^{232}Th, thorium metal, pyrophoric	Thoria, Thorotrast	No data	Thorium tetrafluoride
Chemical formula	Th	ThO_2	$Th(NO_3)_4 \bullet 4H_2O$	$ThF_4 \bullet 4H$
Chemical structure[c]	Th[d]	O═Th═O		
CAS Registry Number	7440-29-1[c]	1314-20-1[c]	13470-07-0	13709-59-6

Characteristic	Thorium dicarbonate	Thorium chloride[e]	Thorium sulfate[e]
Synonym(s)[b] and registered trade name(s)	Thorium carbonate[f]	Thorium tetrachloride; thorium(IV) chloride; thorium chloride; tetrachlorothorium	Thorium disulphate; sulfuric acid, thorium; thorium sulfate nonahydrate; thorium sulfate 9water; thorium (IV) sulfate 9-water
Chemical formula	$Th(CO_3)_2$	$ThCl_4$	$Th(SO_4)_2 \cdot 9H_2O$
Chemical structure[c]	$O_3C═Th═CO_3$		
CAS Registry Number	19024-62-5	10026-08-1, 54327-76-3	10381-37-0

[a]All information obtained from HSDB 1990, except where noted.
[b]Structures are based on tetra valency of thorium unless otherwise stated.
[c]CAS 1990.
[d]SANSS 1988.
[e]Web_elements 2014a, 2014b.
[f]NIH 2018.

CAS = Chemical Abstracts Service

4.2 PHYSICAL AND CHEMICAL PROPERTIES

The physical and chemical properties of elemental thorium and a few representative water-soluble and insoluble thorium compounds are presented in Table 4-2. Water-soluble thorium compounds include the chloride, fluoride, nitrate, and sulfate salts (Weast 1983). These compounds dissolve fairly readily in water. Soluble thorium compounds, as a class, have greater bioavailability than the insoluble thorium compounds. Water-insoluble thorium compounds include the dioxide, dicarbonate, hydroxide, oxalate, and phosphate salts. Thorium dicarbonate is soluble in concentrated sodium carbonate (Weast 1983). Thorium metal and several of its compounds are commercially available. No general specifications for commercially prepared thorium metal or compounds have been established. Manufacturers prepare thorium products according to contractual specifications (Hedrick 1985).

Thorium is a metallic element of the actinide series. It exists in several isotopic forms. The isotope ^{232}Th is a naturally occurring element that is radioactive. It decays through the emission of a series of alpha and beta particles, gamma radiation, and the formation of daughter products, finally yielding the stable isotope of lead, ^{208}Pb. The decay series of ^{232}Th, together with that of ^{238}U and ^{235}U, are shown in Figure 4-1. It can be seen from Figure 4-1 that the isotopes ^{234}Th and ^{230}Th are produced during the decay of naturally occurring ^{238}U, the isotope ^{228}Th during the decay of ^{232}Th, and the isotopes ^{231}Th and ^{227}Th during the decay of naturally occurring ^{235}U. Of these naturally produced isotopes of thorium, only ^{232}Th, ^{230}Th, and ^{228}Th have long enough half-lives to be environmentally significant. More than 99.99% of natural thorium is ^{232}Th; the rest is ^{230}Th and ^{228}Th.

Including artificially produced isotopes, there are 12 isotopes of thorium with atomic masses ranging from 223 to 234. All are radioactive and decay with the emission of alpha or beta particles and/or gamma radiation (Weast 1983). The percent occurrence and the energies of the major alpha and beta particles emitted by these isotopes are shown in Table 4-3. In general, the alpha particles are more intensely ionizing and less penetrating than the beta particles. The gamma radiation is the most penetrating of the three, but it has the least ionizing intensity. Alpha particles do not penetrate external skin to a sufficient depth to produce biological damage due to the protective effect of the epidermis. However, alpha particles emitted from thorium deposited in the lung are able to penetrate lung tissue and produce adverse biological damage since the protective coating of the lung tissue is very thin. In turn, beta particles are able to penetrate the skin to a sufficient depth to cause biological effects in the skin just below the epidermis. Likewise, they penetrate lung tissues to a greater depth. Gamma rays can generally pass through all tissue and interact with tissue at any depth.

Table 4-2. Physical and Chemical Properties of Thorium and Compounds

Property	Thorium (Th)	Thorium dioxide (ThO_2)	Thorium nitrate, tetrahydrate ($Th(NO_3)_4 \bullet 4H_2O$)	Thorium fluoride, tetrahydrate ($ThF_4 \bullet 4H$)
Molecular weight	232.04[a]	264.04[a]	552.12[a]	380.09[a]
Color	Gray[a]	White[b]	Colorless[a]	Not known
Physical state	Solid[a]	Powdery solid[b]	Crystalline solid[a]	Crystalline solid[a]
Odor	Not known	Not known	Not known	Not known
Melting point, °C	≈1,700[b]	3,220±50[a]	500 (decomposes)	100 ($-H_2O$)[a]
Boiling point, °C	≈4,500[b]	4,400[b]	Not applicable	140–100 ($-2H_2O$)[a]
Autoignition temperature	Not applicable	Not applicable	Not applicable	Not applicable
Solubility:				
Water	Insoluble[a]	Insoluble[b]	Very soluble[b]	0.017 g/100 cc H_2O (25°C)[a]
Organic solvents	Soluble in HCl, H_2SO_4, slightly soluble in HNO_3[a]	Soluble in hot H_2SO_4; insoluble in dilute acid alkali[a]	Very soluble in alcohol; slightly soluble in acetone[a]	Insoluble in HF[a]
Density (g/cm^3)	11.7[a]	9.7[b]	Not known	Not known
Partition coefficients	Not applicable	Not applicable	Not applicable	Not applicable
Vapor pressure at 20 °C	Not applicable	Not applicable	Not applicable	Not applicable
Henry's law constant at 25 °C	Not applicable	Not applicable	Not applicable	Not applicable
Refractive index	Not applicable	2.20 (liquid)[a]	Not applicable	Not applicable
Flashpoint	Not applicable	Not applicable	Not applicable	Not applicable
Flammability limits	Not applicable	Not applicable	Not applicable	Not applicable
Conversion factors	1 pCi=1.2 fg[c] of ^{228}Th 1 pCi=9.1 µg of ^{232}Th 1 pCi=48 fg[c] of ^{230}Th	1 pCi=1.2 fg[c] of ^{228}Th 1 pCi=9.1 µg of ^{232}Th 1 pCi=48 fg[c] of ^{2230}Th	1 pCi=1.2 fg[c] of ^{228}Th 1 pCi=9.1 µg of ^{232}Th 1 pCi=48 fg[c] of ^{230}Th	1 pCi=1.2 fg[c] of ^{228}Th 1 pCi=9.1 µg of ^{232}Th 1 pCi=48 fg[c] of ^{230}Th

Table 4-2. Physical and Chemical Properties of Thorium and Compounds

Property	Thorium carbonate $Th(CO_3)_2$	Thorium chloride[d] $ThCl_4$	Thorium sulfate[d] $Th(SO_4)_2\ 9H_2O$
Molecular weight	352.06[a]	373.849	586.303
Color	Not known	White to gray	White
Physical state	Not known	Crystalline solid	Crystalline solid
Odor	Not known	Not known	Not known
Melting point, °C	Not known	770	400 (dehydrates)
Boiling point, °C	Not known	921	Not known
Autoignition temperature	Not applicable	Not known	Not known
Solubility:			
Water	Insoluble[a]	Soluble	4.2 g/100 g H_2O
Organic solvents	Soluble in HCl, H_2SO_4, slightly soluble in HNO_3[a]	Not known	Not known
Density (g/cm^3)	Not known	4.59	2.8
Partition coefficients	Not applicable	Not known	Not known
Vapor pressure at 20 °C	Not applicable	Not known	Not known
Henry's law constant at 25 °C	Not applicable	Not known	Not known
Refractive index	Not applicable	Not known	Not known
Flashpoint	Not applicable	Not known	Not known
Flammability limits	Not applicable	Not known	Not known
Conversion factors	1 pCi=1.2 fg[c] of ^{228}Th 1 pCi=9.1 µg of ^{232}Th 1 pCi=48 fg[c] of ^{230}Th		

[a]Weast 1983.
[b]Hawley 1981.
[c]1 fg = 10^{-9} µg; 1 pCi = 10^{-12} Ci.
[d]Web_elements 2014a, 2014b.

Figure 4-1. Uranium and Thorium Isotope Decay Series Showing the Sources and Decay Products of the Two Naturally Occurring Isotopes of Thorium

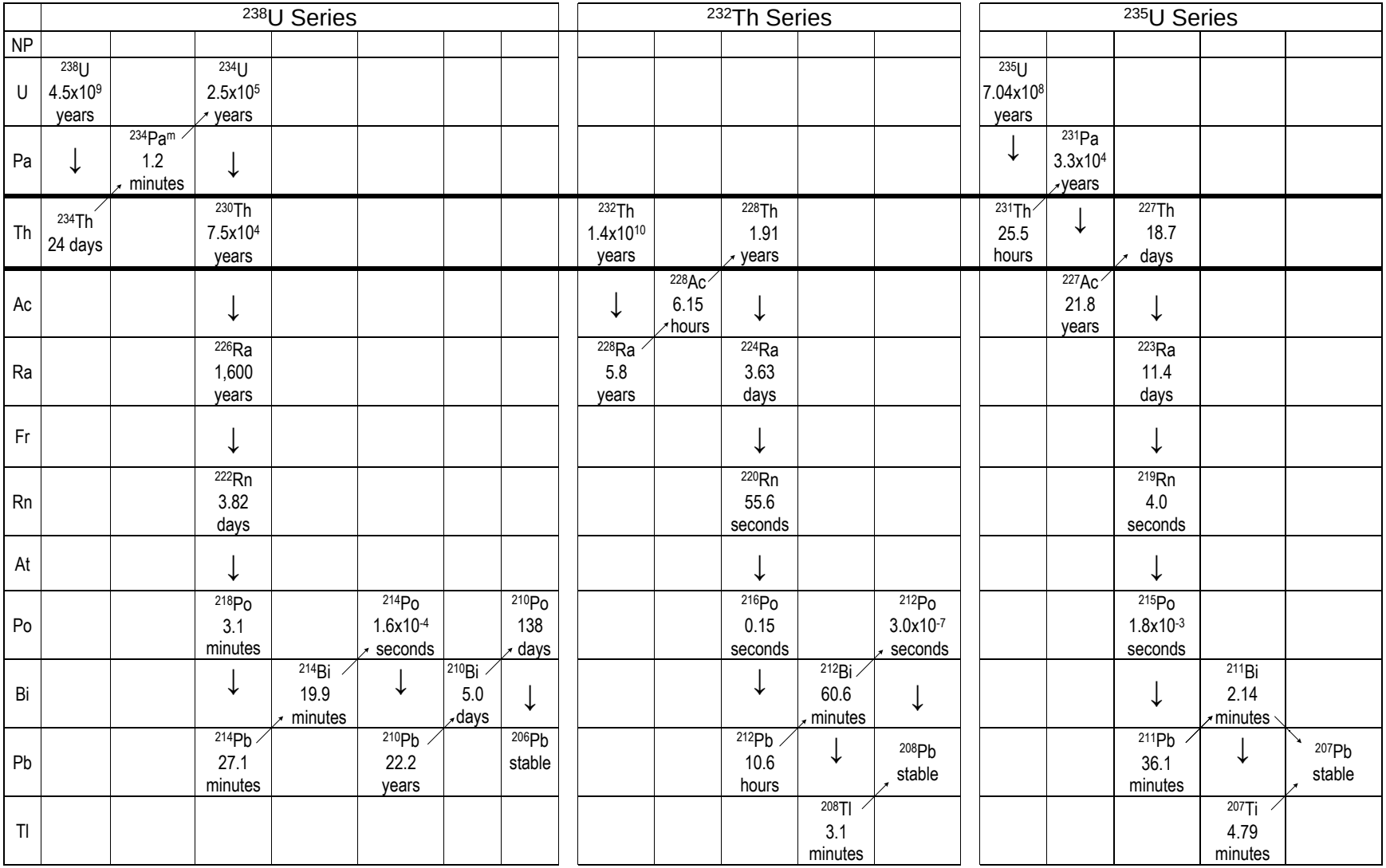


Table 4-3. Percent Occurrence and the Energies of the Major Alpha Particles Emitted by Thorium Isotopes with Atomic Masses Ranging from 223 to 234

Isotope	Percentage in natural thorium	Major alpha energies[a] MEV (abundances)	Half-life
^{223}Th	0	7.286 (26%) 7.298 (66%) 7.323 (13%)	0.60 seconds
^{224}Th	0	7.000 (19%) 7.170 (79%)	1.04 seconds
^{225}Th	0	6.441 (13.5%) 6.478 (39%) 6.501 (12.6%) 6.797 (8.1%)	8.75 minutes
^{226}Th	0	6.234 (22.8%) 6.337 (75.5%)	30.57 minutes
^{227}Th	0	5.757 (20.4%) 5.987 (23.5%) 6.038 (24.2%)	18.70 days
^{228}Th	Very small	5.340 (26.0%) 5.423 (73.4%)	1.91 years
^{229}Th	0	4.815 (9.3%) 4.845 (56.2%) 4.901 (10.2%)	7.93×10^3 years
^{230}Th	Very small	4.621 (23.4%) 4.687 (76.3%)	7.54×10^4 years
^{231}Th	0	Beta-only emitter[b] (0.392 MeV total)	25.52 hours
^{232}Th	>99.99%	3.947 (21.7%) 4.012 (78.2%)	1.40×10^{10} years
^{233}Th	0	Beta-only emitter[b] (1.243 MeV total)	21.8 minutes
^{234}Th	0	Beta-only emitter[b] (0.27e MeV total)	24.10 days

[a]All but a few of these isotopes also emit gamma radiation.
[b]The values in parentheses are the decay energies for the beta particles.

MeV = million electron volt

Source: Weast 1983; NNDC 2018

Alpha particles give up all of their energy in a very short distance and, hence, produce ionization. Beta particles produce less dense ionization, and gamma rays produce less yet. In general, the severity of biological effects of exposures to ionizing radiations is proportional to the density of the ionization produced by their passage through tissue.

Finely divided thorium metal is pyrophoric in air, and thorium ribbon burns in air to give the oxide. The metal also reacts vigorously with hydrogen, nitrogen, the halogens, and sulfur. Thorium compounds are stable in +4 oxidation state (Katzin 1983). Details of thorium chemistry are given by Katzin (1983).

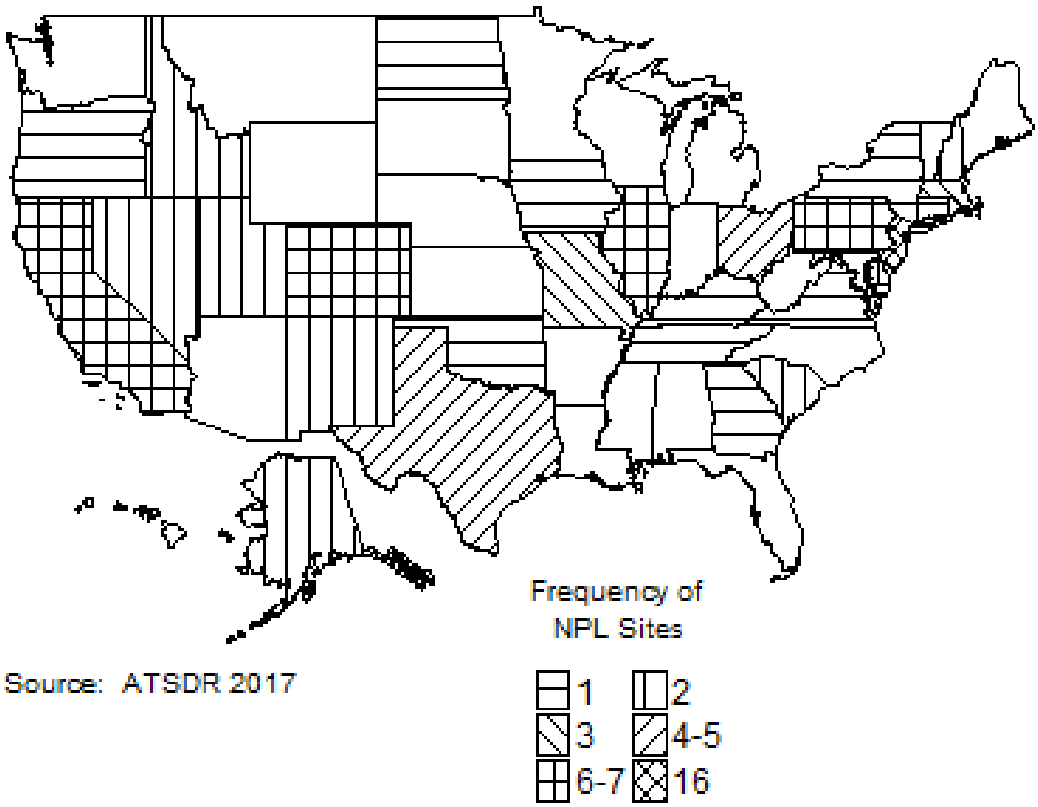
When the solubility of a low-solubility thorium compound is different than expected or reported, the cause could be differences in surface form due to external factors, such as pH or concentrations of two thorium forms at grain boundaries. Vandenborre et al. (2010) scanned the surface of sintered thorium oxide using x-ray photoelectron spectroscopy (XPS) and found it to consist of two forms, 80% ThO_2 and 20% $ThO_x(OH)_y(H_2O)_z$, which have different solubilities. The rate of surface detachment for this oxide was measured, then ^{239}Th was added and the surface attachment rate was determined. The net balance disagreed with the thermodynamic calculation for pure ThO_2.

CHAPTER 5. POTENTIAL FOR HUMAN EXPOSURE

5.1 OVERVIEW

Thorium has been identified in at least 81 of the 1,854 hazardous waste sites that have been proposed for inclusion on the EPA National Priorities List (NPL) (ATSDR 2017). However, the number of sites in which thorium has been evaluated is not known. The number of sites in each state is shown in Figure 5-1. Of these sites, 81 are located within the United States.

Figure 5-1. Number of NPL Sites with Thorium and Thorium Compounds Contamination



- The general population may be exposed to thorium from inhalation of air and ingestion of food and drinking water containing thorium.
- Workers are exposed to higher levels of thorium and other radionuclides in certain thorium industries, as measured in exhaled breath and tissue levels of these chemicals
- Thorium occurs naturally in the environment; thus, background levels occur in air, water, and soil.

- Atmospheric thorium levels above natural background levels occur mainly from mining, milling, and processing operations; phosphate rock processing and phosphate fertilizer production; and coal-fired utilities and industrial boilers.

- Concentrations of thorium in air, food, and/or drinking water are normally very low and thorium-containing substances are not generally readily absorbed by the body.

- Wet and dry deposition are expected to be mechanisms for removal of atmospheric thorium. The rate of deposition will depend on the meteorological conditions, the particle size and density, and the chemical form of thorium particles.

- In water, thorium will be present in suspended matters and sediment and the concentration of soluble thorium will be low.

- Thorium will remain strongly sorbed to soil and its mobility will be very slow.

- Thorium in soil will not bioconcentrate in plants.

Thorium is ubiquitous in our environment. Release of thorium to the atmosphere can occur both from natural and anthropogenic sources, and emissions from the latter sources can produce locally elevated atmospheric levels of thorium over the background. Windblown terrestrial dust and volcanic eruptions are two important natural sources of thorium in the air (Fruchter et al. 1980; Kuroda et al. 1987). Uranium and thorium mining, milling and processing, tin processing, phosphate rock processing and phosphate fertilizer production, and coal fired utilities and industrial boilers are the primary anthropogenic sources of thorium in the atmosphere (Hu and Kandaiya 1985; McNabb et al. 1979; Nakoaka et al. 1984; Sill 1977). The major industrial releases of thorium to surface waters are effluent discharges from uranium and thorium mining, milling and processing, tin processing, phosphate rock processing, and phosphate fertilizer production facilities (Hart et al. 1986; McKee et al. 1987; Moffett and Tellier 1978; Platford and Joshi 1988). The primary sources of thorium at the Superfund sites are perhaps from the processing and extraction of thorium, uranium, and radium from ores and concentrates (EPA 1988a).

Data regarding the fate and transport of thorium in the air are limited. Wet and dry deposition are expected to be mechanisms for removal of atmospheric thorium. The rate of deposition will depend on the meteorological conditions, the particle size and density, and the chemical form of thorium particles. Although atmospheric residence times for thorium and compounds were not located, judging from residence times of other metals (e.g., lead) and their compounds, they are likely to be a few days. Thorium particles with small aerodynamic diameters (<10 micron aerodynamic diameter) will travel long distances from their sources of emission. In water, thorium will be present in suspended matters and

sediment and the concentration of soluble thorium will be low (Platford and Joshi 1987). Sediment resuspension and mixing may control the transport of particle-sorbed thorium in water. The concentration of dissolved thorium in some waters may increase due to formation of soluble complexes with carbonate, humic materials, or other ligands in the water (LaFlamme and Murray 1987). Thorium has been found to show significant bioconcentration in lower trophic animals in water, but the bioconcentration factors decrease as the trophic level of aquatic animals increases (Fisher et al. 1987; Poston 1982). The fate and mobility of thorium in soil will be governed by the same principles as in water. In most cases, thorium will remain strongly sorbed to soil and its mobility will be very slow (Torstenfelt 1986). However, leaching into groundwater is possible in some soils with low sorption capacity and the ability to form soluble complexes. The plant/soil transfer ratio for thorium is <0.01 (Garten 1978), indicating that it will not bioconcentrate in plants from soil. However, plants grown at the edge of impoundments of uranium tailings containing elevated levels of thorium had a plant/soil concentration ratio of about 3 (Ibrahim and Whicker 1988).

The atmospheric mass concentration of thorium ranged from 0.2 to 1.0 ng/m^3, with a mean value of 0.3 ng/m^3 in air samples collected from 250 sites in the United States (Lambert and Wilshire 1979). In another study, the mean activity concentrations of ^{228}Th, ^{230}Th, and ^{232}Th in New York City air were 36, 36, and 37 aCi/m^3 (aCi=10^{-18} Ci), respectively (Wrenn et al. 1981). The average population-weighted concentrations of ^{232}Th and ^{230}Th in United States community water supplies derived both from surface and groundwater were <0.01 and <0.04 pCi/L, respectively (Cothern 1987; Cothern et al. 1986). The maximum concentration of ^{232}Th in several fruits, vegetables, and other type of foods from New York City was reported to be <0.01 pCi/g (Fisenne et al. 1987). The daily intakes of ^{230}Th and ^{232}Th for residents of New York City were estimated to be 0.17 and 0.11 pCi, respectively. Significant exposure to thorium requires special exposure scenarios (Fisenne et al. 1987). People who consume foods grown in high background areas, reside in homes with high thorium background levels, or live near radioactive waste disposal sites may be exposed to higher than normal background levels of thorium. Workers in uranium, thorium, tin, and phosphate mining, milling, and processing industries, and gas mantle manufacture may also be exposed to higher than normal background levels of thorium (Bulman 1976; Hannibal 1982; Hu et al. 1984; Kotrappa et al. 1976; Metzger et al. 1980).

5.2 PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL

5.2.1 Production

Table 5-1 summarizes information on U.S. companies that reported the manufacture or use of thorium dioxide in 2016 (TRI16 2017). Toxics Release Inventory (TRI) data should be used with caution since only certain types of industrial facilities are required to report. This is not an exhaustive list.

Table 5-1. Facilities that Produce, Process, or Use Thorium Dioxide

State[a]	Number of facilities	Minimum amount on site in pounds[b]	Maximum amount on site in pounds[b]	Activities and uses[c]
TX	2	10,000	99,999	10, 12

[a]Post office state abbreviations used.
[b]Amounts on site reported by facilities in each state.
[c]Activities/Uses:

1. Produce
2. Import
3. Used Processing
4. Sale/Distribution
5. Byproduct
6. Reactant
7. Formulation Component
8. Article Component
9. Repackaging
10. Chemical Processing Aid
11. Manufacture Aid
12. Ancillary
13. Manufacture Impurity
14. Process Impurity

Source: TRI16 2017 (Data are from 2016)

The principal source of thorium is monazite (phosphate of rare earth metals, usually with thorium), a mineral produced as a byproduct of mineral sands mined for titanium and zirconium. Thorium compounds are extracted from monazite by acid and alkali treatment processes (Hedrick 1985). Associated Minerals, a subsidiary of the Australian-owned firm Associated Minerals Consolidated Ltd., was the only commercial operation in the United States to produce purified monazite in 1987. This company produced monazite as a byproduct of mineral sands mined for titanium and zirconium minerals at Green Cove Springs, Florida. The monazite produced in the United States was exported. Thorium products used domestically were obtained from imported material, existing company stocks, and thorium nitrate previously released from the National Defense Stockpile (Hedrick 1987). In 1984, the mine production capacity for thorium in the United States was 20 metric tons of thorium oxide equivalent (Hedrick 1985). Actual mine production data have not been released over the years to avoid disclosure of proprietary information. Nevertheless, the domestic mine production volume of monazite or other thorium ore is expected to be approximately the same as the U.S. export volume. The principal processors of thorium-containing ores in the United States during 1987 were W.R Grace & Co. in

Chattanooga, Tennessee, and Rhone-Poulenc Inc. in Freeport, Texas (Hedrick 1987). United States companies that had thorium processing and fabricating capacities in 1987 are listed in Table 5-2.

Table 5-2. United States Companies with Thorium Processing and Fabricating Capacity

Company	Plant location	Operations and products
Atomergic Chemetals Corporation	Plainview, New York	Produces oxide, flouride, metal
Bettis Atomic Power Laboratory	West Mifflin, Pennsylvania	Nuclear fuels; Government research and development
Cerac Inc.	Milwaukee, Wisconsin	Produces ceramics
Ceradyne Inc.	Santa Ana, California	Produces advanced technical ceramics
Chicago Magnesium Castings Co.	Blue Island, Illinois	Magnesium-thorium alloys
Coleman Co., Inc.	Wichita, Kansas	Produces thoriated mantles
GA Technologies, Inc.	San Diego, California	Nuclear fuels
W.R. Grace & Co., Davison Chemical Division	Chattanooga, Tennessee	Produces thorium from compounds in monazite
GTE Sylvania	Towanda, Pennsylvania	Produces thoriated welding rods
Hitchcock Industries Inc.	South Bloomington, Minnesota	Magnesium-thorium alloys
Philips Elmet	Lewiston, Maine	Produces thoriated welding rods
Rhône-Poulenc, Inc.	Freeport, Texas	Produces thorium nitrate from an intermediate compound of monazite
Spectrulite Consortium, Inc.	Madison, Illinois	Magnesium-thorium alloys
Teledyne Cast Products	Pomona, California	Magnesium-thorium alloys
Teledyne Wah Chang	Huntsville, Alabama	Produces thoriated welding rods
Union Carbide Corporation, Nuclear Division	Oak Ridge, Tennessee	Nuclear fuels; test quantities
Wellman Dynamics Corporation	Creston, Iowa	Magnesium-thorium alloys
Westinghouse Materials Co. of Ohio[b]	Cincinnati, Ohio	Produces compounds and metals; manages Department of Energy thorium stocks

[a]Manager of U.S. Department of Energy stocks; formerly NLO, Inc., prior to January 1, 1986.

Source: Hedrick 1987

5.2.2 Import/Export

Imports of thorium into the United States in metric tons of thorium oxide equivalent were 45.8 in 1983, 45.4 in 1984, 69.3 in 1985, 19.7 in 1986, and 30.7 in 1987. Additionally, concentrated monazite containing 350–550 tons of ThO_2 has been imported annually (Hedrick 1987). Imports of thorium by the

United States may decrease as a result of increased costs of processing thorium. These increased costs are primarily due to increasing concerns about the radiological risks of handling, storing, and disposing of thorium, thereby encouraging the search for nonradioactive substitutes (Hedrick 1987). Exports of thorium metal, waste, and scrap from the United States in metric tons of thorium oxide equivalent were 1.1 in 1983, 1.0 in 1984, 1.6 in 1985, 17.0 in 1986, and 20.4 in 1987 (Hedrick 1987).

5.2.3 Use

Thorium can be used as fuel in the generation of nuclear energy. However, there was only one plant in the United States in 1987 that was using thorium for the production of energy (Hedrick 1987). In 1983, 3 metric tons of thorium oxide equivalent were used for energy uses in the United States (Hedrick 1985). Nonenergy uses accounted for almost all of the thorium used in the United States during 1987. The 1987 use pattern for thorium was as follows: refractory applications (57%); lamp mantles (18%); aerospace alloys (15%); welding electrodes (5%); nuclear weapon production; and other applications including ceramics and special use lighting (5%). Specific applications include production of investment molds for casting high-temperature metals and alloys, crucibles, and alloys of special shapes for use in high-temperature vacuum or oxidizing furnaces. Other special applications include production of core-retention beds used in nuclear reactors to contain and possibly diffuse heat generated by accidental core meltdown; magnesium-thorium alloys for strategic aircraft such as military jet fighters and bombers; mantles for incandescent lanterns such as those used on camping trips; thoriated tungsten electrodes used to join stainless steels and other alloys that require controlled weld applications; special lighting such as airport runway lighting; computer memory components; photoconductive film; and target material for x-rays (Hedrick 1985). Natural thorium is also used in ceramic tableware glaze and in flints for lighters (UNSCEAR 1977). Domestic nonenergy thorium consumption was estimated to be 39.4 metric tons of thorium oxide equivalent in 1987, a decrease of 33 metric tons from 1986 usage. The drop in consumption was primarily the result of reduced demand for thorium oxide in high-temperature refractory molds, because suitable substitutes had been developed (Hedrick 1987).

Trastuzumab is a humanized monoclonal antibody approved by the Food and Drug Administration for treating metastatic breast cancer in individuals who overexpress the human epidermal growth factor receptor 2 (HER2) oncogene. Heyerdahl et al. (2012) evaluated the relative efficacy of subcutaneously-injected single dose (1 MBq/kg; 27.02 µCi/kg) versus fractionated dose (4x0.25 MBq/kg; 4x6.76 µCi/kg) therapy with ^{227}Th-DOTA-pbenzyl-trastuzumab (^{227}Th-trastuzumab) for cancer treatment in nude mice. Fractionating the dose of ^{227}Th-trastuzumab reduced toxicity while maintaining therapeutic value,

indicating that fractionation might allow for increased treatment doses aimed at improving cancer therapy. Heyerdahl et al. (2011) also found that ^{227}Th-trastuzumab at clinically relevant concentrations inhibited cell growth, decreased cell survival, and increased apoptosis in human breast cancer cell lines (BT-474 and SKBR-3) as well as in an ovarian cancer cell line (SKOV-3) in a dose-dependent manner.

^{227}Th has been proposed for the palliative treatment of skeletal pain associated with cancers metastasized from other organs so as to improve the quality of life. ^{227}Th deposits on bone surfaces based on its chemical properties independent of its radiological properties and radioactive progeny. Deposition sites receive 28 MeV of localized alpha energy (within micrometers of the deposition sites) over a short period of weeks resulting from its 18.7-day half-life and rapidly-approached secular equilibrium with its alpha-emitting progeny. Ogawa and Washiyama (2012) suggested that bonding ^{227}Th to ethylenediaminetetra-methylenephosphonic acid (EDTPM) should enhance the efficacy of pain treatment since the complex increases the skeletal deposition and retention of thorium and its progeny. It also speeds excretion from soft tissue and blood, thus reducing radiation dose to those tissues. Similar ^{227}Th complexes involve bonding with diethylenetriaminepentamethylenephosphonic acid (DTPMP) and 1,4,7,10-tetraazacyclo-dodecane-1,4,7,10-tetramethylenephosphonic acid (DOTMP).

In addition to DTPA being tested as a thorium chelator, it has been studied as a radiotherapy agent. Le Du et al. (2012) identified that DTPA could be labeled *in vitro* with ^{226}Th to produce a complex with thorium. When injected, the thorium would interact strongly with human serum transferrin such that the complex might be used as a delivery system in targeted alpha therapy.

In February 1976, the European Union made it illegal to commercially export African elephant raw tusk ivory. Schmied et al. (2012) determined that the ratio of ^{228}Th/^{232}Th in the ivory can be used in conjunction with ^{14}C and ^{90}Sr dating to help confirm the time of death. One method involves removing ~10 g of ivory from the base (the area of newest growth) and analyzing the ashed, extracted, and electrodeposited sample by alpha spectroscopy. The accuracy and relevance of this approach was validated using standard reference materials.

5.2.4 Disposal

Disposal of radioactive wastes is a serious environmental problem for which there is, as yet, no completely satisfactory solution. Intensive research is being conducted by both government and industry for the disposal of this type of waste. Small amounts of low-level wastes containing radioisotopes can be

diluted with an inert material sufficiently to reduce its activity to an acceptable level for further storage or disposal. At one nuclear waste disposal site, high-level reactor wastes are stored in concrete tanks lined with steel, which are buried under a foot of concrete and 5–6 feet of soil. Use of compressed alumina (corundum) containers has been recommended, since this material remains impervious to water indefinitely. The Department of Energy has recommended disposal in deep geologic formations. Disposal in salt formations is being considered since they are self-sealing and free from water (Hawley 1981). The Department of Defense Authorization Act of 1987 (Public Law 99-661) authorized 4,536 kg (10,000 pounds) of thorium nitrate for disposal in fiscal year 1987. Further information regarding the amount of thorium disposed of in the United States was not located. Regulations established by the EPA regarding release limits that apply to the storage and disposal of spent nuclear fuel, high-level radioactive wastes, and transuranic radioactive wastes can be found in 40 CFR 191 and 40 CFR 192.

Akkaya (2013) synthesized a polymerized derivative of pumice (poly-hydroxyethylmethacrylate-pumice or P(HEMA-Pum)) and evaluated its effectiveness in adsorbing Th^{4+} ions from solution in order to assess its potential for decontaminating ground and surface water. A total of 0.1 g of adsorbent was agitated for 24 hours in 10 mL of thorium nitrate solution of various concentrations and pH. The adsorption process was endothermic, increased system entropy, was spontaneous, and peaked at pH 3.0. Results demonstrated that P(HEMA)Pum has the potential to adsorb up to 0.21 μmol Th/g medium from a liquid solution. Repetitive testing and cleaning demonstrated the medium to be reusable at least 5 times.

Chandramouleeswaran et al. (2011) tested two boroaluminosilicate glasses with surface area 102 cm^2/g for their ability to adsorb thorium from a solution containing thorium nitrate with or without uranium. Such glasses are used to vitrify and immobilize high level liquid radioactive waste. The glass with the lower B_2O_3:Na_2O ratio (0.23 versus 9.8) was more effective at removing thorium. Its thorium uptake peaked at pH 7.5–8, reached saturation at 12 mg Th/g glass, and was selective against uranium.

Li et al. (2011) evaluated 15 plant species for ability to bioaccumulate thorium and other metals from a uranium mill tailings repository in South China. *Phragmites australis* was found to have the greatest capability for removing uranium, thorium, barium, and lead, with respective “phytoremediation factors” of 17, 9, 10, and 10. However, none of the species were classified as hyperaccumulators for these metals.

5.3 RELEASES TO THE ENVIRONMENT

The Toxics Release Inventory (TRI) data should be used with caution because only certain types of facilities are required to report (EPA 2005). This is not an exhaustive list. Manufacturing and processing facilities are required to report information to the TRI only if they employ ≥10 full-time employees; if their facility is included in Standard Industrial Classification (SIC) Codes 10 (except 1011, 1081, and 1094), 12 (except 1241), 20–39, 4911 (limited to facilities that combust coal and/or oil for the purpose of generating electricity for distribution in commerce), 4931 (limited to facilities that combust coal and/or oil for the purpose of generating electricity for distribution in commerce), 4939 (limited to facilities that combust coal and/or oil for the purpose of generating electricity for distribution in commerce), 4953 (limited to facilities regulated under RCRA Subtitle C, 42 U.S.C. section 6921 et seq.), 5169, 5171, and 7389 (limited S.C. section 6921 et seq.), 5169, 5171, and 7389 (limited to facilities primarily engaged in solvents recovery services on a contract or fee basis**); and if their facility produces, imports, or processes ≥25,000 pounds of any TRI chemical or otherwise uses >10,000 pounds of a TRI chemical in a calendar year (EPA 2005).**

5.3.1 Air

The data in Table 5-3 are the reported releases of thorium to the atmosphere from the two domestic manufacturing and processing facilities in 2016 required to report to the TRI (TRI16 2017; see Table 5-3).

Releases of thorium to the atmosphere can occur from both natural and anthropogenic sources. The release of thorium in volcanic ash containing as much as 0.116 pCi/g (1.06 μg/g) of ^{232}Th was reported by Fruchter et al. (1980). Increased concentrations of thorium in rain water following a volcanic eruption have also been observed (Kuroda et al. 1987). Since the average level of thorium in soil is about 6 μg/g of thorium (Harmsen and De Haan 1980), windblown terrestrial dust is also a likely natural source of thorium in the atmosphere. Since coal contains 0.5–7.3 μg/g thorium (Nakaoka et al. 1984), burning of coal for power generation produces thorium in the fly ash and is a man-made source of this chemical in the atmosphere. The amount of thorium in the fly ash from coal-burning power plants depends on the nature of coal burned and the emission control devices of the plant, but concentrations usually range from 4.5 to 37 μg/g (Abel et al. 1984; Coles et al. 1979; Tadmor 1986; Weissman et al. 1983). However, the concentrations of all natural radioactive isotopes in (including thorium isotopes) the stack effluents from coal-fired power plants are usually much lower than those from the natural background concentrations of

these radionuclides (Nakaoka et al. 1984; Roeck et al. 1987). Similarly, fly ash from oil- and peat-fired power plants can also be atmospheric sources of thorium (Mustonen and Jantunen 1985).

Table 5-3. Releases to the Environment from Facilities that Produce, Process, or Use Thorium Dioxide[a]

		Reported amounts released in pounds per year[b]							
							Total release		
State[c]	RF[d]	Air[e]	Water[f]	UI[g]	Land[h]	Other[i]	On-site[j]	Off-site[k]	On- and off-site
TX	2	0	0	0	0	0	0	0	0

[a]The TRI data should be used with caution since only certain types of facilities are required to report. This is not an exhaustive list. Data are rounded to nearest whole number.
[b]Data in TRI are maximum amounts released by each facility.
[c]Post office state abbreviations are used.
[d]Number of reporting facilities.
[e]The sum of fugitive and point source releases are included in releases to air by a given facility.
[f]Surface water discharges, waste water treatment-(metals only), and publicly owned treatment works (POTWs) (metal and metal compounds).
[g]Class I wells, Class II-V wells, and underground injection.
[h]Resource Conservation and Recovery Act (RCRA) subtitle C landfills; other onsite landfills, land treatment, surface impoundments, other land disposal, other landfills.
[i]Storage only, solidification/stabilization (metals only), other off-site management, transfers to waste broker for disposal, unknown.
[j]The sum of all releases of the chemical to air, land, water, and underground injection wells.
[k]Total amount of chemical transferred off-site, including to POTWs.

RF = reporting facilities; UI = underground injection

Source: TRI16 2017 (Data are from 2016)

^{230}Th has been detected in air dust from uranium ore processing and mill tailings. These concentrations of ^{230}Th (a decay product of ^{238}U) may be particularly high in ore crushing areas (Sill 1977). Similarly, processing of thorium ores is expected to be an atmospheric source of thorium. Elevated levels of thoron (thoron or ^{220}Rn originating from ^{232}Th) daughters, such as bismuth-212 (^{212}Bi) and polonium-216 (^{216}Po), were present at a former thorium and rare-earth extraction facility waste site, although the concentrations of thorium in air particulate samples were not significant (Jensen et al. 1984). Since phosphate ores usually contain ^{230}Th, phosphate-ore processing plants are also atmospheric sources of ^{230}Th (McNabb et al. 1979; Metzger et al. 1980). The byproducts obtained during processing of tin ores usually contain ^{232}Th. Therefore, tin processing industries are sources of atmospheric ^{232}Th emissions (Hu and Kandaiya 1985; Hu et al. 1981, 1984).

EPA (1984) estimated that about 0.2 Ci of ^{230}Th is annually emitted into the air from uranium mill facilities, coal-fired utilities and industrial boilers, phosphate rock processing and wet-process fertilizer

production facilities, and other mineral extraction and processing facilities. About 0.084 Ci of ^{234}Th from uranium fuel cycle facilities and 0.0003 Ci of ^{232}Th from underground uranium mines are emitted into the atmosphere annually (EPA 1984).

5.3.2 Water

The data in Table 5-3 are the reported releases of thorium to water from the two domestic manufacturing and processing facilities in 2016 required to report to the TRI (TRI16 2017; see Table 5-3).

The acidic leaching of uranium tailing piles in certain areas is a source of ^{230}Th in surface water and groundwater (Moffett and Tellier 1978; Platford and Joshi 1988). The contamination of surface waters and benthic organisms by ^{230}Th (a decay product of ^{238}U) from uranium mining and milling operations and from radium and uranium recovery plants has been reported (Hart et al. 1986; McKee et al. 1987). Similarly, effluents from thorium mining, milling, and recovery plants are expected to be sources of thorium in water. Other industrial processes that are expected to be sources of thorium contamination into water are phosphorus and phosphate fertilizer production and processing of some tin ores. Since both phosphate rocks and the tailings from tin ore processing contain thorium mainly as ^{230}Th and ^{232}Th, respectively, discharges of processed or unprocessed effluents and leaching from tailing piles can be sources of thorium in water. Leaching from landfill sites containing uranium and thorium may result in the contamination of surface water and groundwater with thorium (Cottrell et al. 1981).

5.3.3 Soil

The data in Table 5-3 are the reported releases of thorium to the soil from the two domestic manufacturing and processing facilities in 2016 required to report to the TRI (TRI16 2017; see Table 5-3).

Thorium occurs naturally in the earth's crust at an average lithospheric concentration of 8–12 μg/g (ppm). The typical concentration range of naturally-occurring thorium in soil is 2–12 μg/g, with an average value of 6 μg/g (Harmsen and De Haan 1980). Man-made sources of thorium contamination in soil are mining, milling, and processing operations and uranium, thorium, tin, and phosphate fertilizer production (Chong et al. 1985; Hu and Kandaiya 1985; Joshi 1987; McNabb et al. 1979; Sill 1977). The two principal processes that can contaminate soil from these industries are precipitation of airborne dusts and land disposal of uranium or thorium-containing wastes.

According to EPA (1988a), the primary sources of thorium at the Superfund sites are processing and extraction of thorium, uranium and radium from ores or ore-concentrates. The following radioactive waste Superfund sites were found to contain one or more isotopes of thorium (VIEW 1989): Shpack and adjacent landfills, Norton, Massachusetts; Maywood Chemical Co., Sears Property, Maywood, New Jersey; W.R. Grace and Co., Wayne, New Jersey; West Chicago Sewage Treatment Plant, West Chicago, Illinois; Reed-Keppler Park, West Chicago, Illinois; Kerr-McGee (Residential Areas), West Chicago, Illinois; Kress Creek and the West Branch of the DuPage River, West Chicago, Illinois; United Nuclear Corporation, Church Rock, New Mexico; Homestake Mining Co., Milan, New Mexico; Kearsarge Metallurgical Corporation, Conway, New Hampshire; Naval Air Engineering Center, Lakehurst, New Jersey: Teledyne Wah Chang, Albany, Oregon; Woodland Route 72 Dump, Woodland Township, New Jersey; Weldon Spring Quarry, St. Charles City, Missouri; Monticello Radioactivity-Contaminated Properties, Monticello, Utah; and Uravan Uranium Project, Montrose City, Colorado. Disposal of incandescent lights and lanterns containing ^{232}Th will be an additional source of thorium at waste disposal sites.

5.4 ENVIRONMENTAL FATE

Thorium occurs in nature in four isotopic forms, ^{228}Th, ^{230}Th, ^{232}Th, and ^{234}Th. Of these, ^{228}Th is the decay product of naturally-occurring ^{232}Th, and both ^{234}Th and ^{230}Th are decay products of natural ^{238}U. To assess the environmental fate of thorium, these isotopes of thorium, with the exception of ^{234}Th, which has a short half-life (24.1 days), should be considered.

5.4.1 Transport and Partitioning

Air. Data regarding the transport and partitioning of thorium in the atmosphere are limited. Release of atmospheric thorium from mining, milling, and processing operations of thorium will mainly consist of ^{232}Th particulate matter. Emissions from mining, milling, and processing of uranium and the airblown dust from uranium tailing piles will contribute to the presence of ^{230}Th as an atmospheric particulate aerosol. The aerodynamic diameters of both ^{230}Th and ^{232}Th in atmospheric aerosols are >2.5 μm. The aerodynamic diameter of ^{228}Th, however, is <1.6 pm (Hirose and Sugimura 1987) and ^{228}Th may therefore travel longer distances than both ^{230}Th and ^{232}Th. Like other particulate matter in the atmosphere, thorium will be transported from the atmosphere to soil and water by wet and dry deposition.

The deposition of thorium through snow and rain water has been observed (Jiang and Kuroda 1987). Dry deposition of thorium through impaction and gravitational settling has also been observed. The

atmospheric residence time of thorium depends on the aerodynamic diameter of the particles. Those with small diameters are likely to be transported longer distances. For example, high $^{230}Th/^{232}Th$ activity ratios observed in surface air of the Western North Pacific Ocean are thought to be due to long distance transport of small particles of ^{228}Th (Hirose and Sugimura 1987).

The dry deposition velocity of ^{212}Pb, a thoron (thoron or ^{220}Rn itself originating from ^{232}Th) decay product has been reported to be in the range 0.03–0.6 cm/set (Bigu 1985; Rangarajan et al. 1986). These low deposition velocities indicate that the thoron daughter, stable lead, may have a long residence time in the atmosphere with respect to dry deposition.

Thorium discharged as ThO_2 into surface waters from mining, milling, and processing will be present as suspended particles or sediments in water because of the low solubility of thorium in water (Platford and Joshi 1986). Other soluble thorium ions will hydrolyze at pH >5, forming $Th(OH)_4$ precipitate or hydroxy complexes; for example, $Th(OH)_{2+2}$, $Th_2(OH)_2^{+6}$, and $Th_3(OH)_5^{+7}$ (Bodek et al. 1988; Hunter et al. 1988; Milic and Suranji 1982). The hydroxy complexes will be adsorbed by particulate matter in water, e.g., goethite (alpha-FeOOH), with the result that most of the thorium will be present in suspended matter or sediment, and the concentration of soluble thorium in water will be low (Hunter et al. 1988; Sheppard 1980). The adsorption of thorium to suspended particles or sediment in water depends on the particle size, and the adsorption and subsequent removal from aqueous phase is expected to be higher for finer grained particles (Carpenter et al. 1987). The residence times for thorium with respect to removal by adsorption onto particles were reported to be shorter in nearshore waters than in deeper waters, probably because of the availability of more adsorbents (particulate matter). The residence time may vary from 1 to 70 days (Cochran 1984). The scavenging rate varied seasonally and was inversely related to the sediment resuspension rate. Therefore, the removal rate was found to be dependent on both sediment resuspension rate and the concentration of iron and manganese compounds (good adsorption properties) in water (Cochran 1984).

Water. The transport of thorium in water is principally controlled by the particle flux in the water, i.e., most of the thorium will be carried in the particle-sorbed state (Santschi 1984), and sediment resuspension and mixing may control the transport of particle-sorbed thorium in water (Santschi et al. 1983). Although the concentration of dissolved thorium is low in most waters, its value could be higher in some waters. For example, the concentration of dissolved thorium in an alkaline lake was up to 4.9 dpm/L (2.21 pCi/L) compared to about $1.3x10^{-5}$ dpm/L ($0.59x10^{-5}$ pCi/L) in sea water (LaFlanune and Murray 1987). The dissolved thorium concentration can increase by the formation of soluble complexes. The anions or

ligands likely to form complexes with thorium in natural water are CO_3^{-2} and humic materials, although some of the thorium-citrate complexes may be stable at pH >5 (LaFlamme and Murray 1987; Miekeley and Kuchler 1987; Platford and Joshi 1986; Raymond et al. 1987; Simpson et al. 1984).

The transport of thorium from water to aquatic species has been reported. The bioconcentration factor (concentration in dry organism/concentration in water) (dry weight basis) in algae may be as high as $975x10^4$, but the maximum value in zooplankton (calanoids and cyclopoids) may be $2x10^4$ (Fisher et al. 1987). Fisher et al. (1987) suggested that sinking plankton and their debris may account for the sedimentation of most of the thorium from oceanic surface waters. The highest observed thorium bioconcentration factor in the whole body of rainbow trout (*Salmo gairdneri*) was 465 (Poston 1982). The succeedingly lower bioconcentration factors in higher trophic animals indicate that thorium will not biomagnify in the aquatic environment. It was also noted that the majority of thorium body burden in fish is in the gastrointestinal tract (Poston 1982).

Sediment and Soil. The mobility of thorium in soil will be governed by the same principles as in water. In most soil, thorium will remain strongly sorbed onto soil and the mobility will be very slow (Torstenfelt 1986). The presence of ions or ligands (CO_3^{-2}, humic matter) that can form soluble complexes with thorium should increase its mobility in soil. The contamination of groundwater through the transport of thorium from soil to groundwater will not occur in most soils, except soils that have low sorption characteristics and have the capability to form soluble complexes. Chelating agents produced by certain microorganisms (*Pseudomonas aeruginosa*) present in soils may enhance the dissolution of thorium in soils (Premuzic et al. 1985).

The transport of atmospherically deposited thorium from soil to plants is low. The soil to plant transfer coefficients (concentration in dry plant to concentration in dry soil) were estimated to be 10^{-4}–$7x10^{-3}$ by Garten (1978) and $0.6x10^{-4}$ for ^{232}Th by Linsalata et al. (1989). The root systems of grasses and weeds adsorb thorium from the soil but the transport of thorium from the root to the above-ground parts of the plant is not very extensive, as indicated by l00-fold higher concentrations of all three isotopes (^{228}Th, ^{230}Th, and ^{232}Th) in the root than in the above-ground parts of the plant (Taskayev et al. 1986). However, Ibrahim and Whicker (1988) showed that under certain conditions, vegetation can accumulate ^{230}Th, as indicated by the plant/soil concentration ratio (dry weight) of 1.9–2.9 for mixed grasses, mixed forbs, and sagebrush plants grown at the edge of uranium tailings impoundments. Vegetation concentration ratios for ^{232}Th (a concentration ratio of about 0.1) and ^{228}Th (a maximum concentration ratio of about 0.4) were lower than that of ^{230}Th. It was postulated that the acidity and wet conditions at this site enhanced the

solubility of thorium in soil and that the difference in solubility was responsible for the difference in plant uptake of the three thorium isotopes (Ibrahim and Whicker 1988). However, it is possible that the observed difference in the uptake of the three isotopes by plants is due to a difference in the chemical compounds formed by the isotopes, making one more leachable than the other (therefore more available for uptake) under the prevailing local conditions.

More recent studies provide support to previous findings that thorium in soil can adhere to plant roots (Shtangeeva 2010), while relatively little transfers to the upper parts and is slowly taken up by plants (Chen et al. 2005; Morton et al. 2002; Pulhani et al. 2005; Rayno 1989; Shtangeeva 2010; Shtangeeva et al. 2005). Baeza and Guillen (2006) reported that mushrooms remove thorium from soil, with uptake being an order of magnitude higher for Munõveros than Bazagona mushrooms. For both varieties combined, the soil-to-mushroom transfer factors (the ratio of meat to gross soil concentration) ranged from 0.030 to 0.62, which is comparable to factors for uranium, strontium-90 (^{90}Sr), americium-241 (^{241}Am), and plutonium-239+240 ($^{239+240}$Pu). The available transfer factor (considering only that portion of the thorium in soil that is available for transfer to plants) was 2 orders of magnitude higher and ranged from 3 to 371 (which is comparable to factors for cesium-137 [^{137}Cs]).

The presence of EDTA in soil (e.g., at a mill or waste disposal site) can increase the rate at which a thorium plume moves through the earth. Abdel-Fattah et al. (2013) passed mixtures of thorium (0.4–4 mM) and EDTA (4–40 mM) with Th:EDTA ratios of 1:1 to 10:1 through sand at rates of 20–100 m/year to simulate conditions at the U.K. low level waste repository at Drigg. May et al. (2012) studied the migration of thorium-EDTA mixtures through sand-packed columns. Thorium migrated very slowly when EDTA was absent. Migration rate changed as functions of thorium and EDTA concentration, as well as with thorium species. The relative abundances of 10 identified thorium species depended on the thorium:EDTA concentration ratio. At low thorium concentrations, the thorium-EDTA complex was considered to interact with sand surfaces, and transport depended on groundwater flow rate. But at higher thorium concentrations, plume flow was higher than expected. This might be due to the formation of a thorium colloid associated with natural minerals and not necessarily with EDTA, as has been reported for plutonium colloids.

Other Media. Ishikawa et al. (2004) observed relatively high concentrations of ^{234}Th in livers (50–400 Bq/kg dry; 1.35–10.81 nCi/kg) and excrement (2,000–2,900 Bq/kg dry; 54.05–78.38 nCi/kg) from marine ascidians, whereas parent ^{238}U concentrations were <3 Bq/kg dry (<0.081 nCi/kg). These findings indicate biomagnification of ^{234}Th in the liver.

Historical soil-to-plant transfer coefficients (concentration in dry plant to concentration in dry soil) were reported in the range of 10^{-4}–$7x10^{-3}$, but could be as high as 2.9 for mixed grasses under certain conditions. Jeambrun et al. (2012) conducted a study of uranium and thorium uptake in plants from five French areas. Soil-to-plant transfer factors were lower for ^{232}Th than ^{238}U, and those factors for ^{232}Th were lower in wheat (mean 0.0014) than in lettuce (0.013).

Soudek et al. (2013) artificially exposed the roots of hydroponically grown tobacco plant seedlings (*Nicotiana tabacum* cv. La Burley 21) over a 16-day period to media containing thorium nitrate (50, 100, 250, or 500 μM) with various concentrations of organic acid chelators (citric, tartaric, and oxalic) or in the absence of phosphate or iron. The absence of phosphate most significantly affected thorium uptake. Levels in all plant parts increased gradually as a function of thorium concentration and extent of phosphate and iron depletion. The highest thorium dose with no phosphate resulted in thorium levels of 82 μg/kg dry weight in roots, 6 μg/kg dry weight in stems, and 1 μg/kg dry weight in leaves, while the addition of 2 mM phosphate retarded thorium uptake. Effects of iron deprivation were less, while the impact of acids peaked for 0.5 mM citric or tartaric acids resulted in thorium increases in roots and stems, but not in leaves. The phosphate deficient thorium uptake factor for tobacco seedling leaves can be calculated as 0.002.

5.4.2 Transformation and Degradation

Air. Thorium may change from one chemical species to another in the atmosphere (such as ThO_2 to $Th(SO_4)_2$) as a result of chemical reactions, but nothing definitive is known about the atmospheric chemical reactions of thorium. The chemical forms in which thorium may reside in the atmosphere are also not known, but it is likely to be present mostly as ThO_2.

Water. The principal abiotic processes that may transform thorium compounds in water are complexation by anions/organic ligands and hydroxylation. The increase in the mobility of thorium through the formation of soluble complexes with CO_3^{-2}, humic materials, and other anions or ligands and the decrease in the mobility due to formation of $Th(OH)_4$ or anionic thorium-hydroxide complexes were discussed in Section 5.4.1. In a model experiment with seawater at pH 8.2 and freshwater at pH 6 and pH 9, it was estimated that almost 100% of the thorium resides as hydroxo complexes (Boniforti 1987).

Sediment and Soil. No published data were located referencing biotic transformation of thorium in soil. Abiotic transformation processes that can convert immobile thorium in soil into mobile forms through the formation of complexes were discussed in Section 5.4.1.

5.5 LEVELS IN THE ENVIRONMENT

Reliable evaluation of the potential for human exposure to thorium depends, in part, on the reliability of supporting analytical data from environmental samples and biological specimens. Concentrations of thorium in unpolluted atmospheres and in pristine surface waters are often so low as to be near the limits of current analytical methods. In reviewing data on thorium 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 bioavailable.

Table 5-4 shows the lowest limit of detections for thorium that are achieved by analytical analysis in environmental media. An overview summary of the range of concentrations detected in environmental media is presented in Table 5-5.

Table 5-4. Lowest Limit of Detection Based on Standards[a]

Media	Detection limit	Reference
Air	5 fCi/m^3	Percival and Martin 1974
Drinking water	Not available	
Surface water and groundwater	<1 ng/g 0.03 pCi/L	ASTM 1986 Lauria and Godoy 1988
Soil	0.01 pCi	Singh and Wrenn 1988
Sediment	Not available	
Whole blood	<0.2 pg/mL	Picer and Strohal 1968

[a]Detection limits based on using appropriate preparation and analytics. These limits may not be possible in all situations.

Table 5-5. Summary of Environmental Levels of Thorium

Media	Low	High	For more information
Outdoor air (pCi/m^3)	36 x 10^{-6}	0.66 x 10^{-3}	Section 5.5.1
Indoor air (pCi/m^3)	No data	No data	
Surface water (pCi/L)	0.23 x 10^{-6}	1.4	Section 5.5.2
Ground water (pCi/L)	0.009	1.3	Section 5.5.2
Drinking water (pCi/L)	<0.1	1.3	Section 5.5.2
Food (pCi/g)	1x10^{-3}	9.8x10^{-2}	Table 5-6
Soil (pCi/g)	0.716	16,000	Section 5.2.3

No data are available on levels of thorium and thorium compounds in air, water, and soil at NPL sites (ATSDR 2017).

5.5.1 Air

The level of thorium in air has not been measured as frequently as it has for uranium. The concentration of thorium in the atmosphere of the South Pole measured in 1970 ranged between 18 and 83 fg/m^3, with a mean value of 59 fg/m^3 (1 fg=10^{-15} g). The origin of thorium in the polar atmosphere was speculated to be either crustal weathering or the ocean water (Zoller et al. 1974). The thorium level in the air of Algonquin Park, Ontario, Canada was reported to be 7.1 pg/m^3 (Sheppard 1980). The level of thorium measured in 1969 in East Chicago, Indiana, a heavily polluted industrial area, was 1.3 ng/m^3 compared to a value of 0.27 ng/m^3 at a rural location in Niles, Michigan (Dams et al. 1970). The air particulate samples collected from 250 sites in the United States by the National Air Surveillance Network (NASN) of EPA during 1975 and 1976 were analyzed for ^{232}Th by neutron activation analysis. The measured concentrations at 250 urban and nonurban sites in the United States ranged from 0.2 to 1.0 ng/m^3, with a mean concentration of 0.3 ng/m^3 (Lambert and Wilshire 1979). The mean concentrations of ^{228}Th, ^{230}Th, and ^{232}Th in New York City air (sample collected on the roof above the 14th floor) were 36, 36, and 37 aCi/m^3, respectively (Wrenn et al. 1981).

The air concentrations of thorium and other airborne radioactivity near a former thorium and rare-earth extraction facility in the United States were measured. The maximum radioactivity due to all three isotopes of thorium at a site about 450 feet from the primary waste pile was 0.66 fCi/m^3. Although the background thorium radioactivity was not reported, the total radioactivity at a site about 4,000 feet south of the waste pile was about 3.5 times lower than a site 450 feet from the pile (Jensen et al. 1984).

The concentrations of thorium in rainwater over Fayetteville, Arkansas were 2.8–123 fCi/L for ^{228}Th, 1.7–123 fCi/L for ^{230}Th, and 0.8118 fCi/L for ^{232}Th. The peak values in thorium concentrations correlated well with the 1980 eruption of Mount St. Helen and the 1982 eruption of El Chichon (Jiang and Kuroda 1987; Jiang et al. 1986; Salaymeh and Kuroda 1987).

The natural decay of ^{238}U and ^{232}Th will produce ^{222}Rn and thoron (^{220}Rn). The indoor air levels of radon (^{222}Rn) and thoron (^{220}Rn) daughters arising from some building materials and the soil have been reported by several authors. It was generally believed that the effective dose equivalent from ^{220}Rn (thoron) daughters (originating from ^{232}Th) might average about one-fifth of that due to ^{222}Rn daughters (originating from ^{238}U) in the temperate regions (Schery 1985). However, more recent measurements at varied indoor locations within the United States and Germany have shown that the potential alpha energy concentrations from ^{220}Rn daughters may be as high as 60% of that originating from ^{222}Rn. It has also been shown that the concentrations of thoron (^{220}Rn) and ^{222}Rn daughters in the indoor air are dependent on the air exchange rate in the dwellings and that the indoor concentrations are about 3–4 times higher than the outdoor concentrations (Keller and Folkerts 1984; Schery 1985).

5.5.2 Water

Compared to uranium, relatively less information was located on the levels of thorium in natural waters. The concentrations of dissolved thorium in water with high pH (more than 8) are expected to be very low, and the concentration may increase with the decrease of pH (Harmsen and De Haan 1980). Cothern et al. (1986) reported ^{232}Th concentrations rarely exceed 0.1 pCi/L in natural waters, but that the concentrations of ^{230}Th, a progeny of ^{238}U, may be as high as 0.4 pCi/L. In a natural surface water in Austria, the concentration of thorium (isotope undefined) was reported to be 1.24–2.90 μg/L (Harmsen and De Haan 1980). The concentration of thorium (isotope undefined but probably ^{230}Th) in water under low pH conditions, which may occur from the leaching of uranium tailings, may be as high as 38 mg/L (Harmsen and De Haan 1980). The individual concentrations of ^{228}Th, ^{230}Th, and ^{232}Th in an area of Great Bear Lake in Canada contaminated with mine wastes (silver and uranium mines) were <0.5 pCi/L (Moore and Sutherland 1981). The concentrations of ^{228}Th, ^{230}Th, and ^{232}Th in a highly alkaline (pH of about 10) lake (Mono Lake) in California have been reported to be as high as 1.02, 1.41, and 0.7 pCi/L, respectively (Anderson et al. 1982; Simpson et al. 1982).

The concentrations of thorium in seawater at various depths and locations have been reported by several authors. Because of the very low concentrations of thorium and the differences in location and the

varying characteristics of the water, the reported results are different. The concentration of total thorium in seawater ranges from $4x10^{-5}$ to <0.5 µg/kg (Greenberg and Kinston 1982; Sheppard 1980) and the world average concentration in seawater is 0.05 µg/L (Harmsen and De Haan 1980). The concentrations of the individual isotopes ^{232}Th, ^{230}Th, and ^{228}Th in seawater have been reported to be 0.00023–0.032, 0.014–0.72, and 0.023–3.153 fCi/L, respectively (Anderson et al. 1982; Hirose 1988; Huh and Bacon 1985; Livingston and Cochran 1987; Simpson et al. 1982). The concentrations of thorium in sediments are much higher than in seawater. In several sediments, concentrations of ^{232}Th, ^{230}Th, and ^{228}Th were 0.52–1.96, 1.01–30.77, and 0.36–1.93 pCi/g, respectively (Huh et al. 1987; Yang et al. 1986).

Thorium has also been detected in groundwaters. In groundwater in Austria, concentrations ranged from 0.5 to 2.90 µg/L (Harmsen and De Haan 1980). Briny groundwater from a well in Palo Duro Basin, Washington, contained 0.009, 0.1, and 0.59 pCi/L of ^{232}Th, ^{230}Th, and ^{228}Th, respectively (Laul et al. 1987). In a California well, ^{230}Th was detected at a concentration as high as 1.3 pCi/L (Aieta et al. 1987). The average population-weighted concentrations of ^{232}Th and ^{230}Th in U.S. community water supplies derived from both surface water and groundwater are <0.01 and <0.04 pCi/L, respectively (Cothern 1987; Cothern et al. 1986).

5.5.3 Sediment and Soil

The typical concentration range of thorium in soil is 2–12 µg/g (ppm), with an average value of 6 µg/g (Harmsen and De Haan 1980). The thorium content of soil normally increases with an increase in clay content of soil (Harmsen and De Haan 1980). The thorium contents in most soils from the Superfund sites listed in Section 5.3.3 were above background levels. The soil concentrations of ^{232}Th at the Reed-Keppler Park, West Chicago, Illinois, site and the Kerr-McGee Residential areas in West Chicago, Illinois, were 11,000 and 16,000 pCi/g, respectively (EPA 1988a). Soils near processing and milling operations, and concentrations of uranium and thorium ores, phosphate ores, and tin ores may contain thorium at concentrations higher than the background levels. Higher concentrations of thorium in soils near uranium ore crushing facilities have been reported (Jensen et al. 1984; Sill 1977).

Gallegos (1995) reported mean ^{232}Th levels of 0.0265, 0.0259, and 0.0351 Bq/g dry (0.716, 0.7, and 0.949 pCi/g dry) in soil samples taken from sampling sites in the vicinity of the Lawrence Livermore National Laboratory in California. Powell et al. (2007) found much higher levels in sediment samples taken from the Reedy River and surrounding creeks in Simpsonville, South Carolina that averaged 45.3 Bq/kg (1.22 pCi/g).

Hydraulic fracturing (fracking) operations to enhance natural gas production use water and additives injected under pressure and the process results in pits, ponds, and impoundments, referred to as reserve pits, on the surface. Rich and Crosby (2013) collected water and residual sludge from two reserve pits in the Barnett Shale East Newark Field and found ^{228}Th concentrations ranging from 0.36 to 0.72 pCi/g. Water concentrations were not reported.

Coal combustion residues (CCRs) from coal-fired power plants contain thorium, uranium, and a range of other substances. Spills from containment impoundments, such as the one in Kingston, Tennessee in 2008, can adversely affect the environment, so EPA undertook evaluation of such sites. Roper et al. (2013) analyzed samples from a 74-site subset of that larger EPA study. The concentration of ^{232}Th in fly ash averaged 73±26 Bq/kg (1.97±0.70 nCi/kg) for bituminous coals and 81±18 Bq/kg (2.19±0.49 nCi/kg) for subbituminous coals, 10±6 Bq/kg (0.27±0.16 nCi/kg) in scrubber sludges, and 1±1 Bq/kg (0.027±0.027 nCi/kg) in flue gas desulfurization gypsum.

Normally, thorium concentrations in drinking water are low and EPA does not require levels to be measured. Since thorium and other elements can become trapped in solids that deposit on sediment and walls of distribution system piping, levels can build up over time. Lytle et al. (2014) collected and analyzed samples of solids from the flushing of deposits (primarily from fire hydrants) in 25 distribution systems from 12 water utilities. Total thorium averaged 40±25 pCi/g and consisted of >90% ^{228}Th (36±24 pCi/g), ~8% ^{230}Th (3.3±3.0 pCi/g), and ~3% ^{232}Th (1.2±1.1 pCi/g). The flushing of water distribution systems can remove thorium and result in lower levels at the tap, especially if the system is otherwise undisturbed.

5.5.4 Other Media

Because concentrations of thorium in foods are very low, very few data exist. The ^{232}Th content in fresh fruits, vegetables, and tea was determined (in pCi/g), and the values are listed in Table 5-6. Vegetables grown in an area of high natural activity in Brazil had the following concentrations of thorium (μg/g in dry sample) (Linsalata et al. 1987): brown beans, 0.011; potato, 0.0019; zucchini, 0.011; corn, 0.0022; carrot, 0.0074; and sweet potato, 0.0027. These authors did not observe rapid transport of ^{232}Th from soil to the edible parts of the plants.

Table 5-6. ^{232}Th Content in Fresh Fruits, Vegetables, and Tea

Food	Concentration in pCi/g (wet weight)
Apples	≤6.9×10^{-3}
Asparagus	≤9.8×10^{-2}
Bananas	≤8.2×10^{-3}
Bell peppers	≤6.7×10^{-3}
Brazil nut	<7×10^{-3}–9×10^{-3}
Broccoli	≤3.6×10^{-3}
Cabbage	≤3.3×10^{-3}
Carrots	≤4.2×10^{-3}
Celery	≤9.0×10^{-3}
Cucumbers	≤2.9×10^{-3}
Egg plant	≤3.3×10^{-3}
Grapefruit	≤9.8×10^{-3}
Green beans	≤4.9×10^{-3}
Green tea	2×10^{-3}–3×10^{-3}
Irish potatoes	≤3.9×10^{-3}
Lettuce	≤2.8×10^{-3}
Oranges	≤4.1×10^{-3}
Pears	≤8.5×10^{-3}
Raisins	≤1.2×10^{-2}; 2×10^{-3}–3×10^{-3}
Sesame seed	1×10^{-2}
Soybean	1×10^{-3}
Sweet potatoes	≤7.5×10^{-3}
Tangelos	≤2.3×10^{-3}
Tangerines	4.7×10^{-3}
Tomatoes	≤1.1×10^{-2}
Turnips	≤2.6×10^{-3}
Yellow squash	≤3.9×10^{-3}

Sources: Oakes et al. 1977; Kobashi and Tominaga 1985

The concentrations of thorium in both hard and soft tissues of humans have been determined by a few authors. The concentration of ^{232}Th in the blood of normal populations (not occupationally or otherwise known to be exposed to levels higher than background level of thorium) in the United Kingdom was 2.42 μg/L. The ^{232}Th level in the urine of the same population was below the detection limit of 0.001 μg/L, although the concentration in the urine of exposed workers ranged from <0.001 to 2.24 μg/L. The highest value (2.24 μg/L) was found in a worker in the thorium nitrate gas mantle industry (Bulman 1976; Clifton et al. 1971).

The ^{232}Th concentrations in rib bones from several control humans from the United States ranged from <0.1 to 72 ng/g (ppb) and were found to increase with age (Lucas et al. 1970). A similar increase in thorium concentration with age was seen in bones (primarily vertebral wedges) of a Colorado population (Wrenn et al. 1981). The level of ^{232}Th in rib bones of individuals in the United Kingdom not occupationally exposed to thorium ranged from 0.8 to 163.8 ng/g, with a mean value of 28.7 ng/g in dry ash (Clifton et al. 1971). The concentration of thorium in the fibula of a Thorotrast patient was reported to be 2.0 μg/g (ppm) (Edgington 1967). Singh et al. (1985) reported more recent measurements of isotopic concentrations of thorium in different human bones from the general population of Colorado and Pennsylvania. These values are shown in Table 5-7. The authors concluded that the concentrations of ^{230}Th in ribs of the Colorado population were significantly higher (statistically), probably because of exposure to uranium tailings, than those from the Pennsylvania population.

Table 5-7. Thorium Levels in Bones of Colorado and Pennsylvania Residents

Source of bone	Mean thorium levels [(pCi/kg) wet weight] in residents from two locations					
	Colorado			Pennsylvania		
	^{232}Th	^{230}Th	^{228}Th	^{232}Th	^{230}Th	^{228}Th
Ribs	0.50	1.57	1.0	0.20	0.54	1.19
Vertebrae	0.096	0.96	0.88	0.10	0.27	1.31
Sternum	Not detected[a]	Not detected[a]	0.02[a]	0.33	0.63	2.73

[a]Only one sample analyzed.

Source: Singh et al. 1985

The levels of thorium in the tissues of a hard-rock miner, a uranium miner, and the levels in two uranium millers (^{230}Th is a decay product of ^{238}U, and ^{228}Th and ^{232}Th are impurities in uranium) were compared with the levels in the 50th percentile for the general population (Singh et al. 1987; Wrenn et al. 1981). These data are given in Table 5-8. The levels of ^{230}Th in the hard-rock miner were about 10 times higher than the median levels in most tissues of the general population. In the case of the uranium miner and millers, the values were >2 orders of magnitude higher than the median tissues levels in the general population.

Wrenn et al. (1981) determined the median concentrations of ^{228}Th, ^{230}Th, and ^{232}Th in the lungs of smokers and nonsmokers; the respective values were 0.22, 0.56, and 0.43 pCi/kg for smokers and 0.37, 0.84, and 0.60 pCi/kg for nonsmokers. The investigators concluded that cigarette smoking had no effect relative to increasing the concentration of thorium isotopes in lungs.

Table 5-8. Thorium Isotopic Concentration in Three Occupational Cases and the General Population of Grand Junction, Colorado (pCi/kg)

	Uranium miner[a]			Hard rock miner[a]			Uranium miller[b]			50th percentile for the general population[a]		
	^{228}Th	^{230}Th	^{232}Th	^{228}Th	^{230}Th	^{232}Th	^{228}Th	^{230}Th	^{232}Th	^{228}Th	^{230}Th	^{232}Th
Lung	1.1±0.18	54.0±0.81	1.4±0.13	0.70±0.24	12.0±0.79	0.61±0.18	0.49	141	2.35	0.21	0.88	0.37
Lymph nodes	NA	NA	NA	12.0±2.4	37.0±3.9	4.6±1.4	168	1,687	31.7	4.8	13.0	8.1
Liver	0.25±0.04	32.0±0.36	0.12±0.2	0.05±0.01	0.82±0.07	0.06±0.02	0.73	120	0.09	0.08	0.13	0.07
Spleen	0.69±0.18	32.0±1.0	0.80±0.15	0.06±0.02	1.5±0.16	0.12±0.04	1.81	1.81	0.38	0.06	0.13	0.09
Bone	0.24±0.3	132.0±1.1	0.42±0.06	0.54±0.13	10.0±0.40	0.32±0.07	1.47	86.9	0.31	0.54	0.89	0.20
Kidney	0.11±0.05	10.0±0.40	0.09±0.04	0.09±0.04	1.4±0.15	0.11±0.04	0.82	2.80	0.18	0.09	0.23	0.07

[a]Wrenn et al. 1981.
[b]Singh et al. 1987; the averages of two samples are given.

NA = not analyzed; Th = thorium

5.6 GENERAL POPULATION EXPOSURE

The general population will be exposed to thorium through the inhalation of air and ingestion of food and drinking water containing trace amounts of the chemical. Because the concentration of thorium is normally very low in air, drinking water, and foods, few studies were located that determined the daily human intake of thorium. According to Cothern (1987), the estimated daily intakes of ^{230}Th in the United States population through inhalation of air and ingestion of drinking water are 0.0007 and <0.06 pCi, respectively. The corresponding values for ^{232}Th are 0.0007 and <0.02 pCi. Cothern (1987) assumed that the intake from food would be negligible. Based on these values, the total daily intakes of ^{230}Th and ^{232}Th are expected to be <0.06 and <0.02 pCi, respectively. However, other authors estimated the contribution of food to the total human thorium intake may not be negligible and may be the most significant. Based on a survey of the levels of thorium in air, water, and food, Fisenne et al. (1987) estimated the daily intake of ^{230}Th and ^{232}Th by New York City residents. The daily dietary, water, and inhalation intake of ^{230}Th was estimated to be 0.164, 0.005, and 0.0003 pCi, respectively, giving a total daily intake of 0.17 pCi. The corresponding estimated values for ^{232}Th are 0.110, 0.002, and 0.0002 pCi, with a total daily intake being 0.112 pCi. From the measured values of thorium in feces and the assumed values for uptake and elimination rates, Linsalata et al. (1985) estimated a daily ingestion intake of ^{232}Th for New York residents to be about 0.08 pCi or 0.7 μg. This value is considerably smaller than the value estimated by Fisenne et al. (1987). The value from Linsalata et al. (1985) is again considerably smaller than the daily dietary, water, and inhalation intakes of 2.24, 0.02, and 0.02 μg, respectively, as estimated for residents of Bombay, India (Dang et al. 1986). It can be concluded from the above discussion that the total intake of thorium by the United States population may vary depending on the thorium content in the consumed food and that no firm U.S. average thorium intake value is yet available. The importance of the intake of thorium from foods is overshadowed by the relative absorption of thorium by lung compared with its uptake by gut.

Occupational exposures to higher levels of thorium isotopes occur primarily to workers in uranium, thorium, tin, and phosphate mining, milling, and processing industries, radium dial workers, and gas lantern mantle workers. From the measurement of airborne thorium concentrations in workplaces of the uranium and thorium industry, it was concluded that radioactive dust, particularly from crushing areas, represents an important route of exposure (Hannibal 1982; Kotrappa et al. 1976). It has also been reported that exposure of workers in the fertilizer industry to natural radioactivity may increase by 100% over normal background (Metzger et al. 1980). Measuring external gamma radiation dosages to a person working 8 hours/day has shown that monazite and xenotime storage rooms of Amang upgrading plants

(tin processing) on the west coast of Malaysia exhibited exposure rates exceeding the ICRP recommended maximum value of 5 rem/year (Hu et al. 1984). From the radioactivity released by a burning gas mantle (contains thorium), it was concluded that the user would be at minimal risk unless the person was in a small unventilated room (Leutzelschwab and Googins 1984). However, workers in the gas mantle manufacturing industry are expected to be exposed to higher concentrations of radioactivity than the normal population.

Workers are exposed to higher levels of thorium and other radionuclides in certain thorium industries, as indicated by the measured exhaled breath and tissue levels of these chemicals. The significantly higher level of ^{220}Rn (a decay product of ^{232}Th) in the exhaled breath of some thorium plant workers (Mayya et al. 1986) is indirect evidence of higher thorium intakes. Similarly, other authors have found higher tissue and body fluid levels (compared to background) of thorium in workers in the thorium processing industry (Clifton et al. 1971; Mausner 1982; Twitty and Boback 1970), workers in the radium dial industry (Keane et al. 1986), in uranium mill crushermen (Fisher et al. 1983), and in uranium and hard rock miners and uranium millers (Singh et al. 1987; Wrenn et al. 1981).

Thorium-doped glass is also used in the production of some camera lenses (Waligorski et al. 1985). A relatively recent measurement has shown that the external dose rate from exposure to a camera lens can be 10 times higher (as high as 9.25 mrem/hour at the front glass surface of the lens) than previously reported (Waligorski et al. 1985). Therefore, professional photographers and workers in the thorium-doped photographic lens manufacturing industry may be at slightly higher risk of exposure to thorium and its daughter products from inhalation and/or external radiation.

An autopsy study from the U.S. Transuranium and Uranium Registry reported that the maximum concentrations of ^{232}Th for an individual who was not occupationally exposed to thorium were 20–400 ng/g in lung and 160–400 ng/g in lymph nodes (Hare et al. 2010).

Thorium concentrations in the air of an ore-crushing workshop associated with a rare-earth mine in China ranged from 9.30 to 875 mg/m^3 and averaged 188.7 mg/m^3 (Chen et al. 2003).

5.7 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

Neonatal animals have been found to absorb 20–40 times more thorium through the gastrointestinal tract than adult animals (Sullivan 1980a, 1980b; Sullivan et al. 1983), indicating that children may be more susceptible to both the chemical and radiological effects of thorium than adults.

The three groups of the general population that have the potential of exposure to thorium and its decay products at levels higher than background are people who consume large amounts of foods grown in high background areas, people who reside in homes built with high thoron (^{220}Rn) emitting building materials and constructed on soil with high background levels of thorium, and people who live near radioactive waste disposal sites. Linsalata et al. (1987) analyzed vegetables grown in two areas near Sao Paulo, Brazil, which contained high natural radioactivity, and found that thorium is not bioaccumulated in the vegetables but maintained a mean concentration ratio (concentration in dry vegetable/concentration in dry soil) of 10^{-4}. Root vegetables (e.g., carrots and potatoes) showed lower concentration ratios than zucchini and beans. Therefore, it can be concluded that vegetables grown in these soils would contain more thorium than vegetables grown in soil with normal background levels.

Linsalata et al. (1985) also estimated that the intake of thorium by populations residing in these parts of Brazil was 6–10 times higher than the population in New York City, as indicated by the analysis of human bones from the two areas. The concentration of thorium in human bones was found to be 100 times higher in high background monazite areas in India than in areas with normal thorium concentration in soils (Pillai and Matkar 1987).

The building construction materials that contain higher levels of ^{232}Th are granite, clay bricks, and certain kinds of concrete blocks and gypsum, particularly the materials in which waste products from uranium mining and milling industry are used (Beretka and Mathew 1985; Ettenhuber and Lehmann 1986; Hamilton 1971). Ettenhuber and Lehmann (1986) reported that the indoor gamma radiation dose equivalent in buildings made from bricks and concrete is mainly due to ^{222}Rn (originating from ^{238}U) and ^{220}Rn (originating from ^{232}Th), and can be over 7 times higher than outdoors.

The effect of soil on the level of thorium and its decay products in indoor air has been discussed by Gunning and Scott (1982). Homes near the Elliot Lake (Canada) uranium mines were suspected to contain higher than normal levels of thoron (^{220}Rn) and its daughters, because of higher levels of thorium in the surface soil and building materials used in the town. The ratio of the concentration of decay

products of thoron (^{220}Rn) to ^{222}Rn found in these homes was 0.3. Therefore, the concentrations of thoron in decay products originating from ^{232}Th inside the homes were lower than ^{222}Rn decay products originating from ^{238}U, and the levels were insignificant compared with the remedial action limit of 20 mWL (1 WL is the concentration of short-lived radon decay products that will result in $1.3x10^5$ MeV of potential alpha energy per liter of air) (Gunning and Scott 1982).

The concentrations of ^{232}Th in soil from several residential lots near the Kerr-McGee ore processing facilities in West Chicago, Illinois, have been determined to be up to 16,000 pCi/g (EPA 1988a). Therefore, homes built on such lots or homes that are close to other radioactive disposal sites may be sources of higher thorium exposure.

Both cigarette tobacco and its smoke contain thorium (Munita and Mazzilli 1986; Neton and Ibrahim 1978). However, the effect of cigarette smoking on potential thorium exposure remains unclear. Joyet (1971) analyzed the lungs of 10 autopsied smokers and two nonsmokers. In 5 of 10 smokers, the lungs contained significantly higher levels of thorium than the nonsmokers, and the thorium levels in the residual five were not significantly different from the nonsmokers. Limited data suggest that cigarette smoking has no effect on the concentration of thorium isotopes in the lungs (Wrenn et al. 1981).

Welders are exposed to elevated airborne thorium levels when using thoriated tungsten welding electrodes during the process of tungsten inert gas (TIG) welding (Gafvert et al. 2003; Ludwig et al. 1999; McElearney and Irvine 1993; Saito et al. 2003), even though the welding process is not intended to consume the electrode. Additional inhalation exposure of those welders could occur while grinding one end of each electrode to a point in preparation for its use.

Firefighters may be exposed to elevated levels of thorium when inhaling smoke from forest fires. Carvalho et al. (2014) found that the complete combustion of plants in the Viesu district of Portugal resulted in fly ash with a thorium concentration of 412 Bq/kg ($11.14x10^3$ pCi/kg), which was >100 times that of the original vegetation, which ranged from 0.023 to 5.5 Bq/kg (0.62 to 148.65 pCi/kg).

Lenka et al. (2013) estimated the ingestion radiation doses from thorium and other environmental radionuclides in food and water to the population of Chhatrapur, Odisha, India. The area is rich in monazite sand, which contains elevated levels of uranium and thorium series radionuclides. The respective average doses from cereals, pulses, and drinking water were 50, 2.4, and 0.2 μSv/year (5,000,

240, and 20 µrem/year). Cereals were highest due to their combined radioactivity concentration (up to 2 mBq/g; 0.054 pCi/g) and intake rate.

CHAPTER 6. 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 thorium 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 adverse health effects (and techniques for developing methods to determine such health effects) of thorium.

Data needs are defined as substance-specific informational needs that, if met, would reduce the uncertainties of human health risk 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.

6.1 Information on Health Effects

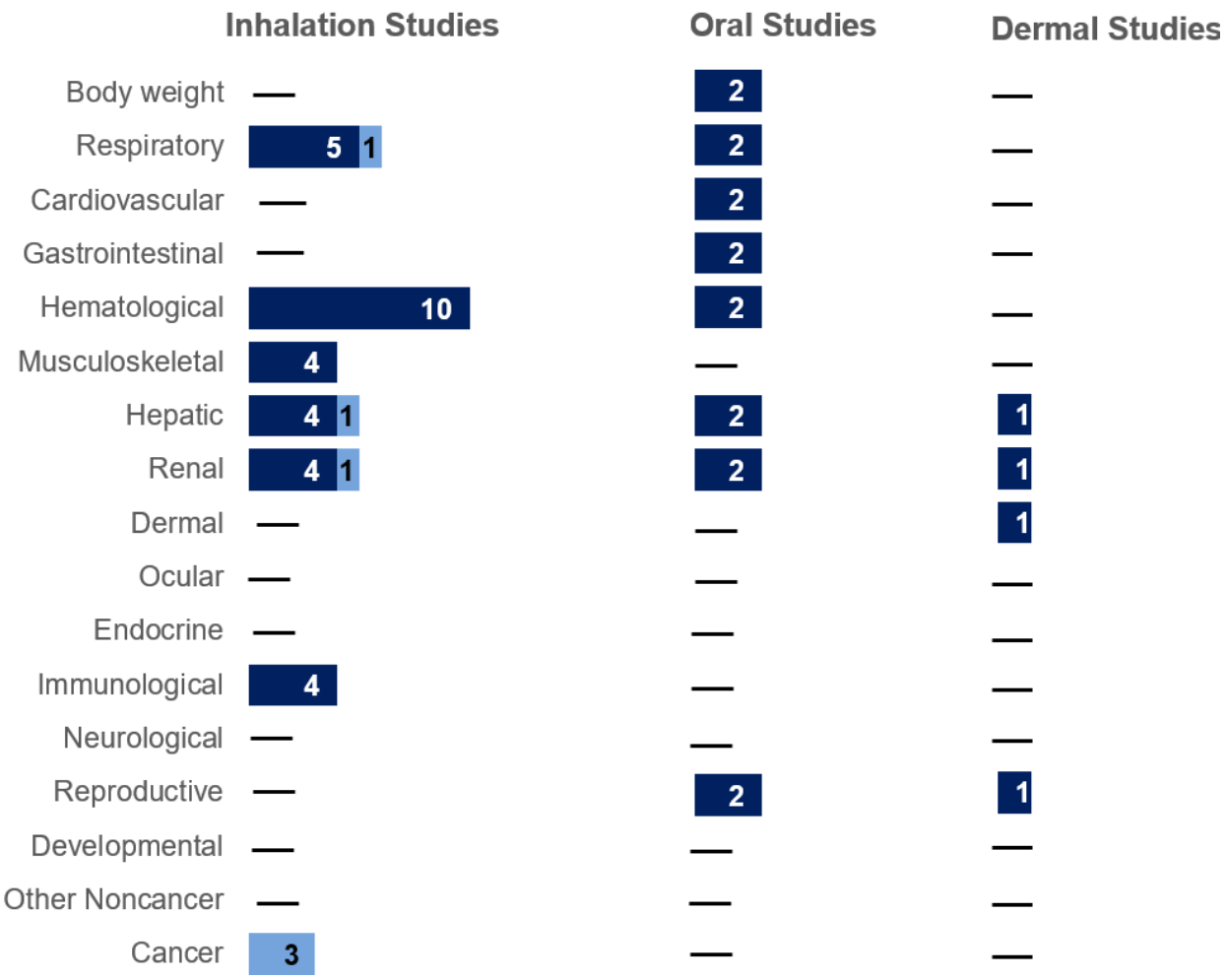
Studies evaluating the health effects of inhalation, oral, and dermal exposure of humans and animals to thorium that are discussed in Chapter 2 are summarized in Figure 6-1. The purpose of this figure is to illustrate the information concerning the health effects of thorium. The number of human and animal studies examining each endpoint is indicated regardless of whether an effect was found and the quality of the study or studies.

6.2 Identification of Data Needs

Missing information in Figure 6-1 should not 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* (ATSDR 1989), is substance-specific information necessary to conduct comprehensive public health assessments. Generally, ATSDR defines a data gap more broadly as any substance-specific information missing from the scientific literature.

Figure 6-1. Summary of Existing Health Effects Studies on Thorium By Route and Endpoint*

Potential hematological, respiratory, hepatic, and renal effects were the most studied endpoints
The majority of the studies examined inhalation exposure in **animals** (versus **humans**)



Acute-Duration MRLs. No studies were located regarding the effects of thorium in humans following acute exposure by any relevant route. Intravenous injection of thorium as an x-ray contrast medium into people resulted in death from various malignancies 20–30 years following injection. Animals studies were limited to determining dose levels resulting in death following inhalation and oral exposure, and in dermal and reproductive effects following dermal administration to the lateroabdominal and scrotal skin, Inhalation-based pharmacokinetic data indicate that the lymph nodes, lungs, and bone may be the target organs of thorium toxicity. Oral pharmacokinetic data indicate that bone may be the target organ of toxicity following ingestion of thorium. The acute toxicity of thorium in animals has also been tested by routes of exposure (intravenous, intraperitoneal, intratracheal) that are difficult to interpret, and it would be useful to compare these toxic levels to toxic levels found after administration by a relevant route (inhalation, oral, dermal). Knowledge about the acute toxicity of thorium is important because people living near hazardous waste sites might be exposed for brief periods.

Intermediate-Duration MRLs. No studies were located regarding the effects of thorium in humans following intermediate-duration exposure by any route of exposure. Two animal studies were reported: one inhalation study in rats showing lung damage and one oral study in mice resulting in death. Intermediate-duration dermal studies in animals were not located. The lungs appear to be the target organs following intermediate-duration inhalation exposure to thorium. Oral pharmacokinetic data indicate that bone may be the target organ of toxicity following ingestion of thorium. More extensive studies by all relevant routes (inhalation, oral, dermal) would be useful in assessing both the chemical and radiological toxicity of thorium. Intermediate-duration toxicity information is important because people living near hazardous waste sites might be exposed for corresponding time periods.

Chronic-Duration MRLs. Several studies have been reported regarding the toxic effects on workers occupationally exposed to thorium or monazite sand found in refinery dust. In these studies, effects on the lungs and chromosomes and an increased cancer incidence were reported. Because the workers were exposed to many toxic agents, however, effects cannot be attributed directly to thorium. Epidemiology studies investigating workers exposed primarily to thorium (e.g., during the production of gas lamp mantles) would be useful. No human studies were located regarding chronic oral or dermal exposure. Studies have shown that the lungs and the hematological system are the target organ systems for thorium toxicity. Oral pharmacokinetic data indicate that bone may be the target organ of toxicity following ingestion of thorium. Chronic studies by relevant routes of exposure, inhalation and oral, are important because people living near hazardous waste sites might be exposed to thorium for years.

Studies in workers occupationally exposed to thorium have reported an increase in the incidence of pancreatic, lung, and hematopoietic cancers. These effects were observed in workers exposed to many toxic agents, so they cannot be attributed directly to thorium. Intermediate duration inhalation exposure of rats to thorium dioxide resulted in lung tumors. No data were located regarding the carcinogenic effects of oral or dermal thorium exposure in humans or animals. Further chronic exposure studies by all relevant routes of exposure (inhalation, oral, dermal) using wider exposure level ranges and a number of species of animals may be useful in assessing the carcinogenic potential of thorium in humans.

Health Effects.

Reproductive Toxicity. No studies were located regarding the reproductive effects of thorium in humans following exposure by any route. Neither inhalation nor oral reproduction studies in animals were located. Pharmacokinetic data following inhalation or oral exposure were not located to allow the prediction of possible reproductive effects. One dermal rat study found testicular effects after administration directly onto the scrotal skin. Additional inhalation, oral, and dermal reproduction studies and multigenerational studies would be helpful in assessing the potential risk to humans.

Developmental Toxicity. No studies were located regarding the developmental effects of thorium in humans or animals following exposure by any route. Also, pharmacokinetic data do not exist that may predict whether thorium crosses the placental barrier. Further developmental studies in animals by all relevant routes of exposure may clarify the potential developmental effects of thorium in humans.

Immunotoxicity. No studies were located regarding the immunological effects of thorium in humans or animals following any relevant route of exposure (inhalation, oral, dermal). One report, however, showed that intraperitoneal and intravenous injection of thorium dioxide in mice resulted in a suppression of the immune response. Studies on the immunotoxic effects of thorium, both histopathological and effects on the immune response, by all relevant routes of exposure in animals may determine the potential immunotoxic effects in humans.

Neurotoxicity. No studies were located regarding the neurological effects of thorium in humans or animals following exposure by any route. Other metals, such as lead, however, have been shown to have more severe neurological effects on children than adults; therefore, it is possible that children may be more susceptible than adults to the effects of thorium. Studies on

the neurological effects of thorium, both histopathological and effects on behavior by all relevant routes of exposure in animals, may determine the potential neurological effects in humans.

Epidemiology and Human Dosimetry Studies. Epidemiology studies have investigated the relationship between long-term exposure to thorium and systemic effects, genotoxic effects, and cancer in humans. The authors of these studies found increases in respiratory disease and certain types of cancer (lung, pancreatic, hematopoietic) in exposed thorium workers, but the findings were not definitive. The existing epidemiological studies are often weakened by not sufficiently accounting for smoking habits or exposure to other chemicals and by relying too heavily on the accuracy of death certificates. Increased incidences of chromosomal abnormalities were found in exposed workers (approximately 4% dicentric in controls versus 20% in exposed workers). The occupational studies focus primarily on adult males. It would be useful to study groups that include women, children, and neonates that have been exposed to greater than normal levels of thorium to determine their level of susceptibility. Epidemiology studies investigating workers exposed primarily to thorium (e.g., during the production of gas lamp mantles) would also be useful. Further studies assessing the cause/effect relationship between thorium exposure and human health effects would be helpful in monitoring individuals living near a hazardous waste site.

Biomarkers of Exposure and Effect. The major route of excretion of inhaled or ingested thorium is in the feces. Exposure to thorium can be determined by measurement of thorium and/or its daughters in the feces, urine, blood, or expired air. The body burden of thorium may be estimated by the measurement of external gamma rays emitted from thorium daughters in the body. Further studies correlating thorium exposure with thorium and/or thorium daughters in the urine, feces, blood, and expired air would be helpful in more accurately quantifying thorium exposure.

No relationship was found between the measured body burden of thorium and complete blood count parameters (e.g., hemoglobin, red and white blood cells) in humans occupationally exposed to thorium. Further studies may reveal thorium-specific biomarkers that may alert health professionals to thorium exposure before toxicological effects occur.

Absorption, Distribution, Metabolism, and Excretion. The absorption of thorium from the lungs and gastrointestinal tract and the tissue distribution of thorium have been studied in both humans and animals. Inhalation was found to be the major route of exposure with gastrointestinal absorption being very low (see Section 3.1). The data in humans correlate well with the animal data. The excretion of systemic thorium in humans has not been extensively studied, especially the partition between feces and

urine, and work in this area in both humans and animals would be helpful. No studies were located regarding the pharmacokinetics in humans or animals following dermal exposure to thorium. Studies on the dermal route of exposure may be helpful in determining whether thorium is a human health hazard by this route.

Comparative Toxicokinetics. No data were located regarding species-specific differences in the toxicokinetics or toxicity of thorium compounds. It does not appear necessary to perform comparative toxicokinetic studies at this time.

Children's Susceptibility. Neonatal animals have been found to absorb 20–40 times more thorium through the gastrointestinal tract than adult animals (Sullivan 1980a, 1980b; Sullivan et al. 1983), indicating that children may be more susceptible to both the chemical and radiological effects of thorium than adults. Additional studies could be designed to further evaluate the potential for age-related differences in thorium toxicity.

Physical and Chemical Properties. Some of the physical and chemical properties (i.e., K_{ow}, K_{oc}, and Henry's law constant) that are often used in the estimation of environmental fate of organic compounds are not useful or relevant for most inorganic compounds including thorium and its compounds. Relevant data concerning the physical and chemical properties, such as solubility, stability, and oxidation-reduction potential of thorium salts and complexes, have been located in the existing literature.

Production, Import/Export, Use, Release, and Disposal. In the absence of experimental or estimated population exposure data, information concerning production volume, uses, release, and disposal are sometimes useful indicators of potential population exposure. For example, if the production volume of a chemical is high, it is likely that the release of the chemical in the workplace and in the environment will be high. The exposure of population groups to a certain substance is dependent on its use pattern. The frequency of general population exposure will be high for substances that have widespread uses in homes. The production volumes and their past and future trends of the commercially important thorium compounds are known. The use pattern of thorium and compounds is well described in the literature. It is also known that occupational groups are most susceptible to thorium exposure. Data regarding the amounts of thorium disposed in the past, the present rates of disposal, and future disposal trends in the United States were not located. These data would be helpful in determining the potential for and extent of general population exposure to thorium. The current disposal and storage

methods for thorium or its byproducts must be efficient in order to meet the Nuclear Regulatory Commission (NRC) and EPA guidelines and regulations regarding their release into the accessible environment and exposure of the general population.

Environmental Fate. It can be concluded from the transport characteristics that surface water sediment will be the repository for atmospheric and aquatic thorium. Normally, thorium compounds will not transport long distances in soil. They will persist in sediment and soil. There is a lack of information on the fate and transport of thorium and its compounds in air. Data regarding measured particulate size and deposition velocity (that determines gravitational settling rates), and knowledge of the chemical forms and the lifetime of the particles in air would be useful.

Bioavailability from Environmental Media. The absorption and distribution of thorium as a result of inhalation and ingestion exposures have been discussed in Sections 3.1.1 and 3.1.2. However, quantitative data relating physical/chemical properties, such as particle size, chemical form of thorium, and degree of adsorption with the bioavailability of thorium in inhaled air particles and inhaled and/or ingested soil particles, are lacking. Such studies would be useful in assessing potential thorium toxicity to people living near a hazardous waste site.

Food Chain Bioaccumulation. Information about bioaccumulation in fish and food exists, as does information on the levels of thorium in various foods. Existing data in the literature indicate that thorium does not biomagnify in predators due to consumption of contaminated prey organisms.

Exposure Levels in Environmental Media. Because of the paucity of data on the levels of thorium in air, water, and food, there are conflicting reports on the importance of each medium to the total human dietary intake of this substance. Data on the levels of thorium in foods grown in contaminated areas, particularly in the vicinity of hazardous waste sites, are limited, and further development of these data would be useful. There is also a lack of air monitoring data around hazardous waste sites.

Exposure Levels in Humans. Although some data on the levels of thorium in human tissues exist, neither consensus values of the background levels for thorium in human tissues nor thorium levels in tissues of populations residing in the vicinity of hazardous waste sites were located. Conflicting data also exist regarding the level of thorium in the lungs of smokers and nonsmokers. Further research would be useful to provide conclusive evidence regarding the effect of cigarette smoking on thorium content in the lung. In addition, there are no reliable data on urinary and fecal excretion of thorium in general

populations in the United States. The skeleton is the main organ for the accumulation of thorium, yet there are also no reliable data on macro and micro distribution of thorium in human bone necessary to quantify its body burden.

Exposures of Children. No studies are available to assess whether children are at a higher exposure risk than adults. Studies examining potential exposure sources for children would be useful.

Analytical Methods. Methods are available that can detect the isotopes of thorium in both biological and environmental samples. Quantification and identification typically occurs through alpha- or gamma-ray spectroscopy. These methods are reliable and sensitive enough to detect thorium at levels that may cause harmful effects. No data needs are identified.

6.3 Ongoing Studies

No ongoing studies were identified for thorium

CHAPTER 7. REGULATIONS AND GUIDELINES

Pertinent international and national regulations, advisories, and guidelines regarding thorium in air, water, and other media are summarized in Table 7-1. This table is not an exhaustive list, and current regulations should be verified by the appropriate regulatory agency.

ATSDR develops MRLs, which are substance-specific guidelines intended to serve as screening levels by ATSDR health assessors and other responders to identify contaminants and potential health effects that may be of concern at hazardous waste sites. See Section 1.3 and Appendix A for detailed information on MRLs and the rationale for not deriving MRLs for thorium.

Table 7-1. Regulations and Guidelines Applicable to Thorium

Agency	Description	Information	Reference
	Air		
EPA	RfC	No data	IRIS 2017
WHO	Air quality guidelines	No data	WHO 2010
NRC	Dose limits for individual members of the public		NRC 2017c
	Radiation		
	Total effective dose equivalent	0.1 rem (1 mSv) in a year	
IAEA	Recommended dose limits for the public		IAEA 2014
	Radiation		
	Effective dose	1 mSv in a year	
	Lens of the eye equivalent dose	15 mSv in a year	
	Skin equivalent dose	50 mSv in a year	
	Hands and feet equivalent dose	No data	
	Water & Food		
EPA	Drinking water standards and health advisories		EPA 2012
	Gross alpha particle activity		
	10^{-4} Cancer risk	15 pCi/L	
	National primary drinking water regulations		EPA 2009
	Alpha and beta/photon emitters		
	Alpha emitters		
	MCL	15 pCi/L	
	Public health goal	zero	
	Beta/gamma emitters		
	MCL	4 mrem/year	

Table 7-1. Regulations and Guidelines Applicable to Thorium

Agency	Description	Information	Reference
EPA	RfD	No data	IRIS 2017
WHO	Drinking water quality guidelines		WHO 2017
	^{228}Th, ^{230}Th, or ^{232}Th	1 Bq/L	
FDA	EAFUS	No data[a]	FDA 2013
	Allowable level in bottled water		FDA 2017
	Gross alpha particle activity	15 pCi/L	
	Cancer		
HHS	Carcinogenicity classification		NTP 2016
	Thorium dioxide	Known to be a human carcinogen	
EPA	Carcinogenicity classification	No data	IRIS 2017
IARC	Carcinogenicity classification		IARC 2012
	^{232}Th (as Thorotrast)	Group 1[b]	
	Occupational		
OSHA	PEL (8-hour TWA) for general industry, shipyards and construction	No data	OSHA 2016a, 2016b, 2017
NIOSH	REL (up to 10-hour TWA)	No data	NIOSH 2016
NRC	Lung clearance class[c]		NRC 2017a
	Thorium oxides and hydroxides	Y	
	All other thorium compounds	W	
	Occupational ALIs and DACs for inhalation		

Isotope	Class[c]	ALI (µCi)[d]	DAC (µCi/mL)
^{226}Th	W	$2x10^{2}$	$6x10^{-8}$
	Y	$1x10^{+2}$	$6x10^{-8}$
^{227}Th	W	$3x10^{-1}$	$1x10^{-10}$
	Y	$3x10^{-1}$	$1x10^{-10}$
^{228}Th	W	$1x10^{+2}$ bone surface ($2x10^{-2}$)	$4x10^{-12}$
	Y	$2x10^{-2}$	$7x10^{-12}$
^{229}Th	W	$9x10^{-4}$ bone surface ($2x10^{-3}$)	$4x10^{-13}$
	Y	$2x10^{-3}$ bone surface ($3x10^{-3}$)	$1x10^{-12}$
^{230}Th	W	$6x10^{-3}$ bone surface ($2x10^{-2}$)	$3x10^{-12}$
	Y	$2x10^{-2}$ bone surface ($2x10^{-2}$)	$6x10^{-12}$
^{231}Th	W	$6x10^{3}$	$3x10^{-6}$
	Y	$6x10^{3}$	$3x10^{-6}$
^{232}Th	W	$1x10^{-3}$ bone surface ($3x10^{-3}$)	$5x10^{-13}$
	Y	$3x10^{-3}$ bone surface ($4x10^{-3}$)	$1x10^{-12}$
^{234}Th	W	$2x10^{2}$	$8x10^{-8}$
	Y	$2x10^{2}$	$6x10^{-8}$

Table 7-1. Regulations and Guidelines Applicable to Thorium

Agency	Description	Information	Reference
	Occupational ALIs for ingestion		
	Isotope	ALI (µCi)[d]	
	^{226}Th	$5x10^{3}$ stomach wall ($5x10^{3}$)	
	^{227}Th	$1x10^{2}$	
	^{228}Th	$6x10^{0}$ bone surface ($1x10^{1}$)	
	^{229}Th	$6x10^{-1}$ bone surface ($1x10^{0}$)	
	^{230}Th	$4x10^{0}$ bone surface ($9x10^{0}$)	
	^{231}Th	$4x10^{3}$	
	^{232}Th	$7x10^{-1}$ bone surface ($2 x10^{0}$)	
	^{234}Th	$3x10^{2}$ lower large intestine wall ($4x10^{2}$)	
NRC	Quantity of radioactive material requiring licensing		NRC 2017a
	Isotope	Activity (Ci)	
	^{226}Th	10	
	^{227}Th	0.01	
	^{228}Th	0.001	
	^{229}Th	0.001	
	^{230}Th	0.001	
	$^{23`}$Th	100	
	^{232}Th	100	
	^{234}Th	10	
	Thorium (natural)	100	
NRC	Occupational dose limits		NRC 2017b
	Radiation		
	Adults		
	Annual limit, the more limiting of:		
	Total effective dose equivalent	5 rem (0.05 Sv) in a year	
	-or-		
	Sum of the deep-dose equivalent and the committed dose equivalent to any individual organ or tissue other than the lens of the eye	50 rem (0.5 Sv) in a year	
	Lens of the eye dose equivalent	15 rem (0.15 Sv) in a year	
	Shallow-dose equivalent to the skin of the whole body or to the skin of any extremity	50 rem (0.5 Sv) in a year	
	Minors	10% of the annual dose limits specified for adult workers	
	Embryo/fetus, dose equivalent during entire pregnancy for a declared pregnant woman	0.5 rem (5 mSv)	

Table 7-1. Regulations and Guidelines Applicable to Thorium

Agency	Description	Information	Reference
IAEA	Recommended occupational dose limits		IAEA 2014
	Radiation		
	Effective dose	20 mSv per year, averaged over 5 consecutive years, and not to exceed 50 mSv in any single year	
	Lens of the eye equivalent dose	20 mSv per year, averaged over 5 consecutive years, and not to exceed 50 mSv in any single year	
	Skin equivalent dose	500 mSv in a year	
	Hands and feet equivalent dose	500 mSv in a year	
	Recommended public dose limits		
	Radiation		
	Effective dose	1 mSv in a year	
	Lens of the eye equivalent dose	15 mSv in a year	
	Skin equivalent dose	50 mSv in a year	
	Emergency Criteria		
EPA	AEGLs-air	No data	EPA 2016
DOE	Protective Action Criteria (PACs)-air		DOE 2016b
	Thorium		
	PAC-1[e]	30 mg/m^3	
	PAC-2[e]	330 mg/m^3	
	PAC-3[e]	2,000 mg/m^3	
	Thorium hydroxide		
	PAC-1[e]	30 mg/m^3	
	PAC-2[e]	330 mg/m^3	
	PAC-3[e]	2,000 mg/m^3	
	Thorium dioxide		
	PAC-1[e]	30 mg/m^3	
	PAC-2[e]	330 mg/m^3	
	PAC-3[e]	2,000 mg/m^3	
	Thorium(IV) nitrate		
	PAC-1[e]	2.9 mg/m^3	
	PAC-2[e]	32 mg/m^3	
	PAC-3[e]	190 mg/m^3	
	Thorium nitrite		
	PAC-1[e]	30 mg/m^3	
	PAC-2[e]	330 mg/m^3	
	PAC-3[e]	2,000 mg/m^3	

Table 7-1. Regulations and Guidelines Applicable to Thorium

Agency	Description	Information	Reference
	Thorium oxalate		
	PAC-1[e]	30 mg/m^3	
	PAC-2[e]	330 mg/m^3	
	PAC-3[e]	2,000 mg/m^3	

[a]The EAFUS list of substances contains ingredients added directly to food that FDA has either approved as food additives or listed or affirmed as GRAS.
[b]Group 1: carcinogenic to humans
[c]Class refers to the retention (approximately days, weeks, or years) in the pulmonary region of the lung. This classification applies to a range of clearance half-times of <10 days for D, 10–100 days for W, and >100 days for Y.
[d]When an ALI is defined by the stochastic dose limit, this value alone is given. When an ALI is determined by the non-stochastic dose limit to an organ, the organ or tissue to which the limit applies is shown, and the ALI for the stochastic limit is shown in parentheses.
[e]Definitions of PAC terminology are available from U.S. Department of Energy (DOE 2016a).
PAC-1 values are based on the applicable AEGL-1, ERPG-1, or TEEL-1 values
PAC-2 values are based on the applicable AEGL-2, ERPG-2, or TEEL-2 values
PAC-3 values are based on the applicable AEGL-3, ERPG-3, or TEEL-3 values

AEGL = acute exposure guideline levels; ALI = annual limit on intake; DAC = derived air concentration; DOE = Department of Energy; EAFUS = Everything Added to Food in the United States; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; GRAS = generally recognized as safe; HHS = Department of Health and Human Services; IAEA = International Atomic Energy Agency; IARC = International Agency for Research on Cancer; IRIS = Integrated Risk Information System; MCL = maximum contaminant level; NIOSH = National Institute for Occupational Safety and Health; NRC = Nuclear Regulatory Commission; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; PAC = Protective Action Criteria; PEL = permissible exposure limit; REL = recommended exposure limit; RfC = inhalation reference concentration; RfD = oral reference dose; TLV = threshold limit values; TWA = time-weighted average; WHO = World Health Organization

CHAPTER 8. REFERENCES

Abbatt JD. 1979. History of the use and toxicity of Thorotrast. Environ Res 18:6-12.

*Abdel-Fattah AI, Zhou D, Boukhalfa H, et al. 2013. Dispersion stability and electrokinetic properties of intrinsic plutonium colloids: Implications for subsurface transport. Environ Sci Technol 47(11):5626-5634.

*Abe H, Kawahara T, Gondou K, et al. 1999. The reticuloendothelial system and macrophage-monocyte system in Thorotrast patients. Radiat Res 152(6 Suppl):S115-S117.

*Abel KJ, Young JA, Rancitelli LA. 1984. Atmospheric chemistry of inorganic emissions. In: Randerson D, ed. Atmospheric science and power production. Oak Ridge, TN: U.S. Department of Energy, The Technical Information Center, Office of Scientific and Technical Information, 423-465.

ACGIH. 2014. 2014 TLVs and BEIs: Based on the documentation of the threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinnati, OH: American Conference of Governmental Industrial Hygienists. OH241-54.

ACGIH. 2016. In: TLVs and BEIs based on the documentation of the threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.

Adelglass JM, Samara M, Cantor JO, et al. 1980. Thorotrast induced multiple carcinomatosis of the frontal sinus. Bull NY Acad Med 56:453-457.

*Aieta EM, Singley JE, Trussell AR, et al. 1987. Radionuclides in drinking water: An overview. Am Water Works Assoc J 79:144-152.

*Akkaya R. 2013. Uranium and thorium adsorption from aqueous solution using a novel polyhydroxyethylmethacrylate-pumice composite. J Environ Radioact 120:58-63.

*Albert R, Klevin P, Fresco J, et al. 1955. Industrial hygiene and medical survey of a thorium refinery. Arch Ind Health 11:234-242.

*Ali M, Kumar A, Pandey BN. 2014. Thorium induced cytoproliferative effect in human liver cell HepG2: Role of insulin-like growth factor 1 receptor and downstream signaling. Chem Biol Interact 211:29-35.

*Anderson RF, Bacon MP, Brewer PG. 1982. Elevated concentrations of actinides in Mono Lake (California, USA). Science 216:514-516.

*Andersson M, Storm HH. 1992. Cancer incidence among Danish Thorotrast-exposed patients. J Natl Cancer Inst 84(17):1318-1325.

*Andersson M, Carstensen B, Storm HH. 1995a. Mortality and cancer incidence after cerebral arteriography with or without Thorotrast. Radiat Res 142(3):305-320.

*Andersson M, Carstensen B, Visfeldt J. 1993a. Leukemia and other related hematological disorders among Danish patients exposed to Thorotrast. Radiat Res 134(2):224-233.

*Andersson M, Jonsson M, Nielsen LL, et al. 1995b. Mutations in the tumor suppressor gene p53 in human liver cancer induced by α-particles. Cancer Epidemiol Biomarkers Prev 4(7):765-770.

*Andersson M, Juel K, Ishikawa Y, et al. 1994a. Effects of preconceptional irradiation on mortality and cancer incidence in the offspring of patients given injections of Thorotrast. J Natl Cancer Inst 86(24):1866-1867.

*Andersson M, Juel K, Storm HH. 1993b. Pattern of mortality among Danish Thorotrast patients. J Clin Epidemiol 46(7):637-644.

*Andersson M, Vyberg M, Visfeldt J, et al. 1994b. Primary liver tumors among Danish patients exposed to Thorotrast. Radiat Res 137(2):262-273.

*Andersson M, Wallin H, Jonsson M, et al. 1995c. Lung carcinoma and malignant mesothelioma in patients exposed to Thorotrast: Incidence, histology and p53 status. Int J Cancer 63(3):330-336.

---

* Cited in text

8. REFERENCES

*APHA/AWWA/WPCF. 1985. Standard methods for the examination of water and wastewater. 16th ed. Washington, DC: American Public Health Association/American Water Works Association/Water Pollution Control Federation, 162-164.

*Archer VE, Wagoner JK, Lundin FE. 1973. Cancer mortality among uranium mill workers. J Occup Med 15:11-14.

*Arden JW, Gale NH. 1974. Separation of trace amounts of uranium and thorium and their determination by mass spectrometric isotope dilution. Anal Chem 46:687-691.

*Arnold AG, Oelbaum MH. 1980. Thorotrast administration followed by myelofibrosis. Postgrad Med J 56:124-127.

*ASTM. 1986. 1986 annual book of ASTM standards, Vol 11.01 (Section 11). Method D2333-80: Test method for thorium in water. American Society for Testing of Materials, 714-717.

*ATSDR. 1989. Decision guide for identifying substance-specific data needs related to toxicological profiles; Notice. Agency for Toxic Substances and Disease Registry. Fed Regist 54(174):37618-37634.

*ATSDR. 1990a. Toxicological profile for thorium. Atlanta, GA: Agency for Toxic Substances and Disease Registry, U.S. Department of Health and Human Services. Public Health Service

*ATSDR. 1990b. Toxicological profile for radium. Atlanta, GA: Agency for Toxic Substances and Disease Registry, U.S. Department of Health and Human Services. Public Health Service

*ATSDR. 1990c. Toxicological profile for radon. Atlanta, GA: Agency for Toxic Substances and Disease Registry, U.S. Department of Health and Human Services. Public Health Service.

*ATSDR. 1990d. Toxicological profile for uranium. Atlanta, GA: Agency for Toxic Substances and Disease Registry, U.S. Department of Health and Human Services. Public Health Service.

*ATSDR. 2012. Toxicological Profile for Radon. Atlanta, GA: Agency for Toxic Substances and Disease Registry, Department of Health and Human Services. Public Health Service

*ATSDR. 2013. Toxicological Profile for Uranium. Atlanta, GA: Agency for Toxic Substances and Disease Registry, Department of Health and Human Services. Public Health Service

*ATSDR. 2017. Thorium. Full SPL data. Substance priority list (SPL) resource page. Agency for Toxic Substances and Disease Registry, Centers for Disease Control and Prevention. http://www.atsdr.cdc.gov/SPL/resources/index.html. October 6, 2017.

*Baeza A, Guillen J. 2006. Influence of the soil bioavailability of radionuclides on the transfer of uranium and thorium to mushrooms. Appl Radiat Isot 64(9):1020-1026.

*Baglan N, Cossonnet C, Ritt J. 2001. Determination of 232Th in urine by ICP-MS for individual monitoring purposes. Health Phys 81(1):76-81.

Ballou JE, Hursh JB. 1972. The measurement of thoron in the breath of dogs administered inhaled or injected ThO2. Health Phys 22:155-159.

*Barnes DG, Dourson M. 1988. Reference dose (RfD): Description and use in health risk assessments. Regul Toxicol Pharmacol 8(4):471-486.

Baserga R, Yokoo H, Henegar GC. 1960. Thorotrast induced cancer in man. Cancer 13:1021-1031.

Baxter PJ, Anthony PP, Macsween RNM, et al. 1980a. Angiosarcoma of the liver: Annual occurrence and aetiology in Great Britain. Br J Ind Med 37:213-221.

*Baxter PJ, Langlands AO, Anthony PP, et al. 1980b. Angiosarcoma of the liver: A marker tumour for the late effects of Thorotrast in Great Britain. Br J Cancer 41:446-453.

*Becker N, Liebermann D, Wesch H, et al. 2008. Mortality among Thorotrast-exposed patients and an unexposed comparison group in the German Thorotrast study. Eur J Cancer 44(9):1259-1268.

Behari JR, Tandon SK, Mathur AK, et al. 1975. Histological and biochemical alterations in rat's liver and kidney induced by thorium nitrate. Arh Hig Rada Toksikol 26:267-274.

*BEIR III. 1980. The effects on populations of exposure to low levels of ionizing radiation. Committee on the Biological Effects of Ionizing Radiations, National Research Council. Washington, DC: National Academy Press.

8. REFERENCES

*BEIR IV. 1988. Health risks of radon and other internally deposited alpha-emitters. Committee on the Biological Effects of Ionizing Radiations, National Research Council. Washington, DC: National Academy Press, 245-275.

*BEIR V. 1990. Health effects of exposure to low levels of ionizing radiation. Committee on the Biological Effects of Ionizing Radiations, National Research Council. Washington, DC: National Academy Press.

*Beretka J, Mathew PJ. 1985. Natural radioactivity of Australian building materials, industrial wastes and by-products. Health Phys 48:87-95.

*Bernabee RP. 1983. A rapid method for the determination of americium, curium, plutonium and thorium in biological and environmental samples. Health Phys 44:688-692.

*Bigu J. 1985. Radon daughter and thoron daughter deposition velocity and unattached fraction under laboratory-controlled conditions and in underground uranium mines. J Aerosol Sci 16:157-165.

*Bodek I, Lyman WJ, Reehl RF, et al., eds. 1988. Environmental inorganic chemistry: Properties, processes and estimation methods. SETAC Special Publication Series, New York, NY: Pergamon Press, 9.2-19.

*Boecker BB. 1963. Thorium distribution and excretion studies. Am Ind Hyg Assoc J 24:155-163.

*Boecker BB, Thomas RG, Scott JK. 1963. Thorium distribution and excretion studies. II. General patterns following inhalation and the effect of the size of the inhaled dose. Health Phys 9:165-176.

*Boniforti R. 1987. Lanthanides, uranium, and thorium as possible simulators of the behavior of transuranics in the aquatic environment. Sci Total Environ 64:181-189.

*Boone IU, Rogers BS, White DC, et al. 1958. Toxicity excretion and tissue distribution of ionium (Th-230) in rats. Am Ind Hyg Assoc J 19:285-295.

*Bowen JH, Woodward BH, Mossler JA, et al. 1980. Energy dispersive x-ray detection of thorium dioxide. Arch Pathol Lab Med 104:459-461.

Brody H, Cullen M. 1957. Carcinoma of the breast seventeen years after mammography with Thorotrast. Surgery 42:600-606.

Brown WM, Buckton KE, Langlands AO, et al. 1967. The identification of lymphocyte clones with chromosome structural aberrations in irradiated men and women. Int J Radiat Biol 13:155-169.

*Bruenger FW, Miller SC, Lloyd RD. 1991. A comparison of the natural survival of beagle dogs injected intravenously with low levels of 239Pu, 226Ra, 228Ra, 228Th, or 90Sr. Radiat Res 126(3):328-337.

Brues AM. 1979. The long term follow-up of radium dial painters and thorium workers. Med Bases Radiat Accident Prep:441-450.

*Buckton KE, Langlands AO. 1973. The Edinburgh Thorotrast series - report of a cytogenetic study. In: 3rd International Meeting: Toxicity of Thorotrast, April 25-27, 1973. RISO Report No. 294:114-125.

*Bulman RA. 1976. Concentration of actinides in the food chain. United Kingdom: National Radiological Protection Board. NRPB-R-44.

Burnett WC. n.d. US-New Zealand cooperative research into the development and application of a new method for separation of uranium-series isotopes. Washington, DC: National Science Foundation, Division of International Programs.

Cantor JO, Adelglass J, Cerreta JM, et al. 1981. Collision tumor of the frontal sinus: Evidence of prior intrasinus instillation of Thorotrast. Laryngoscope 91:798-803.

*Carpenter R, Beasley TM, Zahnie D, et al. 1987. Cycling of fallout (plutonium, americium-241, cesium-137) and natural (uranium, thorium, lead210) radionuclides in Washington continental slope sediments. Geochim Cosmochim Acta 51:1897-1921.

*Carvalho FP, Oliveira JM, Malta M. 2014. Exposure to radionuclides in smoke from vegetation fires. Sci Total Environ 472:421-424.

CAS. 1990. Chemical Abstract Service. February 14, 1989.

*Chandramouleeswaran S, Ramkumar J, Sudarsan V, et al. 2011. Boroaluminosilicate glasses: Novel sorbents for separation of Th and U. J Hazard Mater 198:159-164.

8. REFERENCES

*Chen SB, Zhu YG, Hu QH. 2005. Soil to plant transfer of 238U, 226Ra and 232Th on a uranium mining-impacted soil from southeastern China. J Environ Radioact 82(2):223-236.

Chen XA, Cheng YE, Xiao H, et al. 2003. A 20-year follow-up study on the effects of long-term exposure to thorium dust. Chin Med J 116(5):692-694.

Chen XA, Cheng YE, Xiao H, et al. 2004. Health effects following long-term exposure to thorium dusts: A twenty-year follow-up study in China. Radioprotection 39(4):525-533.

*Chong CS, Chong HY, Fun HK, et al. 1985. Gamma radioactivity level in Sn slag dumps. Health Phys 49:1008-1010.

*Christensen P, Madsen MR, Jensen OM. 1983. Latency of Thorotrast-induced renal tumours. Survey of the literature and a case report. Scand J Urol Nephrol 17:127-130.

*Clewell HJ, Andersen ME. 1985. Risk assessment extrapolations and physiological modeling. Toxicol Ind Health 1(4):111-131.

*Clifton RJ, Farrow M, Hamilton EI. 1971. Measurements of Th-232 in normal and industrially exposed humans. Ann Occup Hyg 14:303-308.

*Cochran JK. 1984. The fates of uranium and thorium decay series nuclides in the estuarine environment. Estuary Filter, 179-220.

*Coles DG, Ragaini RC, Ondov JM, et al. 1979. Chemical studies of a stack fly ash from a coal-fired power plant. Environ Sci Technol 13:455-459.

*Conibear SA. 1983. Long term health effects of thorium compounds on exposed workers: The complete blood count. Health Phys 44(Suppl 1):231-237.

*Coorey KD. 1983. Thorotrast granuloma of the neck with local complications. Med J Aust 2:580-581.

*Costa-Ribeiro C, Barcinski MA, Figueiredo N, et al. 1975. Radiobiological aspects and radiation levels associated with the milling of monazite sand. Health Phys 28:225-231.

*Cothern CR. 1987. Development of regulations for radionuclides in drinking water. In: Graves B ed. Conference: NWWA, April 7-19, Somerset, NJ. Michigan: Lewis Publishers, 1-11.

*Cothern CR, Lappenbusch WL, Michel J. 1986. Drinking water contribution to natural background radiation. Health Phys 50:33-47.

*Cottrell WD, Haywood, FF, Witt, et al. 1981. Radiological survey of the Shpack Landfill, Norton, Massachusetts. Report DOE/EV-ORNL-5799, 0005/31. Oak Ridge, TN: Oak Ridge National Laboratory.

Dahlgren S. 1961. Thorotrast tumors: A review of the literature and report of two cases. Acta Pathol Microbial Scand 53:147.

*Dalheimer AR, Kaul A, Said MD. 1988. Analysis of tissue samples containing colloidal thorium dioxide (Thorotrast) or zirconium dioxide (Zirconotrast): Radiochemical preparation and alpha-spectrometry. Sci Total Environ 70:335-353.

*Dams R, Robbins JA, Rahn KA, et al. 1970. Nondestructive neutron activation analysis of air pollution particles. Anal Chem 42:861-867.

*da Motta LC, da Silva Horta J, Tavares MH. 1979. Prospective epidemiological study of Thorotrast exposed patients in Portugal. Environ Res 18:152-172.

*Dang HS, Jaiswal DD, Sunta CM. 1986. Daily intake of thorium by an Indian urban population. Sci Total Environ 57:73-77.

*Dang HS, Jaiswal DD, Sunta CM, et al. 1989. A sensitive method for the determination of Th in body fluids. Health Phys 57(3):393-396.

*da Silva Horta J. 1956. Late lesions in man caused by colloidal thorium dioxide (Thorotrast). Arch Pathol 62:403-418.

*da Silva Horta J. 1967a. Late effects of Thorotrast on the liver and spleen, and their efferent lymph nodes. Ann NY Acad Sci 145:675-699.

*da Silva Horta J. 1967b. Effects of colloidal thorium dioxide extravasates in the subcutaneous tissues of the cervical region in man. Ann NY Acad Sci 145:776.

da Silva Horta J, Moura NJ. 1979. Movement of Thorotrast aggregates in the bone marrow. Environ Res 18:184-191.

8. REFERENCES

*da Silva Horta J, Cayolla Da Motta L, Tavares MH. 1974. Thorium dioxide effects in man. Epidemiological clinical and pathological studies (experience in Portugal). Environ Res 8:131-159.

*Davis MW. 1985. Radiological significance of thorium processing in manufacturing. Report. INFO-0150.

*Dejgaard A, Krogsgaard K, Jacobsen M. 1984. Veno-occlusive disease and peliosis of the liver after Thorotrast administration. Virchows Archiv Pathol Anat 403:87-94.

*DOE. 2014a. Calculation of slope factors and dose coefficients. Oak Ridge, TN: U.S. Department of Energy. Oak Ridge National Laboratory. ORNL/TM-2013/00. https://epa-prgs.ornl.gov/radionuclides/SlopesandDosesFinal.pdf. June 20, 2018.

DOE. 2014b. [Appendices to:] Calculation of slope factors and dose coefficients. Oak Ridge, TN: U.S. Department of Energy. Oak Ridge National Laboratory. ORNL/TM-2013/00. https://epa-prgs.ornl.gov/radionuclides/SlopesandDosesMasterTableFinal.pdf. June 20, 2018.

*DOE. 2016a. Protective Action Criteria (PAC) with AEGLs, ERPGs, & TEELs: Rev. 29 for Chemicals of Concern - May 2016. Oak Ridge, TN: U.S. Department of Energy. https://energy.gov/ehss/protective-action-criteria-pac-aegls-erpgs-teels-rev-29-chemicals-concern-may-2016. March 2, 2017.

*DOE. 2016b. Table 3: Protective Action Criteria (PAC) Rev. 29 based on applicable 60-minute AEGLs, ERPGs, or TEELs. The chemicals are listed by CASRN. May 2016. Oak Ridge, TN: U.S. Department of Energy. https://sp.eota.energy.gov/pac/teel/Revision_29_Table3.pdf. February 28, 2017.

*dos Santos Silva I, Jones M, Malveiro F, et al. 1999. Mortality in the Portuguese Thorotrast study. Radiat Res 152(6 Suppl):S88-S92.

*dos Santos Silva I, Malveiro F, Jones ME, et al. 2003. Mortality after radiological investigation with radioactive Thorotrast: A follow-up study of up to fifty years in Portugal. Radiat Res 159(4):521-534.

Dougherty JH, Rosenblatt LS. 1971. Long term hematological effects of internal emitters in beagles. Radiat Res 48:319-331.

*Dougherty TF, Stover BJ, Dougherty JH, et al. 1962. Studies of the biological effects of Ra^{226} Pu^{239} $Ra^{228}(MsTH_1)$,Th^{228}(RdTh), and Sr^{90} in adult beagles. Radiat Res 17:625-681.

*Downs WL, Scott KJ, Maynard EA, et al. 1959. Studies on the toxicity of thorium nitrate. Report UR-561, Contract W-7401-eng-49. Atomic Energy Project, University of Rochester, Rochester, NY, 1-35.

Dudley RA. 1978. Bone irradiation in Thorotrast cases: Results of measurements at IAEA. Health Phys 35: 103-112.

*Early P, Razzak M, Sodee D. 1979. Nuclear medicine technology, 2nd ed. St. Louis: C.V. Mosby Company.

*Edgington DN. 1967. The estimation of thorium and uranium at the submicrogram level in bone by neutron activation. Int J Appl Radiat Isot 18:11-18.

*Eichholz G. 1982. Environmental aspects of nuclear power. Ann Arbor, MI: Ann Arbor Science.

Einck-Rosskamp P, Rajewsky B, Stahlhofen W. 1969. Cross placental passage of radium-228 and its daughters after intravenous injection of colloidal thorium. AEC Symp Ser 17:121-135.

*Ellis LC, Berliner DL. 1967. The effects of ionizing radiations on endocrine cells. Radiat Res 32:520-537.

*EPA. 1980. U.S. Environmental Protection Agency. Guidelines and methodology used in the preparation of health effect assessment chapters of the consent decree water criteria documents. Fed Regist 45:79347-79357.

*EPA. 1984. Background information document (integrated risk assessment). Final rules for radionuclides. Vol I. Washington, DC: U.S. Environmental Protection Agency, Office of Radiation Programs. EPA5201840221.

*EPA. 1987. Radiation protection guidance to federal agencies for occupational exposure; approval of Environmental Protection Agency recommendations. Fed Regist 52:2823-2834.

8. REFERENCES

*EPA. 1988a. Technological approaches to the cleanup of radiologically contaminated superfund sites. Washington, DC: U.S. Environmental Protection Agency, Office of Research and Development. EPA540288002.

*EPA. 1988b. Limiting values of radionuclide intake and air concentration and dose conversion factors for inhalation, submersion, and ingestion. Federal Guidance Report No. 11. Washington, DC: U.S. Environmental Protection Agency, Office of Radiation Programs. EPA520188020.

*EPA. 1988c. Maximum contaminant levels for radium-226, radium-228, and gross alpha-particle radioactivity in community water systems. 40 CFR 141.15. Fed Regist 533.

*EPA. 1989a. Interim Methods for Development of Inhalation References Doses. Washington, DC: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment. EPA600888066F.

*EPA. 1989b. Reportable quantity adjustment-radionuclides; Final rules. Fed Regist 54:22524-22543.

*EPA. 1993. Federal Guidance Report No. 12. External exposure to radionuclides in air, water, and soil. U.S. Environmental Protection Agency. EPA402R93081. https://www.epa.gov/sites/production/files/2015-05/documents/402-r-93-081.pdf. December 14, 2017.

*EPA. 1999. Federal Guidance Report No. 13: Cancer risk coefficients for environmental exposure to radionuclides. U.S. Environmental Protection Agency. EPA402R99001. https://www.epa.gov/radiation/federal-guidance-report-no-13-cancer-risk-coefficients-environmental-exposure. December 14, 2017.

*EPA. 2005. Toxic chemical release inventory reporting forms and instructions: Revised 2004 version. Section 313 of the Emergency Planning and Community Right-to-Know Act (Title III of the Superfund Amendments and Reauthorization Act of 1986). U.S. Environmental Protection Agency, Office of Environmental Information. EPA260B05001.

*EPA. 2009. National primary drinking water regulations. Washington, DC: U.S. Environmental Protection Agency, Office of Ground Water and Drinking Water. EPA816F090004. https://www.epa.gov/sites/production/files/2016-06/documents/npwdr_complete_table.pdf. September 7, 2017.

*EPA. 2012. Drinking water standards and health advisories. Washington, DC: U.S. Environmental Protection Agency, Office of Water. EPA822S12001. https://www.epa.gov/sites/production/files/2015-09/documents/dwstandards2012.pdf. April 25, 2013.

*EPA. 2014. National primary drinking water regulations. Washington, DC: U.S. Environmental Protection Agency, Office of Ground Water and Drinking Water.

*EPA. 2016. Acute Exposure Guideline Levels (AEGLs) values. U.S. Environmental Protection Agency. https://www.epa.gov/sites/production/files/2016-03/documents/compiled_aegl_update_.pdf. September 8, 2017.

*Ettenhuber E, Lehmann R. 1986. The collective dose equivalent due to the naturally occurring radionuclides in building materials in the German Democratic Republic. Part I: External exposure. Health Phys 50:49-56.

*Faber M. 1973. Effect of Thorotrast enriched with thorium-230. Danish Atomic Energy Commission, In: 3rd International Meeting: Toxicity of Thorotrast, April 25-27, 1973. RISO Report No. 294:294-302.

*Faber M. 1979. 28 years of continuous follow-up of patients injected with Thorotrast for cerebral angiography. Environ Res 18:37-43.

*Falk H, Telles NC, Ishak KG. 1979. Epidemiology of Thorotrast induced hepatic angiosarcoma in the USA. Environ Res 18:67-73.

*Farid I, Conibear SA. 1983. Hepatic function in previously exposed thorium refinery workers as compared to normal controls from the health and nutrition survey. Health Phys 44(Suppl 1):221-230.

8. REFERENCES

*FDA. 2013. Everything Added to Food in the United States (EAFUS). Washington, DC: U.S. Food and Drug Administration. http://www.accessdata.fda.gov/scripts/fcn/fcnnavigation.cfm?rpt=eafuslisting. January 8, 2014.

*FDA. 2017. Subpart B - Requirements for specific standardized beverages. Bottled water. U.S. Food and Drug Administration. Code of Federal Regulations 21 CFR 165.110 https://www.gpo.gov/fdsys/pkg/CFR-2017-title21-vol2/pdf/CFR-2017-title21-vol2-sec165-110.pdf. September 7, 2017.

FEDRIP. 1990. Federal Research in Progress. Databank. July 24, 1990.

*Filer TD. 1970. Fluorometric determination of submicrogram quantities of thorium. Anal Chem 42:1265-1267.

*Fischer P, Golob E, Kunze-Muehl E. 1967. Chromosomal aberrations in thorium dioxide patients. Ann NY Acad Sci 145:759-766.

*Fisenne IM, Perry PM, Decker KM, et al. 1987. The daily intake of 234,235,238U 228,230,232Th, and 226,228Ra by New York City residents. Health Phys 53:357-363.

*Fisher DR, Jackson PO, Brodaczynski GG, et al. 1983. Level of 234U, 238U and 230Th in excreta of uranium mill crushermen. Health Phys 45:617-630.

*Fisher NS, Teyssie JL, Krishnaswami S, et al. 1987. Accumulation of thorium, lead, uranium, and radium in marine phytoplankton and its geochemical significance. Limnol Oceanogr 32:131-142.

Fishman EK, Gayler BW, Kashima HK, et al. 1984. Computed tomography in the evaluation of cervical Thorotrast granuloma. J Comput Assist Tomogr 8:224-228.

*Frank AL. 1980. Diseases associated with exposure to metals-thorium. In: Last JMM-R, ed. Public health and preventive medicine. 11th ed. New York, NY: Appleton-Century-Crofts, 681-682.

*FRC. 1960. Federal Radiation Council. Radiation protection guidance for federal agencies. Fed Regist 60:4402-4403.

*Fried JF, Schubert J. 1961. Effect of chelating agent administration on the removal of monomeric and polymeric thorium. Radiat Res 15:227-235.

*Fruchter JS, Robertson DE, Evans JC, et al. 1980. Mount St. Helen's ash from the 18 May 1980 eruption: Chemical, physical, mineralogical, and biological properties. Science 29:1116-1125.

*Gafvert T, Pagels J, Holm E. 2003. Thorium exposure during tungsten inert gas welding with thoriated tungsten electrodes. Radiat Prot Dosimetry 103(4):349-357.

*Gaidova ES, Syao-Shan Y. 1970. Morphological changes in the lungs and other organs in rats on intratracheal administration of thorium dioxide. In: Letavet AA, Kurlyandskaya EB, eds. The toxicology of radioactive substances, Vol. 4. New York: Pergamon Press, 66-82.

*Gallegos G. 1995. Surveillance monitoring of soils for radioactivity: Lawrence Livermore National Laboratory 1976 to 1992. Health Phys 69(4):487-493.

*Garten CT Jr. 1978. A review of parameter values used to assess the transport of plutonium, uranium and thorium in terrestrial food chains. Environ Res 17:437-452.

*Gilbert GE, Casella VR, Bishop CT, et al. 1985. Isotopes of uranium and thorium, lead-210, and polonium-210 in the lungs of coal miners of Appalachia and the lungs and livers of residents of central Ohio. Energy Res Abstr 11:4090.

*Gilman JPW, Ruckerbauer GM. 1962. Metal carcinogenesis. I. Observations on the carcinogenicity of a refinery dust, cobalt oxide and colloidal thorium dioxide. Cancer Res 22:152-156.

*Glover SE, Traub RJ, Grimm CA, et al. 2001. Distribution of natural thorium in the tissues of a whole body. Radiat Prot Dosimetry 97(2):153-160.

*Golchert NW, Iwami FS, Sedlet J. 1980. Determination of actinides in soil. In: Lyon WS, ed. Radioelement analysis: Progress and problems. 23rd conference: Analytical Chemistry in Energy Technology, Gatlinburg, TN, October 9-11, 1979. Ann Arbor, MI: Ann Arbor Science Publishers, Inc., 215-222.

*Gonzalez-Vasconcellos I, Domke T, Kuosaite V, et al. 2011. Differential effects of genes of the Rb1 signalling pathway on osteosarcoma incidence and latency in alpha-particle irradiated mice. Radiat Environ Biophys 50(1):135-141.

8. REFERENCES

Goren AD, Harley N, Eisenbud L, et al. 1980. Clinical and radiobiologic features of Thorotrast induced carcinoma of the maxillary sinus. Oral Surg Oral Med Oral Pathol 49:237-242.

*Gossner W. 1982. Thorium II: Biological effects of thorium. In: Galle P, Masse R, eds. Radionuclide metabolism and toxicity symposium proceedings. Masson Publications, 273-280.

*Grampa G. 1967. Liver distribution of colloidal thorium dioxide and development of liver epithelial tumors in rats. Ann NY Acad Sci 145:738.

*Grampa G. 1971. Radiation injury with particular reference to Thorotrast. Pathol Ann 6:147-169.

*Greenberg RR, Kinston HM. 1982. Simultaneous determination of 12 trace elements in estuarine and sea water using pre-irradiation chromatography. In: 1981 International Conference: Modern trends in activation analysis, Part 3, Toronto, Ontario, Canada, June 15-16, 1981. J Radioanal Chem 71:147-168.

*Gridgeman NT. 1971. Methods of assay of the relative toxicity of certain bone seeking radionuclides. Radiat Res 48:291-302.

*Guimaraes JP, Lamerton LF. 1956. Further experimental observations on the late effects of Thorotrast administration. Br J Cancer 10:527.

*Guimaraes JP, Lamerton LF, Christensen WR. 1955. The late effects of Thorotrast administration: A review and experimental study. Br J Cancer 9:253.

*Gunning C, Scott AG. 1982. Radon and thoron daughters in housing. Health Phys 42:527-528.

*Hall RH, Stroud CA, Scott JK, et al. 1951. Acute toxicity of inhaled thorium compounds. Atomic Energy Project, University of Rochester, Rochester, NY. Report No. UR-190.

*Hallegot PH, Galle P. 1988. Microanalytical study of thorium 232 deposits in bone marrow and liver. Radiat Environ Biophys 27:67-78.

*Hamilton EI. 1971. The relative radioactivity of building materials. Am Ind Hyg Assoc J 32:398-403.

+Hannibal L. 1982. On the radiological significance of inhaled uranium and thorium ore dust. Health Phys 42:367-371.

*Hare D, Tolmachev S, James A, et al. 2010. Elemental bio-imaging of thorium, uranium, and plutonium in tissues from occupationally exposed former nuclear workers. Anal Chem 82(8):3176-3182.

*Harley NH, Fisenne IM. 1990. Distribution and alpha radiation dose from naturally occurring U, Th, and Ra in the human skeleton. Health Phys 58(4):515-518.

*Harley NH, Pasternack BS. 1979. Potential carcinogenic effects of actinides in the environment. Health Phys 37:291-300.

*Harmsen K, De Haan FAM. 1980. Occurrence and behaviour of uranium and thorium in soil and water. Neth J Agric Sci 28:40-62.

*Harrist TJ, Schiller AL, Trelstad RL, et al. 1979. Thorotrast-associated sarcoma of bone: A case report and review of the literature. Cancer 44:2049-2058.

*Hart DR, McKee PM, Burt AJ, et al. 1986. Benthic community and sediment quality assessment of Port Hope Harbor, Lake Ontario (Canada). J Great Lakes Res 12:206-220.

*Hawley GG, ed. 1981. The condensed chemical dictionary. 10th ed. New York, NY: Van Nostrand Reinhold, 881, 1021-1022.

*Hedrick JB. 1985. Thorium. Preprint from Bulletin 675: Mineral facts and problems, 1985 ed. Washington, DC: Bureau of Mines, U.S. Department of the Interior.

*Hedrick JB. 1987. Thorium. Preprint from the 1987 Bureau of Mines mineral yearbook. Washington, DC: Bureau of Mines, U.S. Department of the Interior.

Hemphill FM, Hesselgren RD. 1971. Thorotrast quantities and whole body counts. Health Phys 21:85-89.

*Hendee W. 1973. Radioactive isotopes in biological research. New York, NY: John Wiley and Sons.

*Hewson GS, Fardy JJ. 1993. Thorium metabolism and bioassay of mineral sands workers. Health Phys 64(2):147-156.

8. REFERENCES

*Heyerdahl H, Abbas N, Brevik EM, et al. 2012. Fractionated therapy of HER2-expressing breast and ovarian cancer xenografts in mice with targeted alpha emitting 227Th-DOTA-p-benzyl-trastuzumab. PLoS ONE 7(8):e42345.
*Heyerdahl H, Krogh C, Borrebaek J, et al. 2011. Treatment of HER2-expressing breast cancer and ovarian cancer cells with alpha particle-emitting 227Th-trastuzumab. Int J Radiat Oncol Biol Phys 79(2):563-570.
*Hirose K. 1988. Determination of thorium isotopes in seawater by using preconcentration of thorium-XO complexes on XAD-2 resin. J Radioanal Nucl Chem-Lett 127:199-207.
*Hirose K, Sugimura Y. 1987. Thorium isotopes in the surface air of the western north Pacific Ocean. J Environ Radioact 5:459-475.
*Hobbs C, McClellan RO. 1986. Radiation and radioactive materials. In: Klassen CD, Amdur MO, Doull J, eds. Casarett and Doull's Toxicology, 3rd ed. New York, NY: Macmillan Publishing Co., Inc., 497-530.
*Hodge HC, Maynard EA, Leach LJ. 1960. The chemical toxicity of thorium dioxide following inhalation by laboratory animals. University of Rochester Atomic Energy Project. Report UR-562. University of Rochester, Rochester, NY, 1-33.
*Hodgson SA, Stradling GN, Hodgson A, et al. 2003. Biokinetics and assessment of intake of thorium dioxide. Radiat Prot Dosimetry 105(1-4):115-118.
*Hoegerman SF, Cummins HT. 1983. Chromosome damage in peripheral lymphocytes from American thorium workers. Health Phys 44(Suppl 1):365-371.
*HSDB. 1990. Hazardous Substances Data Bank. National Library of Medicine, Washington, DC. February 14, 1989.
*Hu SJ, Kandaiya S. 1985. Radium-226 and 232Th concentration in Amang. Health Phys 49:1003-1007.
*Hu SJ, Chong CS, Subas S. 1981. U-238 and Th-232 in Cassiterites samples and Amang by-products. Health Phys 40:248-250.
*Hu SJ, Koo WK, Tan KL. 1984. Radioactivity associated with Amang upgrading plants. Health Phys 46:452-455.
*Huh C-A, Bacon MP. 1985. Determination of thorium concentration in seawater by neutron activation analysis. Anal Chem 57:2138-2142.
*Huh C-A, Zahnle DL, Small LF, et al. 1987. Budgets and behaviors of uranium and thorium series isotopes in Santa Monica basin (California, USA) sediments. Geochim Cosmochim Acta 51:1743-1754.
*Humphreys JA, Priest ND, Ishikawa Y. 1998. Thorotrast distribution in monkey bone marrow at early and late times after injection. Health Phys 74(4):442-447.
*Hunter KA, Hawke DJ, Choo LK. 1988. Equilibrium adsorption of thorium by metal-oxides in marine electrolytes. Geochim Cosmochim Acta 52:627-636.
*Hursh JB, Steadman LT, Looney WB, et al. 1957. The excretion of thorium and thorium daughters after Thorotrast administration. Acta Radiol 47:481-498.
*Hyman C, Paldino RL. 1967. Influence of sex hormones and tissues on colloidal thorium dioxide distribution and effects in rabbits. Ann NY Acad Sci 145:576-584.
*IAEA. 2014. Radiation protection and safety of radiation sources: International basic safety standards. IAEA safety standards series GSR Part 3. Vienna, Austria: International Atomic Energy Agency. http://www-pub.iaea.org/books/IAEABooks/8930/Radiation-Protection-and-Safety-of-Radiation-Sources-International-Basic-Safety-Standards. December 04, 2017.
*IARC. 1997. Silica, some silicates, coal dust and para-aramid fibrils. In: IARC Monograph Volume 68. Geneva: World Health Organization, International Agency for Research on Cancer.
*IARC. 2001. Some internally deposited radionuclides. In: Ionizing radiation, part 2, Volume 78. Geneva: World Health Organization, International Agency for Research on Cancer.

8. REFERENCES

*IARC. 2012. Internalized alpha-particle emitting radionuclides. IARC Monographs on the evaluation of carcinogenic risks to humans. Volume 100D. Radiation. Lyon, France: International Agency for Research on Cancer. http://monographs.iarc.fr/ENG/Monographs/vol100D/mono100D-9.pdf. November 7, 2017.

*IARC. 2014. Agents reviewed by the IARC Monographs. Volumes 1-109. Lyon, France: World Health Organization, International Agency for Research on Cancer.

*Ibrahim SA, Whicker FW. 1988. Comparative uptake of U and Th by native plants at a U production site. Health Phys 54:413-419.

*Ibrahim SA, Wrenn ME, Singh NP, et al. 1983. Thorium concentration in human tissues from two U.S. populations. Health Phys 44(Suppl 1):213-220.

*ICRP. 1966. International Commission on Radiological Protection. ICRP task group on lung dynamics, depositions and retention models for internal dosimetry of the human respiratory tract. Health Phys 21:173-207.

*ICRP. 1975. International Commission on Radiological Protection. Report of the Task Group on Reference Man. ICRP Publication 23. New York: Pergamon Press.

*ICRP. 1977. Recommendations of the International Commission on Radiological Protection. ICRP Publication 26. Vol. 1. No. 3. Oxford: Pergamon Press.

*ICRP. 1979. Limits for intakes of radionuclides by workers. International Commission on Radiological Protection. ICRP Publication 30. New York: Pergamon Press, 31, 32, 37, 100-101.

*ICRP. 1984. A compilation of the major concepts and quantities in use by ICRP. International Commission on Radiological Protection. ICRP Publication 42. Oxford: Pergamon Press.

*ICRP. 1994a. Appendix A: Age-specific biokinetic models for the alkaline earth elements and lead. Age-dependent doses to members of the public from intake of radionuclides: Part 2. Ingestion dose coefficients. International Commission on Radiological Protection. ICRP publication 67. Tarrytown, NY: International Commission on Radiological Protection, 95-120.

*ICRP. 1994b. ICRP Publication 66: Human respiratory tract model for radiological protection. International Commission on Radiological Protection.

*ICRP. 1995. ICRP Publication 69: Age-dependent doses to members of the public from intake of radionuclides: Part 3. Ingestion dose coefficients. The International Commission on Radiological Protection. Smith H, editor. Tarrytown, NY: Elsevier Science, Inc.

*ICRP. 1996. ICRP Publication 71: Age-dependent doses to members of the public from intake of radionuclides: Part 3 Inhalation dose coefficients. The International Commission on Radiological Protection. Smith H, Ed. Tarrytown, NY: Elsevier Science, Inc.

*ICRP. 2001. The ICRP database of dose coefficients workers and members of the public. Version 2.01. Thorium: International Commission on Radiological Protection. Elsevier Science Ltd.

*ICRP. 2006. Description of the model. New York, NY: International Commission on Radiological Protection.

*ICRP. 2007. Publication no. 103. The 2007 recommendations of the International Commission on Radiological Protection. Ann ICRP 37(2-4):98-99. November 27, 2017.

*ICRP. 2010. Conversion coefficients for radiological protection quantities for external radiation exposures. ICRP Publication 116, Ann ICRP 40(2-5). The International Commission on Radiological Protection and The International Commission on Radiation Units and Measurements. http://www.icrp.org/publication.asp?id=icrp%20publication%20116. February 1, 2018.

*ICRP. 2012. Compendium of dose coefficients based on ICRP Publication 60. ICRP Publication 119. Ann ICRP 41 (Suppl). The International Commission on Radiological Protection. http://www.icrp.org/publication.asp?id=ICRP%20Publication%20119. February 1, 2018.

ICRU. 1980. International Commission on Radiation Units and Measurements. ICRU Report No. 33. Washington, DC.

*Inn KGW. 1987. The National Bureau of Standards freshwater lake sediment environmental-level radioactivity standard reference material. J Radioanal Nucl Chem 115:91-112.

*IRIS. 2014. Integrated Risk Information System. Washington, DC.

8. REFERENCES

*IRIS. 2017. Integrated Risk Information System. Washington, DC: U.S. Environmental Protection Agency. http://www.epa.gov/iris/. September 11, 2017.

Ishihara T, Kohno S, Hayta I, et al. 1978. Nine year cytogenetic follow up of a patient injected with Thorotrast. Hum Genet 42:99-108.

Ishikawa Y, Kagaya H, Saga K. 2004. Biomagnification of 7Be, 234Th, and 228Ra in marine organisms near the northern Pacific coast of Japan. J Environ Radioact 76(1-2):103-112.

Ishikawa Y, Mori T, Kato Y, et al. 1992. Lung cancers associated with Thorotrast exposure: High incidence of small-cell carcinoma and implications for estimation of radon risk. Int J Cancer 52(4):570-574.

Ishikawa Y, Mori T, Machinami R. 1995. Lack of apparent excess of malignant mesothelioma but increased overall malignancies of peritoneal cavity in Japanese autopsies with Thorotrast injection into blood vessels. J Cancer Res Clin Oncol 121(9-10):567-570.

*Isner JM, Sazama KJ, Roberts WC. 1978. Vascular complications of thorium dioxide. Am J Med 67:1069-1074.

*Iyengar GV, Kawamura H, Dang HS, et al. 2004. Contents of cesium, iodine, strontium, thorium, and uranium in selected human organs of adult Asian population. Health Phys 87(2):151-159.

*Ito Y, Kojiro M, Nakashima T, et al. 1988. Pathomorphologic characteristics of 102 cases of Thorotrast-related hepatocellular carcinoma, cholangiocarcinoma, and hepatic angiosarcoma. Cancer 62:1153-1162.

*Jadon A, Mathur R. 1983. Gametogenic count and histopathological effect of thorium nitrate and uranyl nitrate on mice testes. Andrologia 15:40-43.

*Jaiswal DD, Singh IS, Nair S, et al. 2004. Comparison of observed lung retention and urinary excretion of thorium workers and members of the public in India with the values predicted by the ICRP biokinetic model. Radiat Prot Dosimetry 112(2):237-243.

*James A. 1987. A reconsideration of cells at risk and other key factors in radon daughter dosimetry. In: Hopke P, ed. Radon and its decay products: Occurrence, properties and health effects. ACS Symposium Series 331. Washington, DC: American Chemical Society, 400-418.

*James A, Roy M. 1988. Dosimetric lung models. In: Gerber G, et al., ed. Age-related factors in radionuclide metabolism and dosimetry. Boston, MA: Martinus Nijhoff Publishers, 95-108.

*Jeambrun M, Pourcelot L, Mercat C, et al. 2012. Potential sources affecting the activity concentrations of 238U, 235U, 232Th and some decay products in lettuce and wheat samples. J Environ Monit 14(11):2902-2912.

*Jeanson A, Ferrand M, Funke H, et al. 2010. The role of transferrin in actinide(IV) uptake: Comparison with iron(III). Chemistry 16(4):1378-1387.

*Jee WS, Dockum NL, Mical RS, et al. 1967. Distribution of thorium daughters in bone. Ann NY Acad Sci 145:660-673.

*Jensen L, Regan G, Goranson S, et al. 1984. Ambient monitoring of airborne radioactivity near a former thorium processing plant. Health Phys 46:1021-1033.

*Jiang FS, Kuroda PK. 1987. Variation of the isotopic composition of thorium in the atmosphere. Radiochim Acta 42123-28.

*Jiang FS, Lee SC, Bakhtiar SN, et al. 1986. Determination of thorium, uranium and plutonium isotopes in atmospheric samples. J Radioanal Nucl Chem 100:65-72.

*Johansen C. 1967. Tumors in rabbits after injections of various amounts of thorium dioxide. NY Acad Sci 145:724

*Johannson L. 1982. Oral intake of radionuclides in the population: A review of biological factors of relevance for assessment of absorbed dose at long term waste storage. FOA Report C40161-W4. DE 83-704553.

Johannsson W, Perrault G, Savoie L, et al. 1968. Action of various metallic chlorides on calcaemia and phosphataemia. Br J Pharamcol Chemother 33:91-97.

*Johnson JR, Lamothe ES. 1989. A review of the dietary uptake of Th. Health Phys 56:165-168.

8. REFERENCES

*Joshi SR. 1987. Nondestructive determination of selected uranium and thorium-series radionuclides in biological samples. Health Phys 53:417-420.
*Joyet G. 1971. The thorium-series in cigarettes and lungs of smokers. Experientia 27:85-89.
*Kamboj MP, Kar AB. 1964. Antitesticular effect of metallic and rare earth salts. J Repro Fertil 7:21-28.
*Kamijo A, Okabe K, Hirose T. 1979. Thorium dioxide granuloma of the neck with resultant fatal hemorrhage. Arch Otolaryngol 105:45-47.
*Kamiyama R, Ishikawa Y, Hatakeyama S, et al. 1988. Clinicopathological study of hematological disorders after Thorotrast administration in Japan. Blut 56:153-160.
Kaneko M, Kamiya Y, Hoshino M, et al. 1981. Identification and mapping of Thorotrast in tissue by analytical electron microscopy. Health Phys 41:677-680.
*Kato H, Schull W. 1982. Studies of the mortality of A-bomb survivors. Report 7, Part 1: Cancer mortality among atomic bomb survivors, 1950-78. Radiat Res 90:395-432.
*Kato I, Kido C. 1987. Increased risk of death in Thorotrast-exposed patients during the late follow-up period. Jpn J Cancer Res 78:1187-1192.
*Kato Y, Mori T, Kumatori T. 1979. Thorotrast dosimetric study in Japan. Environ Res 18:32-36.
*Kato Y, Mori T, Kumatori T. 1983. Estimated absorbed dose in tissues and radiation effects in Japanese Thorotrast patients. Health Phys 44(Suppl 1):273-279.
*Kathren RL, Hill RL. 1992. Distribution and dosimetry of Thorotrast in USUR case 1001. Health Phys 63(1):72-88.
Katzin LI. 1983. Thorium and thorium compounds. In: Grayson M, Eckroth D, eds. Kirk-Othmer encyclopedia of chemical technology, Vol 22, 3rd ed. New York, NY: John Wiley and Sons, 989-1002.
*Kaul A, Heyder J. 1972. Clearance of thorium-232 and daughters from the blood. In: Symposium: Assessment Radioactive Contam Man, 469-481.
*Kaul A, Muth H. 1978. Thorotrast kinetics and radiation dose. Results from studies in Thorotrast patients and from animal experiments. Radiat Environ Biophys 15:241-259.
*Kaul A, Noffz W. 1978. Tissue dose in Thorotrast patients. Health Phys 35:113-121.
Kaul A, Foll U, Haase VA, et al. 1979. Microdistribution of Thorotrast and dose to cellular structures. Environ Res 18:13-22.
*Kauzlaric D, Barmeir E, Luscieti P, et al. 1987. Renal carcinoma after retrograde pyelography with Thorotrast. Am J Radiol 148:897-898.
*Keane AT, Brewster DR. 1983. Calibration of a decay-product collection and counting apparatus for the determination of exhaled thoron. Health Phys 45:801-805.
*Keane AT, Lucas HF, Markun F, et al. 1986. The estimation and potential radiobiological significance of the intake of radium-228 by early radium dial workers in Illinois. Health Phys 51:313-328.
*Keller G, Folkerts KH. 1984. Radon-222 concentrations and decay-product equilibrium in dwellings and in the open air. Health Phys 47:385-398.
*Kemmer W. 1979. A field study in 156 Thorotrast cases: Results of biophysical measurements and clinical examinations. Environ Res 18:147-151.
*Kemmer W, Muth H, Tranekjer F. 1971. Dose dependence of the chromosome aberration rate in Thorotrast patients. Biophysik 7:342-351.
*Kemmer W, Muth H, Trandkjer F, et al. 1973. Chromosome aberrations caused by Thorotrast. In: 3rd International Meeting: Toxicity of Thorotrast, April 25-27, 1973. RISO Report 294:104-113.
*Kemmer W, Steinstraesser A, Muth H. 1979. Chromosome aberrations as a biological dosimeter in Thorotrast patients: Dosimetric problems. Environ Res 18:178-183.
*Kido C, Sasaki F, Hirota Y, et al. 1999. Cancer mortality of Thorotrast patients in Japan: The second series updated 1998. Radiat Res 152(6 Suppl):S81-S83.
*Kobashi A, Tominaga T. 1985. Radium-228-thorium-228 dating of plant samples. Int J Appl Radiat Isot 36:547-554.

8. REFERENCES

*Kojiro M, Nakashima T, Ito Y, et al. 1985. Thorium dioxide-related angiosarcoma of the liver. Pathomorphologic study of 29 autopsy cases. Arch Pathol Lab Med 109:853-857.

*Korte N, Kollenbach M, Donivan S. 1983. The determination of uranium, thorium, yttrium, zirconium and hafnium in zircon. Analyt Chim Acta 146:267-270.

*Kotrappa P, Bhanti DP, Menon VB, et al. 1976. Assessment of airborne hazards in the thorium processing industry. Am Ind Hyg Assoc J 37:613-616.

Krey P, Fiseene I, Perry P, et al. n.d. Natural radioactivity in the biosphere. Environmental Measurements Laboratory, New York, NY.

*Krishnan K, Anderson ME, Clewell HJ, et al. 1994. Physiologically based pharmacokinetic modeling of chemical mixtures. In: Yang RSH, ed. Toxicology of chemical mixtures. Case studies, mechanisms, and novel approaches. San Diego, CA: Academic Press, 399-437.

*Kumar A, Ali M, Mishra P, et al. 2009. Thorium-induced neurobehavioural and neurochemical alterations in Swiss mice. Int J Radiat Biol 85(4):338-347.

*Kumar A, Ali M, Pandey BN, et al. 2010. Role of membrane sialic acid and glycophorin protein in thorium induced aggregation and hemolysis of human erythrocytes. Biochimie 92(7):869-879. http://doi.org/10.1016/j.biochi.2010.03.008.

*Kumar A, Sharma P, Ali M, et al. 2012. Decorporation and therapeutic efficacy of liposomal-DTPA against thorium-induced toxicity in the Wistar rat. Int J Radiat Biol 88(3):223-229.

*Kuppers G. 2001. Determination of 232Th by neutron activation analysis using isotope-related ki factors. Radiat Prot Dosim 97(2):123-125.

Kurlyandskaya EB. 1970. Certain aspects of the toxicology of insoluble compounds of thorium-232 and uranium-238. In: Letavet AA, Kurlyandskaya EB, eds. The toxicology of radioactive substances, Vol. 4. New York: Pergamon Press, 1-8.

*Kuroda PK, Barbod T, Bakhtiar SN. 1987. Effect of the eruptions of Mount St. Helens and El Chichon on the ratios of thorium and uranium isotopes in rain. J Radioanal Nucl Chem 111:137-146.

*Kyle RH, Oler A, Lasser EC, et al. 1963. Meningioma induced by thorium dioxide. New Engl J Med 368:80-82.

*Kyoizumi S, Umeki S, Akiyama M, et al. 1992. Frequency of mutant T lymphocytes defective in the expression of the T-cell antigen receptor gene among radiation-exposed people. Mutat Res 265(2):173-180.

*LaFlamme BD, Murray JW. 1987. Solid/solution interaction: The effect of carbonate alkalinity on adsorbed thorium. Geochim Cosmochim Acta 51:243-250.

*Lambert JPF, Wilshire FW. 1979. Neutron activation analysis for simultaneous determination of trace elements in ambient air collected on glass-fiber filters. Anal Chem 51:1346-1350.

*Laul JC, Smith MR, Thomas CW, et al. 1987. Analysis of natural radionuclides from uranium and thorium series in briney groundwaters. J Radioanal Nucl Chem 110:101-112.

*Lauria DC, Godoy JM. 1988. A sequential analytical method for the determination of uranium-238, thorium-232, thorium-230, thorium-228, radium228, and radium-226 in environmental samples. Sci Total Environ 70:83-99.

*Lazo EN, Roessler GS, Berven BA. 1991. Determination of uranium and thorium concentrations in unprocessed soil samples. Health Phys 61(2):231-243.

*Le Du A, Sabatie-Gogova A, Morgenstern A, et al. 2012. Is DTPA a good competing chelating agent for Th(IV) in human serum and suitable in targeted alpha therapy? J Inorg Biochem 109:82-89.

*Lenka P, Sahoo SK, Mohapatra S, et al. 2013. Ingestion dose from 238U, 232Th, 226Ra, 40K and 137Cs in cereals, pulses and drinking water to adult population in a high background radiation area, Odisha, India. Radiat Prot Dosimetry 153(3):328-333.

*Levowitz BS, Hughes RE, Alford TC. 1963. Treatment of thorium dioxide granulomas of the neck. New Engl J Med 268:340-342.

*Levy DW, Rindsberg S, Friedman AC, et al. 1986. Thorotrast-induced hepatosplenic neoplasia: CT identification. Am J Radiol 146:997-1004.

8. REFERENCES

*Li GY, Hu N, Ding DX, et al. 2011. Screening of plant species for phytoremediation of uranium, thorium, barium, nickel, strontium and lead contaminated soils from a uranium mill tailings repository in South China. Bull Environ Contam Toxicol 86(6):646-652.

*Li WB, Karpas Z, Salonen L, et al. 2009. A compartmental model of uranium in human hair for protracted ingestion of natural uranium in drinking water. Health Phys 96(6):636-645.

*Li WB, Wahl W, Oeh U, et al. 2007. Biokinetic modelling of natural thorium in humans by ingestion. Radiat Prot Dosimetry 125(1-4):500-505.

*Likhachev YuP. 1976. Pathological anatomy, etiology and pathogenesis of remote sequelae of radiation dust exposure. Arkh Patol 38:18-26. [Russian]

*Likhachev YuP, Lyarskii PP, Elovskaya LT. 1973a. Morphological changes in the lungs with chronic inhalation of thorium dioxide. Med Radiol 18:35-41. [Russian]

*Likhachev YuP, Lyarskii PP, Elovskaya LT. 1973b. Pulmonary neoplasms in rats in chronic inhalation of thorium dioxide. Vopr Onkol 19:47-54.

*Linsalata P, Franca EP, Eisenbud M. 1985. Determination of the human intake of thorium and the light rare earth elements from high and typical natural radiation environments. Trace Subst Environ Health 19:257-263.

Linsalata P, Eisenbud M, Franca EP. 1986. Ingestion estimates of thorium and the light rare earth elements based on measurements of human feces. Health Phys 50:163-167.

*Linsalata P, Morse RS, Ford H, et al. 1989. An assessment of soil-to-plant concentration ratios for some natural analogues of the transuranic elements. Health Phys 56:33-46.

*Linsalata P, Penna Franca E, Sachett I, et al. 1987. Radium, thorium, and the light rare earth elements in soils and vegetables grown in an area of high natural radioactivity. DOE Symp Ser 59:131-146.

*Lipchik EO, Russell SB, Raphael MJ, et al. 1972. Effect of Thorotrast on the canine heart. Br J Radiol 45:142-145.

*Little TT, Miller G, Guilmette R. 2003. Internal dosimetry of uranium isotopes using Bayesian inference methods. Radiat Prot Dosimetry 105(1-4):413-416.

*Little TT, Miller G, Guilmette R, et al. 2007. Uranium dose assessment: A Bayesian approach to the problem of dietary background. Radiat Prot Dosimetry 127(1-4):333-338.

*Littlefield LG, Travis LB, Sayer AM, et al. 1997. Cumulative genetic damage in hematopoietic stem cells in a patient with a 40-year exposure to alpha particles emitted by thorium dioxide. Radiat Res 148(2):135-144.

*Liu Z, Lee TS, Kotek TJ. 1992. Mortality among workers in a thorium-processing plant--a second follow-up. Scand J Work Environ Health 18(3):162-168.

*Livingston HD, Cochran JK. 1987. Determination of transuranic and thorium isotopes in ocean water in solution and in filterable particles. J Radioanal Nucl Chem 115:299-308.

*Lloyd RD, Jones CW, Mays CW, et al. 1984. Thorium-228 retention and dosimetry in beagles. Radiat Res 98:614-628.

*Lloyd RD, Angus W, Taylor GN, et al. 1995. Soft tissue tumors among beagles injected with 90Sr, 228Ra, or 228Th. Health Phys 69(2):272-277.

*Lloyd RD, Wrenn ME, Taylor GN, et al. 1985. Toxicity of 228Ra and 228Th relative to 226Ra for bone sarcoma induction in beagles. Strahlentherapie [Sonderb] 80:65-69.

*Lucas HF Jr., Edgington DN, Markun F. 1970. Natural thorium in human bone. Health Phys 19:739-742.

Lucas HF Jr, Markun F, May H, et al. 1972. Thorium daughters in the spleen of a Thorotrast case. Health Phys 23:575-576.

*Ludwig T, Schwass D, Seitz G, et al. 1999. Intakes of thorium while using thoriated tungsten electrodes for TIG welding. Health Phys 77(4):462-469.

*Luetzelschwab JW, Googins SW. 1984. Radioactivity released from burning gas lantern mantles. Health Phys 46:873-881.

*Lung RJ, Harding RL, Herceg SJ, et al. 1978. Long-term survival with Thorotrast cervical granuloma. J Surg Oncol 10:171-177.

8. REFERENCES

*Luz A, Linzner U, Müller WA, et al. 1979. Osteosarcoma induction by simultaneous incorporation of 227Th and 227Ac. Biological implications of radionuclides released from nuclear industries, Vol. 1. Vienna: International Atomic Energy Agency, 141-151.

*Luz A, Müller WA, Schaffer E, et al. 1985. The sensitivity of female NMRI mice of different ages for osteosarcoma induction with 227Thorium. Strahlentherapie [Sonderb] 80:178-182.

*Lytle DA, Sorg T, Wang L, et al. 2014. The accumulation of radioactive contaminants in drinking water distribution systems. Water Res 50:396-407.

*Maletskos DJ, Keane AT, Telles NC, et al. 1969. Retention and absorption of Ra-224 and Th-234 and some dosimetric considerations of Ra-224 in human beings. In: May C, ed. Delayed effects of bone-seeking radionuclides. Salt Lake City, UT: University of Utah Press, 29-49.

*Martling U, Mattsson A, Travis LB, et al. 1999. Mortality after long-term exposure to radioactive Thorotrast: A forty-year follow-up survey in Sweden. Radiat Res 151(3):293-299.

*Mausner LF. 1982. Inhalation exposures at a thorium refinery. Health Phys 42:231-236.

*May CC, Young L, Worsfold PJ, et al. 2012. The effect of EDTA on the groundwater transport of thorium through sand. Water Res 46(15):4870-4882.

*Mays CW. 1978. Endosteal dose to Thorotrast patients. Health Phys 35:123-125.

*Mays CW. 1988. Alpha-particle-induced cancer in humans. Health Phys 55:637-655.

*Mays CW, Dougherty TF. 1972. Progress in the beagle studies at the University of Utah. Health Phys 22:793-801.

*Mays CW, Lloyd RD, Taylor GN, et al. 1987. Cancer incidence and lifespan vs. alpha-particle dose in beagles. Health Phys 52:617-624.

*Mayya YS, Prasad SK, Nambiar PPVJ, et al. 1986. Measurement of 220Rn in exhaled breath of Th plant workers. Health Phys 51:737-744.

*McClinton LT, Schubert J. 1948. The toxicity of some zirconium and thorium salts in rats. J Pharmacol Exp Ther 94:1-6.

*McElearney N, Irvine D. 1993. A study of thorium exposure during tungsten inert gas welding in an airline engineering population. J Occup Med 35(7):707-711.

McInroy JF. n.d. Measurements of plutonium and metals in man. Los Alamos, NM: Los Alamos National Laboratory.

*McInroy JF, Gonzales ER, Miglio JJ. 1992. Measurement of thorium isotopes and 228Ra in soft tissues and bones of a deceased Thorotrast patient. Health Phys 63(1):54-71.

*McKee PM, Snodgrass WJ, Hart DR, et al. 1987. Sedimentation rates and sediment core profiles of uranium-238 and thorium-232 decay chain radionuclides in a lake affected by uranium mining and milling. Can J Fish Aquat Sci 44:390-398.

*McNabb GJ, Kirk JA, Thompson JL. 1979. Radio nuclides from phosphate ore processing plants: The environmental impact after 30 years of operation. Health Phys 34:585-587.

*McNeill KG, Molla MA, Harrison JE. 1973. Distribution of thorium series nuclides in beagles after intraspinal Thorotrast injection. Health Phys 24:403-409.

Mettler F. 1985. Medical effects of ionizing radiation. New York, NY: Grune and Stratton.

*Metzger R, McKlveen JW, Jenkins R, et al. 1980. Specific activity of uranium and thorium in marketable rock phosphate as a function of particle size. Health Phys 39:69-76.

*Michael TH, Murray C. 1970. The effects of a blockading agent on the primary immune response. J Immunol 105:411-415.

*Miekeley N, Kuchler IL. 1987. Interactions between thorium and humic compounds in surface waters. Inorg Chim Acta 140:315-319.

*Milic, NB, Suranji TM. 1982. Hydrolysis of the thorium(IV) ion in sodium nitrate medium. Can J Chem 60:1298-1303.

*Moffett D, Tellier M. 1978. Radiological investigations of an abandoned uranium tailings area. J Environ Qual 7:310-314.

*Mola M, Nieto A, Penalver A, et al. 2014. Uranium and thorium sequential separation from norm samples by using a SIA system. J Environ Radioact 127:82-87.

*Molla MAR. 1975. Radionuclides in the autopsy samples from Thorotrast patients. Health Phys 28:295-297.

Molla MAR, Harrison JE, McNeill KG. 1976. Doses to the cauda equina due to Thorotrast myelography. Health Phys 31:109-114.

Monath TP, Borden EC. 1971. Effects of Thorotrast on humoral antibody viral multiplication and interferon during infection with St. Louis encephalitis virus in mice. J Infect Dis 123:297-300.

*Moore JW, Sutherland DJ. 1981. Distribution of heavy metals and radionuclides in sediments, water, and fish in an area of Great Bear Lake contaminated with mine wastes. Arch Environ Contam Toxicol 10:329-338.

*Moores SR, Black A, Lambert BE, et al. 1980. Deposition of thorium and plutonium oxides in the respiratory tract of the mouse. DOE Symp Ser 53:103-118.

*Mori T, Kato Y. 1991. Epidemiological, pathological and dosimetric status of Japanese Thorotrast patients. J Radiat Res 32(Suppl) 2:34-45.

*Mori T, Fukutomi K, Kato Y, et al. 1999a. 1998 results of the first series of follow-up studies on Japanese Thorotrast patients and their relationships to an autopsy series. Radiat Res 152(6 Suppl):S72-S80.

*Mori T, Kato Y, Aoki N, et al. 1983b. Statistical analysis of Japanese Thorotrast-administered autopsy cases--1980. Health Phys 44(Suppl 1):281-292.

*Mori T, Kato Y, Kumatori T, et al. 1983a. Epidemiological follow-up study of Japanese Thorotrast cases--1980. Health Phys 44(Suppl 1):261.-272.

*Mori T, Kato Y, Shimamini T, et al. 1979. Statistical analysis of Japanese Thorotrast-administered autopsy cases. Environ Res 18:231.

*Mori T, Kido C, Fukutomi K, et al. 1999b. Summary of entire Japanese Thorotrast follow-up study: Updated 1998. Radiat Res 152(6 Suppl):S84-S87.

*Morton LS, Evans CV, Estes GO. 2002. Natural uranium and thorium distributions in podzolized soils and native blueberry. J Environ Qual 31(1):155-162.

Müller WA. 1971. Studies on short-lived internal emitters in mice and rats. Int J Radiat Bio 20:233-243.

*Müller WA, Gijssner W, Hug O, et al. 1978. Late effects after incorporation of the short-lived alpha-emitters radium-224 and thorium-227 in mice. Health Phys 35:33-55.

*Müller WA, Luz A, Schaffer EH, et al. 1983. The role of time-factor and RBE for the induction of osteosarcomas by incorporated short-lived boneseekers. Health Phys 44(Suppl 1):203-212.

*Müller WA, Nenot JC, Daburon ML, et al. 1975. Metabolic and dosimeter studies after inhalation of Th-227 in rats with regard to the risk of lung and bone tumors. Radiat Environ Biophys 11:309-318.

*Munita CS, Mazzilli BP. 1986. Determination of trace elements in Brazilian cigarette tobacco by neutron activation analysis. J Radioanal Nucl Chem 108:217-228.

*Mustonen R, Jantunen M. 1985. Radioactivity of size fractionated fly-ash emissions from a peat- and oil-fired power plant. Health Phys 49:1251-1260.

*Nakaoka A, Fukushima M, Takagi S. 1984. Environmental effects of natural radionuclides from coal-fired power plants. Health Phys 47:407-416.

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

*NCRP 1971. Basic radiation protection criteria. National Council on Radiation Protection and Measurements. NCRP Report No. 39. Washington, DC.

*NCRP. 1985. A handbook of radioactivity measurements procedures. 2nd ed. Bethesda, MD: National Council on Radiation Protection and Measurements. NCRP Report No. 58.

*NCRP. 1997. Deposition, retention and dosimetry of inhaled radioactive substances. NCRP Report No. 125. Bethesda, MD: National Council on Radiation Protection and Measurements.

*Neton JW, Ibrahim SA. 1978. Alpha emitting radio nuclides in cigarette tobacco. Health Phys 35:922.

*Newton D, Rundo J, Eakins JD. 1981. Long-term retention of thorium-228 following accidental intake. Health Phys 40:291-298.

Nielsen M, Albrechtsen R, Johnson NJ, et al. 1979. Carcinoma of the parotid gland following sialography with Thorotrast. Acta Otolaryngol 88:462-467.

*NIH. 2018. PubChem Open Chemistry Database. National Institutes of Health. U.S. National Library of Medicine. National Center for Biotechnology Information. https://pubchem.ncbi.nlm.nih.gov/compound/44150929#section=Top. March 7, 2018.

*NIOSH. 2014. NIOSH pocket guide to chemical hazards. Atlanta, GA.

*NIOSH. 2016. NIOSH pocket guide to chemical hazards. Index of Chemical Abstracts Service Registry Numbers (CAS No.). Atlanta, GA: National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention. https://www.cdc.gov/niosh/npg/npgdcas.html. September 11, 2017.

*Nishioka H. 1975. Mutagenic activities of metal compounds in bacteria. Mutat Res 31:185-190.

*NNDC. 2018. Interactive chart of nuclides. National Nuclear Data Center. http://www.nndc.bnl.gov/chart/. March 5, 2018.

*NRC. 1988. Maximum permissible concentrations for uranium and thorium. Nuclear Regulatory Commission. 10 CFR 20 151:4115 and 151:4117.

*NRC. 2017a. Appendix B - Annual limits on intake (ALIs) and derived air concentrations (DACs) of radionuclides for occupational exposure. Code of Federal Regulations. Occupational Safety and Health Standards. 10 CFR 20, App B. https://www.govinfo.gov/content/pkg/CFR-2012-title10-vol1/pdf/CFR-2012-title10-vol1-part20-appB.pdf. November 27, 2017.

*NRC. 2017b. Subpart C - Occupational dose limits. Code of Federal Regulations. Nuclear Regulatory Commission. 10 CFR 20.1201-1208. https://www.gpo.gov/fdsys/pkg/CFR-2017-title10-vol1/pdf/CFR-2017-title10-vol1-part20-subpartC.pdf. November 28, 2017.

*NRC. 2017c. Subpart D - Radiation dose limits for individual members of the public. Code of Federal Regulations. Nuclear Regulatory Commission. 10 CFR 20.1301-1302. https://www.gpo.gov/fdsys/pkg/CFR-2017-title10-vol1/pdf/CFR-2017-title10-vol1-part20-subpartD.pdf. November 28, 2017.

*NTP. 2011. Ionizing radiation: Thorium dioxide. Report on carcinogens: Carcinogen profiles. National Toxicology Program. U.S. Department of Health and Human Services, Public Health Service, 243-246.

*NTP. 2016. Ionizing radiation. Report on carcinogens, Fourteenth edition. Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Service, National Toxicology Program. https://ntp.niehs.nih.gov/ntp/roc/content/profiles/ionizingradiation.pdf. November 7, 2017.

*Nyberg U, Nilsson B, Travis LB, et al. 2002. Cancer incidence among Swedish patients exposed to radioactive Thorotrast: A forty-year follow-up survey. Radiat Res 157(4):419-425.

*Oakes TW, Shank KE, Easterly CE, et al. 1977. Concentrations of radionuclides and selected stable elements in fruits and vegetables. Trace Subst Environ Health 11:123-132.

*Odegaard A, Ophus EM, Larsen AM. 1978. Identification of thorium dioxide in human liver cells by electron microscopic x-ray microanalysis. J Clin Pathol 31:893-896.

*Ogawa K, Washiyama K. 2012. Bone target radiotracers for palliative therapy of bone metastases. Curr Med Chem 19(20):3290-3300.

*Okubo A, Obata H, Magara M, et al. 2013. Rapid collection of iron hydroxide for determination of Th isotopes in seawater. Anal Chim Acta 804:120-125.

*Oliveira MS, Duarte IM, Paiva AV, et al. 2014. The role of chemical interactions between thorium, cerium, and lanthanum in lymphocyte toxicity. Arch Environ Occup Health 69(1):40-45.

*Ondov JM, Zoller WH, Olmez I, et al. 1975. Elemental concentrations in the National Bureau of Standards' environmental coal and fly ash standard reference materials. Anal Chem 47:1102-1109.

*OSHA. 2014. Limits for air contaminants. 29 CFR 1910.1000, Subpart Z, Table Z-1. Washington, DC: Occupational Safety and Health Administration.

8. REFERENCES

*OSHA. 2016a. Subpart D - Occupational health and environment controls. Gases, vapors, fumes, dusts, and mists. Code of Federal Regulations. Occupational Safety and Health Standards. 29 CFR 1926.55. https://www.gpo.gov/fdsys/pkg/CFR-2016-title29-vol8/pdf/CFR-2016-title29-vol8-sec1926-55.pdf. March 6, 2017.

*OSHA. 2016b. Subpart Z - Toxic and hazardous substances. Air contaminants. Code of Federal Regulations. Occupational Safety and Health Standards. 29 CFR 1910.1000. https://www.gpo.gov/fdsys/pkg/CFR-2016-title29-vol6/pdf/CFR-2016-title29-vol6-sec1910-1000.pdf. March 6, 2017.

*OSHA. 2017. Subpart Z - Toxic and hazardous substances. Air contaminants. Code of Federal Regulations. Occupational Safety and Health Standards. 29 CFR 1915.1000. https://www.gpo.gov/fdsys/pkg/CFR-2017-title29-vol7/pdf/CFR-2017-title29-vol7-sec1915-1000.pdf. September 7, 2017.

*Otake M, Schull W. 1984. Mental retardation in children exposed *in utero* to the atomic bombs: A reassessment. Technical Report RERF TR 1-83, Radiation Effects Research Foundation, Japan.

*Parr RM, Lucas HF Jr., Griem ML. 1968. Metabolism of 232Th decay series radionuclides in man and other animals following intravascular administration of Thorotrast. ANL-7615. U.S. AEC Argonne National Lab, 97115.

*Parreira F, De Moura MC. 1979. Morphological study of the bone marrow in patients injected with thorium oxide. Environ Res 18:61-64.

*Patrick SJ, Cross EM. 1948. Some effects of the administration of thorium nitrate to mice. Can J Res 26:303-316.

*Pavlovskaia NA. 1973. Basic patterns of the metabolism of Th232 and its decay products in the body. Gig Sanit 11:55-58. [Russian]

*Pavlovskaia NA, Makeeva LG, Orlianskaia RL. 1969. Distribution of thorium in rat bones with various routes of administration and different chemical compounds of thorium. Gig Sanit 34:27-31.

*Pavlovskaia NA, Makeeva LG, Zel'tser MR. 1974a. Excretion of radionuclides of the thorium-232 (thorium-228, radium-224, lead-212) series from a rat’s body during the uptake of thorium compounds in respiratory organs. Gig Sanit 9:42-45. [Russian]

*Pavlovskaia NA, Provotorov AV, Makeeva LG. 1974b. Behavior of thorium-228 and its daughter isotopes in the body of rats when administered perorally. Gig Tr Prof Zabol 5:36-39. [Russian]

*Percival DR, Martin DB. 1974. Sequential determination of radium-226, radium-228, actinium-227, and thorium isotopes in environmental and process waste samples. Anal Chem 46:1742-1749.

*Perkins RW, Kalkwarf DR. 1956. Determination of thorium in urine. Anal Chem 28:1989-1993.

Perry DL, Tsao L. n.d. Thorium species on basalt surfaces. Berkeley, CA: Lawrence Berkeley Laboratory.

*Peter E, Lehmann M. 1981. Interaction of thorium with blood serum proteins *in vivo*. Int J Radiat Biol Relat Stud Phys Chem 40:445-450.

*Peter-Witt E, Volf V. 1984. Efficacy of different diethylenetriaminepentaacetic acid treatment schedules for removal of thorium-234 from simulated wounds in rats. Int J Radiat Biol Relat Stud Phys Chem Med 45:45-50.

*Peter-Witt E, Wolf V. 1985. Comparison of diethylenetriaminepentaacetic acid calcium chelate and diethylenetriaminepentaacetic acid zinc chelate in removing thorium-234 from the rat. Health Phys 49:395-404.

Peter-Witt E, Volf V. 1985. The distribution and decorporation of 234Th in the rat as influenced by the mass of thorium administered. Strahlentherapie [Sonderb] 80:183-185.

*Petrow HG, Strehlow CD. 1967. Spectrophotometric determination of thorium in bone ash using arsenazo. 3. Anal Chem 39:265-267.

*Picer M, Strohal P. 1968. Determination of thorium and uranium in biological materials. Anal Chim Acta 40:131-136.

8. REFERENCES

*Pillai KC, Matkar VM. 1987. Determination of plutonium and americium in environmental samples and assessment of thorium in bone samples from normal and high background areas. J Radioanal Nucl Chem 115:217-229.

Planas-Bohne F, Taylor DM, Lamble G, et al. 1982. The localization of metallic radionuclides in abscesses in rats. Br J Radiol 55:289-293.

*Platford RF, Joshi SR. 1986. The chemistry of uranium and related radionuclides in Lake Ontario (USA, Canada) waters. J Radioanal Nucl Chem 106:333-344.

*Platford RF, Joshi SR. 1988. Dose rates to aquatic life near a uranium waste site. Health Phys 54:63-68.

Pleskach SD. 1985. Determination of U and Th in urine by neutron activation. Health Phys 48:303-307.

*Platz EA, Wiencke JK, Kelsey KT, et al. 2000. Chromosomal aberrations and hprt mutant frequencies in long-term American Thorotrast survivors. Int J Radiat Biol 76(7):955-961.

*Polednak AP, Stehney AF, Lucas HF. 1983. Mortality among male workers at a thorium-processing plant. Health Phys 44(Suppl 1):239-251.

*Popper H, Thomas LB, Telles NC. 1978. Development of hepatic angiosarcoma in man induced by vinyl chloride, Thorotrast, and arsenic. Comparison with cases of unknown etiology. Am J Pathol 92:349-376.

*Poston TM. 1982. The bio accumulation potential of thorium and uranium in rainbow trout *Salmo-nairdneri.* Bull Environ Contam Toxicol 28:682-690.

*Powell BA, Hughes LD, Soreefan AM, et al. 2007. Elevated concentrations of primordial radionuclides in sediments from the Reedy River and surrounding creeks in Simpsonville, South Carolina. J Environ Radioact 94(3):121-128.

*Premuzic ET, Francis AJ, Lin M, et al. 1985. Induced formation of chelating agents by *Pseudomonas aeruginosa* grown in presence of thorium and uranium. Arch Environ Contam Toxicol 14:759-768.

*Priest ND, Humphreys JA, Kathren RL, et al. 1992. The distribution of Thorotrast in human bone marrow: A case report. Health Phys 63(1):46-53.

*Pulhani VA, Dafauti S, Hegde AG, et al. 2005. Uptake and distribution of natural radioactivity in wheat plants from soil. J Environ Radioact 79(3):331-46.

*Rae BK, Brodell GK, Haaga JR, et al. 1986. Visceral CT findings associated with Thorotrast. J Comput Assist Tomogr 10:57-61.

*Rangarajan C, Eapen CD, Gopalakrishnan SS. 1986. Measured values of the dry deposition velocities of atmospheric aerosols carrying natural and fallout radionuclides using artificial collectors. Water Air Soil Pollut 27:305-314.

*Raymond DP, Dufield JR, Williams DR. 1987. Complexation of plutonium and thorium in aqueous environments. Inorg Chim Acta 140:309-313.

*Rayno DR. 1989. Assimilation of thorium isotopes into terrestrial vegetation. Sci Total Environ 80(23):243-266.

*Rich AL, Crosby EC. 2013. Analysis of reserve pit sludge from unconventional natural gas hydraulic fracturing and drilling operations for the presence of technologically enhanced naturally occurring radioactive material (TENORM). New Solutions 23(1):117-135.

*Riedel WR, Hirschberg AK, Kaul A, et al. 1979. Comparative investigations on the biokinetics of colloidal thorium, zirconium, and hafnium dioxides in animals. Environ Res 28:127-139.

Riedel W, Dalheimer A, Said M, et al. 1983. Recent results of the German Thorotrast study dose relevant physical and biological properties of Thorotrast equivalent colloids. Health Phys 44:293-298.

*Roeck DR, Reavey TC, Hardin JM. 1987. Partitioning of natural radionuclides in the waste streams of coal-fired utilities. Health Phys 52:311-324.

*Roper AR, Stabin MG, Delapp RC, et al. 2013. Analysis of naturally-occurring radionuclides in coal combustion fly ash, gypsum, and scrubber residue samples. Health Phys 104(3):264-269.

*Roth P, Hollriegl V, Li WB, et al. 2005. Validating an important aspect of the new ICRP biokinetic model of thorium. Health Phys 88(3):223-228.

8. REFERENCES

*RTECS. 1989. Registry of Toxic Effects of Chemical Substances. February 14, 1989.
*Rubin P, Casarett G. 1968. Clinical radiation pathology. Philadelphia, PA: W.B. Sanders Company, 33.
*Ruhmann AG, Berliner DL. 1965. Serum lactic dehydrogenase levels in adult beagle dogs with internally deposited radionuclides. Radiat Res 26:287-294.
*Sadamori N, Miyajima J, Okajima S, et al. 1987. Japanese patients with leukaemia following the use of Thorotrast including a patient with marked chromosomal rearrangements. Acta Haematol 77:11-14.
*Saisho H, Tanaka M, Nakamura K, et al. 1988. Determination of traces of uranium and thorium in microelectronics constituent materials. J Res Natl Bureau Stand 93:398-400.
*Saito H, Hisanaga N, Okada Y, et al. 2003. Thorium-232 exposure during tungsten inert gas arc welding and electrode sharpening. Ind Health 41(3):273-278.
*Salaymeh S, Kuroda PK. 1987. Variation of the thorium to uranium ratio in rain: Thorium-230 chronology of the eruptions of Mt. St. Helens and El Chichon volcanoes. J Radioanal Nucl Chem 116:261-269.
*Saldanha MJ, Shah VR, Nambiar PPUJ. 1975. Health Assessment of thorium nitrate plant workers of Indian rare earths. Indian J Ind Med 21:114-123.
*SANSS. 1989. Structure and Nomenclature Search System. February 14, 1989.
*Santschi PH. 1984. Particle flux and trace metal residence time in natural waters. Limnol Oceanogr 29:1100-1108.
*Santschi PH, Li YH, Adler DM, et al. 1983. The relative mobility of natural (thorium, lead and polonium) and fallout (plutonium, americium, cesium) radionuclides in the coastal marine environment: Results from model ecosystems (MERL) and Narragansett Bay. Geochim Cosmochim Acta 47:201-210.
*Sasaki F, Kido C, Sobue T, et al. 1999. Cancer mortality in Thorotrast-exposed patients in Japan: Aichi series. Int J Clin Oncol 4(2):69-73.
*Sasaki MS, Takatsuji T, Ejima Y, et al. 1987. Chromosome aberration frequency and radiation dose to lymphocytes by alpha-particles from internal deposit of Thorotrast. Radiat Environ Biophys 26:227-238.
*Schery SD. 1985. Measurements of airborne lead-212 and radon-220 at varied indoor locations within the United States. Health Phys 49:1061-1067.
*Schlemmer HP, Liebermann D, Naser V, et al. 2000. Locoregional late effects of paravascular Thorotrast deposits: Results of the German Thorotrast study. J Neuroradiol 27(4):253-263.
*Schmied SA, Brunnermeier MJ, Schupfner R, et al. 2012. Dating ivory by determination of 14C, 90Sr and 228/232Th. Forensic Sci Int 221(1-3):5-10.
*Scott JK, Neuman WF, Bonner JF. 1952. The distribution and excretion of thorium sulphate. J Pharmacol Exp Therapeut 106:286-290.
Serio CS, Henninb CB, Toohey RE, et al. 1983. Measurement of lymphoblastogenic activity from thorium workers. Int J Radiat Biol 44:251-256.
Sheppard MI. 1980. The environmental behavior of uranium and thorium. Atomic Energy Canada Ltd., AECL-6795.
*Shiga J, Maruyama T, Takahashi H, et al. 1993. Effect of PSK, a protein-bound polysaccharide preparation, on liver tumors of Syrian hamsters induced by Thorotrast injection. Acta Pathol Jpn 43(9):475-480.
*Shtangeeva I. 2010. Uptake of uranium and thorium by native and cultivated plants. J Environ Radioact 101(6):458-463.
*Shtangeeva I, Ayrault S, Jain J. 2005. Thorium uptake by wheat at different stages of plant growth. J Environ Radioact 81(2-3):283-293.
*Sill CW. 1977. Simultaneous determination of U-238, U-234, Th-230, Ra226, and PB.210 in uranium ores, dusts, and mill tailings. Health Phys 33:393-404.
*Sill CW, Willis CP. 1962. Fluorometric determination of submicrogram quantities of thorium. Anal Chem 34:954-964.

8. REFERENCES

*Simpson HJ, Trier RM, Li YH, et al. 1984. Field experiment determinations of distribution coefficients of actinide elements in alkaline lake environments. Nucl Waste Geochem, 326-342.
*Simpson HJ, Trier RM, Toggweiler JR, et al. 1982. Radionuclides in Mono Lake, California, USA. Science 216:512-514.
Sindelar WF, Costa J, Ketcham AS. 1978. Osteosarcoma associated with Thorotrast administration: Report of two cases and literature review. Cancer 42:2604-2609.
*Singh NP, Wrenn ME. 1988. Determinations of actinides in biological and environmental samples. Sci Total Environ 70:187-203.
*Singh NP, Bennett D, Saccomanno G, et al. 1985. Concentrations of lead-210 in uranium miners' lungs and its states of equilibria with uranium-238 uranium-234 and thorium-230. Occup Radiat Saf Min 2:503-506.
*Singh NP, Bennett DB, Wrenn ME, et al. 1986. Concentrations of 210Pb and its states of equilibrium with 238U 234U and 230Th in U miners' lungs. Health Phys 51:501-507.
*Singh NP, Bennett DD, Wrenn ME, et al. 1987. Concentrations of alpha-emitting isotopes of uranium and thorium in uranium miners' and millers' tissues. Health Phys 53:261-266.
*Singh, NP, Ibrahim SA, Cohen N, et al. 1979. Simultaneous determination of alpha-emitting radionuclides of thorium plutonium in human tissues including bone. Analytical Chem 51:1978-1981.
*Singh NP, Lewis LL, Wrenn ME. 1985. Uranium thorium and plutonium in bones from the general population of the United States. Comm Eur Communities Issue 9250:231-241.
*Singh NP, Wrenn ME, Archer VE, et al. 1981. Uranium-238, uranium-234 and thorium-230 in uranium miners' lungs. Radiation Hazards in Mining, Control Measurements, Medical Aspects, International Conference 236-239.
Singh NP, Wrenn ME, Ibrahim SA, et al. 1982. Thorium concentration in human tissues from two geographic locations of the United States. In: National radiation environment. New York, NY: John Wiley and Sons, 258-268.
*Singh NP, Wrenn ME, Ibrahim SA. 1983. Plutonium concentration in human tissues: Comparison to thorium. Health Phys 44:469-476.
*Singh NP, Wrenn ME, McInroy JF, et al. 1986. Ratios of 234U, 238U and 230Th in dog lungs exposed to U ore dust: An interlaboratory comparison. Health Phys 50:292-297.
*Singh NP, Zimmerman CJ, Taylor GN, et al. 1988. The beagle: An appropriate experimental animal for extrapolating the organ distribution pattern of Th in humans. Health Phys 54:293-299.
*Sollman T, Brown ED. 1907. Pharmacologic investigations on thorium. Am J Physiol 18:426-456.
*Soudek P, Kufner D, Petrova S, et al. 2013. Composition of hydroponic medium affects thorium uptake by tobacco plants. Chemosphere 92(9):1090-1098.
*Spiers FW, Beddow AH. 1983. Sites of incidence of osteosarcoma in the long bones of man and beagle. Health Phys 44(Suppl 1):49-64.
*Spiethoff A, Wesch H, Wegener K, et al. 1992. The effects of Thorotrast and quartz on the induction of lung tumors in rats. Health Phys 63(1):101-110.
*Stannard JN. 1988. Radioactivity and health: A history. DOE/RL/01830T59.
Stanley RB Jr. 1983. Thorium-dioxide induced pharyngeal hemorrhage. Am J Otolaryngol 4:437-441.
*Stanley RB Jr, Calcaterra TC. 1981. Management of cervical thorium dioxide granulomas. Arch Otolaryngol 107:631-634.
*Stehney AF. 1999. Organ distribution of thorium in thorium workers: Good agreement with new models of the International Commission on Radiological Protection. Radiat Res 152(6 Suppl):S110-S114.
*Stehney AF, Lucas HF. 2000. Thorium isotopes in autopsy samples from thorium workers. Health Phys 78(1):8-14.
*Stehney AF, Polednak AP, Rundo J, et al. 1980. Health status and body radioactivity of former thorium workers. Argonne, IL, Argonne National Laboratory 80-37:44.

8. REFERENCES

*Steinstrasser A. 1981. Biophysical investigations of the dose-effect relationship in chromosome aberrations of human lymphocytes caused by Thorotrast deposits. Radiat Env Biophys 19:1-15.

*Stevens W, Nabors CJ Jr, Berliner DL. 1967. A comparison of serum transaminase levels and other serum constituents in dogs burdened with 239Pu, 228-Th, 228-RA and 226-Ra. NY Acad Sci 145:817-829.

*Stougaard M, Praestholm J, Stoier M. 1984. Late effects of perivascular injection of Thorotrast in the neck. J Laryngol Otol 98:1003-1007.

*Stover BJ. 1981. Toxicology of thorium-228 in young adult beagles: Potential relationship to the thorium fuel cycle. In: Wrenn ME, ed. Actinides in man and animals: Proc Snowbird Actinide Workshop. Salt Lake City, UT: University of Utah, 483-500.

Stover BJ. 1983. Effects of Thorotrast in humans. Health Phys 44:253-257.

Stover BJ, Atherton DR, Buster DS, et al. 1965a. The Th-228 decay series in adult beagles: Ra-224 PB-212 and Bi-212 in selected bones and soft tissues. Radiat Res 26:132-145.

Stover BJ, Atherton DR, Buster DS, et al. 1965b. The Th-228 decay series in adult beagles: Ra224 Pb212 and Bi-212 in blood and excreta. Radiat Res 26:226-243.

*Stover BJ, Atherton DR, Keller, et al. 1960. Metabolism of Th-228 decay series in adult beagle dogs. Radiation Res 12:657-671.

*Stradling N, Phipps A, Hodgson A. 2001. Dosimetric models for thorium and practical problems in assessing intakes. Radiat Prot Dosimetry 97(2):89-94.

*Sullivan MF. 1980a. Absorption of actinide elements from the gastrointestinal tract of rats, guinea pigs and dogs. Health Phys 38:159-171.

*Sullivan MF. 1980b. Absorption of actinide elements from the gastrointestinal tract of neonatal animals. Health Phys 38:173-185.

*Sullivan MF, Miller BM, Ryan JL. 1983. Absorption of thorium and protactinium from the gastrointestinal tract in adult mice and rats and neonatal rats. Health Phys 44:425-428.

*Summers DE, Chung EB. 1986. Thorotrast associated anemia and bone marrow hypoplasia. J Nat1 Med Assoc 78:1161-1165.

*Sunta CM, Dang HS, Jaiswal DD. 1987. Thorium in man and environment: Uptake and clearance. J Radional Nucl Chem 115:149-158.

*Sussman S, Terbrugge KG, Solt LC, et al. 1980. Thorotrast induced meningioma case report. J Neurosurg 52:834-837.

*Syao-Shan Y. 1970a. The behavior of thorium dioxide in rats after intratracheal and intraperitoneal administration. In: Letavet AA, Kurlyandskaya EB, eds. The toxicology of radioactive substances, Vol. 4. New York, NY: Pergamon Press, 30-41.

*Syao-Shan Y. 1970b. Comparative toxicity of soluble and insoluble compounds of thorium-232. In: Letavet AA, Kurlyandskaya EB, eds. The toxicology of radioactive substances, Vol. 4. New York, NY: Pergamon Press, 9-19.

Syao-Shan Y. 1970c. The effect of thorium dioxide on the peripheral blood of rats. In: Letavet AA, Kurlyandskaya EB, eds. The toxicology of radioactive substances, Vol. 4. New York, NY: Pergamon Press, 42-57.

*Syao-Shan, Y. 1970d. The effect of thorium dioxide on arterial pressure and threshold of stimulation of the nerve muscle apparatus in rats. In: Letavet AA, Kurlyandskaya EB, eds. The toxicology of radioactive substances, Vol. 4. New York, NY: Pergamon Press, 58-65.

*Tadmor J. 1986. Atmospheric release of volatilized species of radioelements from coal fired plants. Health Phys 50:270-273.

*Tandon SK, Dikshith TSS, Behari JR, et al. 1975. Effect of thorium nitrate in male albino rats. Ind Health 13:221-225.

*Tanosaki S, Minamihisamatsu M, Ishihara T, et al. 1999. Chromosome aberrations in bone marrow cells from Japanese patients with thorotrastosis. Radiat Res 152(6 Suppl):S128-S132.

*Taskayev AI, Popova ON, Alexakhin RM, et al. 1986. Root absorption of radon-222 and its transfer into above ground plant organs. Health Phys 50:589-594.

*Taylor DM, Chipperfield AR, James AC. 1971. Effects of tetracycline on the deposition of plutonium and related elements in rat bone. Health Phys 21:197-204.
*Taylor GN, Jee WSS, Christensen WR, et al. 1966. Thorium-228 induced fractures in beagles. Health Phys 12:889-893.
*Taylor GN, Mays CW, Lloyd RD, et al. 1986. Liver cancer induction by 241Am and Thorotrast in deer mice and grasshopper mice. Strahlen Therapie 80(Suppl):172-177.
*Teixeira-Pinto AA, Azevedo e Silva MC. 1979. Chromosome radiation induced aberrations in patients injected with thorium dioxide. Environ Res 18:225-230.
*Telles MC, Thomas LB, Popper H, et al. 1979. Evolution of Thorotrast induced hepatic angiosarcomas. Environ Res 18:74-87.
*Terry KW, Hewson GS. 1995. Thorium lung burdens of mineral sands workers. Health Phys 69(2):233-242.
*Terry KW, Hewson GS, Meunier G. 1995. Thorium excretion in feces by mineral sands workers. Health Phys 68(1):105-109.
*Thomas RG. 1957. The metabolism of thorium-230 administered by intratracheal injection to the rat. Rochester, NY: University of Rochester, Atomic Energy Project Report UR-480, 1-26.
Thomas RG. 1968. Transport of relatively insoluble materials from lung to lymph nodes. Health Phys 14:111-117.
*Thomas RG, Lie R, Scott JK. 1963. Thorium distribution and excretion studies. I. Patterns following parenteral administration. Health Phys 9:153-163.
*Thurman GB, Mays CW, Taylor GN, et al. 1971. Growth dynamics of beagle osteosarcomas. Growth 35:119-125.
*Toohey RE, Bertelli L, Sugarman SL, et al. 2011. Dose coefficients for intakes of radionuclides via contaminated wounds. Health Phys 100(5):508-514.
*Torstenfelt B. 1986. Migration of the actinides, thorium, protactinium, uranium, neptunium, plutonium and americium in clay. Radiochem Acta 39:105112.
*Traikovich M. 1970. Absorption, distribution and excretion of certain soluble compounds of natural thorium. In: Letavet AA, Kurlyandskaya EB, eds. The toxicology of radioactive substances, Vol. 4. New York, NY: Pergamon Press, 20-29.
*Travis LB, Hauptmann M, Gaul LK, et al. 2003. Site-specific cancer incidence and mortality after cerebral angiography with radioactive Thorotrast. Radiat Res 160(6):691-706.
*Travis LB, Land CE, Andersson M, et al. 2001. Mortality after cerebral angiography with or without radioactive Thorotrast: An international cohort of 3,143 two-year survivors. Radiat Res 156(2):136-150.
*TRI16. 2017. TRI explorer: Providing access to EPA's toxics release inventory data. Washington, DC: Office of Information Analysis and Access. Office of Environmental Information. U.S. Environmental Protection Agency. Toxics Release Inventory. http://www.epa.gov/triexplorer/. September 11, 2017.
*Twitty BL, Boback MW. 1970. Rapid determination of thorium in urine by thermal neutron activation analysis. Anal Chim Acta 49:19-24.
*Umeki S, Kyoizumi S, Kusunoki Y, et al. 1991. Flow cytometric measurements of somatic cell mutations in Thorotrast patients. Jpn J Cancer Res 82(12):1349-1353.
*UNSCEAR. 1977. Sources and effects of ionizing radiation. United Nations Scientific Committee on the Effects of Atomic Radiation. United Nations Publication E.77.IX.l. New York, NY: United Nations, 95-96.
*UNSCEAR. 1982. Ionizing radiation: Sources and biological effects. United Nations Scientific Committee on the Effects of Atomic Radiation. New York, NY: United Nations.
*UNSCEAR. 1986. Genetic and somatic effects of ionizing radiation. United Nations Scientific Committee on the Effects of Atomic Radiation. New York, NY: United Nations.
*UNSCEAR. 1988. Sources, effects and risks of ionization radiation. United Nations Scientific Committee on the Effects of Atomic Radiation. New York, NY: United Nations.

*Van Kaick G, Dalheimer A, Hornik S, et al. 1999. The German Thorotrast study: Recent results and assessment of risks. Radiat Res 152(6 Suppl):S64-S71.

*Van Kaick G, Lieberman D, Lorenz D, et al. 1983. Recent results on the German Thorotrast study-epidemiological results and dose effect relationships in Thorotrast patients. Health Phys 44:299-306.

Van Kaick G, Wesch H, Luhrs H, et al. 1986. Radiation induced primary liver tumors in Thorotrast patients. Recent Results Cancer Res 100:16-22.

*van Kaick G, Wesch H, Luhrs H, et al. 1991. Neoplastic diseases induced by chronic alpha-irradiation-epidemiological, biophysical and clinical results of the German Thorotrast Study. J Radiat Res 32 Suppl 2:20-33.

*Vandenborre J, Grambow B, Abdelouas A. 2010. Discrepancies in thorium oxide solubility values: Study of attachment/detachment processes at the solid/solution interface. Inorg Chem 49(19):8736-8748.

*Velten RJ, Jacobs BJ. 1982. Determination of thorium in drinking water, Method 910. Cincinnati, OH: U.S. Environmental Protection Agency, Environmental Monitoring and Support Laboratory.

*VIEW Database. 1989. Agency for Toxic Substances and Disease Registry (ATSDR), Office of External Affairs, Exposure and Disease Registry Branch, Atlanta, GA. June 20, 1989.

*Visfeldt J, Andersson M. 1995. Pathoanatomical aspects of malignant haematological disorders among Danish patients exposed to thorium dioxide. APMIS 103(1):29-36.

*Visfeldt J, Poulsen H. 1972. On the histopathology of liver and liver tumors in thorium dioxide patients. Acta Path Micro Scand Sect A:97-108.

*Vocaturo G, Colombo F, Zanoni M, et al. 1983. Human exposure to heavy metals: Rare earth pneumoconiosis in occupational workers. Chest 83:780-783.

*Waligorski MPR, Jasinska M, Schwabenthan J. 1985. Enhanced nuclear radiation from camera lenses. Health Phys 49:491-494.

*Wargotz ES, Sidawy MK, Jannotta FS. 1988. Thorotrast associated gliosarcoma including comments on Thorotrast use and review of sequelae with particular reference to lesions of the central nervous system. Cancer 62:58-60.

*Weast RC, ed. 1983. CRC handbook of chemistry and physics. 64th ed. Boca Raton, FL: CRC Press, Inc., B149-B150.

*Web_elements. 2014a. Thorium compounds: Thorium tetrachloride. The University of Sheffield and Web Elements Ltd., UK [May 29, 2014]. http://www.webelements.com/compounds/thorium/thorium_tetrachloride.html.

*Web_elements. 2014b. Thorium compounds: Thorium sulphate nonahydrate. The University of Sheffield and Web Elements Ltd., UK [May 29, 2014]. http://www.webelements.com/compounds/thorium/Th-1_SO4-2_OH2_9.html.

*Wegener K, Wesch H. 1979. Pathological changes of lymph nodes in Thorotrast patients: Pathoanatomical autoradiographical and quantitative investigations. Environ Res 18:245-255.

Wegener K, Hasenohrl K, Wesch H. 1983. Recent results of the German Thorotrast study pathoanatomical changes in animal experiments and comparison to human thorotrastosis. Health Phys 44(Suppl 1):307-316.

*Wegener K, Wesch H, Kampmann H. 1976. Investigations into human thorotrastosis tissue concentrations of thorium-232 and late effects in 13 autopsy cases. Virchows Arch Path Anat Histol 371:131-143.

*Weissman SH, Carpenter RL, Newton GJ. 1983. Respirable aerosols from fluidized bed coal combustion: Element composition of fly ash. Environ Sci Tech 17:65-71.

*Welford GA, Sutton DC, Morse RS, et al. 1958. Determination of thorium in urine. Am Ind Hyg Assoc J 19:464-468.

*Wesch H, van Kaick G, Riedel W, et al. 1983. Recent results of the German Thorotrast study statistical evaluation of animal experiments with regard to the nonradiation effects in human thorotrastosis. Health Phys 44:317-321.

*West CM. 1962. An evaluation of the health physics problems from thorium and its daughters in a thorium purification and fabrication process. Health Phys 8:279-297.

*Westin J, Lanner LO, Weinfeld A, et al. 1973. Renal pelvic carcinoma after Thorotrast pyelography: Case report. Acta Med Scand 194:141-143.

*Wong SH. 1988. Effects of some metallic compounds on *Klebsiella*. Bull Environ Contam Toxicol 40:525-531.

*WHO. 2005. WHO air quality guidelines for particulate matter, ozone, nitrogen dioxide and sulfur dioxide. 2nd ed. Geneva, Switzerland: World Health Organization.

*WHO. 2010. WHO guidelines for indoor air quality: Selected pollutants. Geneva, Switzerland: World Health Organization. http://www.euro.who.int/__data/assets/pdf_file/0009/128169/e94535.pdf. April 25, 2012.

*WHO. 2011. Guidelines for drinking-water quality, fourth edition. Geneva, Switzerland: World Health Organization.

*WHO. 2017. Guidelines for drinking-water quality. Fourth edition incorporating the first addendum. Geneva, Switzerland: World Health Organization. http://apps.who.int/iris/bitstream/10665/254637/1/9789241549950-eng.pdf?ua=1. February 28, 2017.

*Woodliff HJ, Cohen G, Gallon W. 1972. Chromosome aberrations in lymphocytes from patients exposed to thorium dioxide. Med J Australia 2:768-771.

*Wrenn ME, Singh NP, Cohen N, et al. 1981. Thorium in human tissues. NTIS NUREG/CR-1227, 1-97.

*Wrenn ME, Singh NP, Paschoa AS, et al. 1985. Concentrations of uranium and thorium isotopes in uranium millers' and miners' tissues. NTIS NUREG/CR-4382/GAR, 1-47.

*Wrenn ME, Singh NP, Saccomanno G. 1983. Uranium and thorium isotopes and their state of equilibria in lungs from uranium miners. Health Phys 44:385-389.

*Wrenn ME, Taylor GN, Stevens W, et al. 1986. DOE life-span radiation effects studies in experimental animals at University of Utah, Division of Radiobiology. In: Life-span radiation effects in animals: What can they tell us? Conference: U.S. Department of Energy, 830951.

*Wustrow TP, Behbehani AA, Wiebecks B. 1988. Thorotrast-induced oro- and hypopharyngeal fibrosis with recurrent bleeding. J Cranio-Maxillo-Facial Surg 16:315-319.

*Yamada S, Hosoda S, Tateno H, et al. 1983. Survey of Thorotrast associated liver cancers in Japan. J Natl Cancer Inst 70:31-35.

*Yamamoto Y, Chikawa J, Uegaki Y, et al. 2010. Histological type of Thorotrast-induced liver tumors associated with the translocation of deposited radionuclides. Cancer Sci 101(2):336-340.

*Yamamoto Y, Usuda N, Takatsuji T, et al. 2009. Long incubation period for the induction of cancer by Thorotrast is attributed to the uneven irradiation of liver cells at the microscopic level. Radiat Res 171(4):494-503.

*Yang HS, Nozaki Y, Sakai H, et al. 1986. Natural and man-made radionuclide distributions in Northwest Pacific deep sea sediments: Rates of sedimentation, bioturbation and radium-226 migration. Geochem J 20:29-40.

*Yantasee W, Sangvanich T, Creim JA, et al. 2010. Functional sorbents for selective capture of plutonium, americium, uranium, and thorium in blood. Health Phys 99(3):413-419.

*Young WN, Tebrock HA. 1958. The treatment of exposure to thorium and uranium with a chelating agent and supportive measures. Ind Med Surg (Annual Meeting) 27:229-232.

*Zoller WH, Gladney ES, Duce RA. 1974. Atmospheric concentrations and sources of trace metals at the South Pole. Science 183:198-200.

APPENDIX A. ATSDR MINIMAL RISK LEVEL WORKSHEETS

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 route and duration of exposure. MRLs are based on noncancer health effects only; cancer effects are not considered. 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 NOAEL/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) 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 substance-induced endpoint 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.

APPENDIX A

Proposed MRLs undergo a rigorous review process: Health Effects/MRL Workgroup reviews within the Division of Toxicology and Human Health Sciences, 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 MRLs. For additional information regarding MRLs, please contact the Division of Toxicology and Human Health Sciences, Agency for Toxic Substances and Disease Registry, 1600 Clifton Road NE, Mailstop S102-1, Atlanta, Georgia 30329-4027.

APPENDIX A

MINIMAL RISK LEVEL (MRL) WORKSHEET

***Chemical Name*:** Thorium
CAS Numbers: 7440-29-1
Date: October 1990
June 2017—Updated literature search
Profile Status: Final draft
Route: Inhalation
Duration: Acute

MRL Summary: There are insufficient data for derivation of an acute-duration inhalation MRL.

Rationale for Not Deriving an MRL: No exposure-response data are available for humans. Studies in laboratory animals were limited to a series of studies conducted by Hall et al. (1951) examining the toxicity of thorium nitrate and thorium dioxide in dogs and rabbits exposed for approximately 2 weeks. Hematological effects were reported in dogs; however, the two studies found different effects. In dogs exposed to thorium nitrate (4.0 nCi/m^3 as thorium), leukocytosis, abnormal lymphocytes, and hypersegmented polymonorphonuclear granulocytes were observed; no alterations in erythrocyte counts were observed. In contrast, exposure to 4.8 nCi/m^3 as thorium dioxide resulted in decreases in erythrocyte counts, increased percentage of lymphocytes, and nonfilamented polymorphonuclear neutrophils. No hematological effects were observed in rabbits exposed to 3.5 or 3.8 nCi/m^3 as thorium nitrate. The studies also conducted histological alterations in numerous studies including the lungs and reported no alterations. The Hall et al. (1951) studies were not considered suitable as the basis of an MRL due to the lack of control groups, small number of animals tested in the dog studies (4/group), testing only one exposure level, inadequate reporting of results, and the inconsistency of the findings across studies.

Agency Contacts (Chemical Managers): Sam Keith

APPENDIX A

MINIMAL RISK LEVEL (MRL) WORKSHEET

***Chemical Name*:** Thorium
CAS Numbers: 7440-29-1
Date: October 1990
June 2017—Updated literature search
Profile Status: Final draft
Route: Inhalation
Duration: Intermediate

MRL Summary: There are insufficient data for derivation of an intermediate-duration inhalation MRL.

Rationale for Not Deriving an MRL: No exposure-response data are available for humans. Hall et al. (1951) examined the intermediate-duration toxicity of thorium tetrafluoride in dogs and thorium oxalate in dogs and rabbits. Decreased erythrocyte counts were observed in dogs exposed to 0.9 nCi/m^3 as thorium tetrafluoride and 1.4 nCi/m^3 as thorium oxalate; the dogs received 51 and 45 exposures (6 hours/day, 5 days/week), respectively. No hematological effects were observed in the rabbits exposed to 1.6 nCi/m^3 for 21 exposures. The investigators reported no alterations in histopathological examinations of numerous tissues (including the lungs). The Hall et al. (1951) studies were not considered suitable as the basis of an MRL due to a number of study limitations, including the small number of animals per group (four dogs per compound; histopathology examination conducted in two dogs/compound), no control group, only testing one concentration per compound, and inadequate reporting of results.

Agency Contacts (Chemical Managers): Sam Keith

APPENDIX A

MINIMAL RISK LEVEL (MRL) WORKSHEET

***Chemical Name*:** Thorium
CAS Numbers: 7440-29-1
Date: October 1990
June 2017—Updated literature search
Profile Status: Final draft
Route: Inhalation
Duration: Chronic

MRL Summary: There are insufficient data for derivation of a chronic-duration inhalation MRL.

Rationale for Not Deriving an MRL: No exposure-response data are available for humans. In the only available animal studies, no thorium exposure-related adverse effects were observed in rats, rabbits, guinea pigs, or dogs repeatedly exposed to thorium dioxide by inhalation at 0.55 nCi/m^3 (the only exposure level tested) for 12–14 months (Hodge et al. 1960).

Agency Contacts (Chemical Managers): Sam Keith

MINIMAL RISK LEVEL (MRL) WORKSHEET

***Chemical Name*:** Thorium
CAS Numbers: 7440-29-1
Date: October 1990
June 2017—Updated literature search
Profile Status: Final draft
Route: Oral
Duration: Acute

MRL Summary: There are insufficient data for derivation of an acute-duration oral MRL.

Rationale for Not Deriving an MRL: No human data are available. The only available acute-duration oral study reported only a NOAEL of 84 nCi/kg and the death of 4/20 mice administered thorium nitrate at 110 nCi/kg once by gavage.

Agency Contacts (Chemical Managers): Sam Keith

APPENDIX A

MINIMAL RISK LEVEL (MRL) WORKSHEET

***Chemical Name*:** Thorium
CAS Numbers: 7440-29-1
Date: October 1990
June 2017—Updated literature search
Profile Status: Final draft
Route: Oral
Duration: Intermediate

MRL Summary: There are insufficient data for derivation of an intermediate-duration oral MRL.

Rationale for Not Deriving an MRL: No human data are available. Two intermediate-duration oral studies were located. In one study, the only adverse treatment-related effect among rats administered thorium nitrate in the food for 105–131 days at 130 nCi/kg/day decreased body weight gain; however, this was attributed to decreased food intake (Downs et al. 1959). In the other study, 10/20 mice died during a 4-month exposure to thorium nitrate in the drinking water at an estimated dose of 12 nCi/kg/day (the only exposure level tested); there were no other reported effects (Patrick and Cross 1948).

Agency Contacts (Chemical Managers): Sam Keith

MINIMAL RISK LEVEL (MRL) WORKSHEET

***Chemical Name*:** Thorium
CAS Numbers: 7440-29-1
Date: October 1990
June 2017—Updated literature search
Profile Status: Final draft
Route: Oral
Duration: Chronic

MRL Summary: There are insufficient data for derivation of a chronic-duration oral MRL.

Rationale for Not Deriving an MRL: No chronic-duration oral studies are available for humans or animals.

Agency Contacts (Chemical Managers): Sam Keith

APPENDIX B. LITERATURE SEARCH FRAMEWORK FOR THORIUM

The objective of the toxicological profile is to evaluate the potential for human exposure and the potential health hazards associated with inhalation, oral, or dermal/ocular exposure to thorium.

B.1 LITERATURE SEARCH AND SCREEN

A literature search and screen was conducted to identify studies examining health effects, toxicokinetics, mechanisms of action, susceptible populations, biomarkers, and chemical interactions for thorium. ATSDR primarily focused on peer-reviewed articles without publication date or language restrictions. Non-peer-reviewed studies that were considered relevant to the assessment of the health effects of thorium have undergone peer review by at least three ATSDR-selected experts who have been screened for conflict of interest. The inclusion criteria used to identify relevant studies examining the health effects of thorium are presented in Table B-1.

Table B-1. Inclusion Criteria for the Literature Search and Screen

Health Effects
Species
Human
Laboratory mammals
Route of exposure
Inhalation
Oral
Dermal (or ocular)
Parenteral (these studies will be considered supporting data)
Health outcome
Death
Systemic effects
Body weight effects
Respiratory effects
Cardiovascular effects
Gastrointestinal effects
Hematological effects
Musculoskeletal effects
Hepatic effects
Renal effects
Dermal effects
Ocular effects
Endocrine effects
Immunological effects
Neurological effects
Reproductive effects
Developmental effects
Other noncancer effects
Cancer

Table B-1. Inclusion Criteria for the Literature Search and Screen

Toxicokinetics
Absorption
Distribution
Metabolism
Excretion
PBPK models
Biomarkers
Biomarkers of exposure
Biomarkers of effect
Interactions with other chemicals

B.1.1 Literature Search

The current literature search was intended to update the existing 1990 toxicological profile for thorium; thus, the literature search was restricted to studies published between January 1988 to June 2017. The following main databases were searched in June 2017:

- PubMed
- National Library of Medicine's TOXLINE
- Scientific and Technical Information Network's TOXCENTER

The search strategy used the chemical names, Chemical Abstracts Service (CAS) numbers, synonyms, Medical Subject Headings (MeSH) headings, and keywords for thorium. The query strings used for the literature search are presented in Table B-2.

The search was augmented by searching the Toxic Substances Control Act Test Submissions (TSCATS), NTP website, and National Institute of Health Research Portfolio Online Reporting Tools Expenditures and Results (NIH RePORTER) databases using the queries presented in Table B-3. Additional databases were searched in the creation of various tables and figures, such as the TRI Explorer, the Substance Priority List (SPL) resource page, and other items as needed. Regulations applicable to thorium were identified by searching international and U.S. agency websites and documents.

Review articles were identified and used for the purpose of providing background information and identifying additional references. ATSDR also identified reports from the grey literature, which included unpublished research reports, technical reports from government agencies, conference proceedings and abstracts, and theses and dissertations.

Table B-2. Database Query Strings

Database search date	Query string
PubMed	
6/2017	((((("Thorium/toxicity"[mh] OR "Thorium/adverse effects"[mh] OR "Thorium/poisoning"[mh] OR "Thorium/pharmacokinetics"[mh]) OR ("Thorium"[mh] AND ("environmental exposure"[mh] OR ci[sh])) OR ("Thorium"[mh] AND toxicokinetics[mh:noexp]) OR ("Thorium/blood"[mh] OR "Thorium/cerebrospinal fluid"[mh] OR "Thorium/urine"[mh]) OR

Table B-2. Database Query Strings

Database search date	Query string
	("Thorium"[mh] AND ("endocrine system"[mh] OR "hormones, hormone substitutes, and hormone antagonists"[mh] OR "endocrine disruptors"[mh])) OR ("Thorium"[mh] AND ("computational biology"[mh] OR "medical informatics"[mh] OR genomics[mh] OR genome[mh] OR proteomics[mh] OR proteome[mh] OR metabolomics[mh] OR metabolome[mh] OR genes[mh] OR "gene expression"[mh] OR phenotype[mh] OR genetics[mh] OR genotype[mh] OR transcriptome[mh] OR ("systems biology"[mh] AND ("environmental exposure"[mh] OR "epidemiological monitoring"[mh] OR analysis[sh])) OR "transcription, genetic "[mh] OR "reverse transcription"[mh] OR "transcriptional activation"[mh] OR "transcription factors"[mh] OR ("biosynthesis"[sh] AND (RNA[mh] OR DNA[mh])) OR "RNA, messenger"[mh] OR "RNA, transfer"[mh] OR "peptide biosynthesis"[mh] OR "protein biosynthesis"[mh] OR "reverse transcriptase polymerase chain reaction"[mh] OR "base sequence"[mh] OR "trans-activators"[mh] OR "gene expression profiling"[mh])) OR ("Thorium/antagonists and inhibitors"[mh]) OR ("Thorium/metabolism"[mh] AND ("humans"[mh] OR "animals"[mh])) OR ("Thorium"[mh] AND cancer[sb]) OR ("Thorium/pharmacology"[majr])) OR (("Thorium Compounds/toxicity"[mh] OR "Thorium Compounds/adverse effects"[mh] OR "Thorium Compounds/poisoning"[mh] OR "Thorium Compounds/pharmacokinetics"[mh]) OR ("Thorium Compounds"[mh] AND ("environmental exposure"[mh] OR ci[sh])) OR ("Thorium Compounds"[mh] AND toxicokinetics[mh:noexp]) OR ("Thorium Compounds/blood"[mh] OR "Thorium Compounds/cerebrospinal fluid"[mh] OR "Thorium Compounds/urine"[mh]) OR ("Thorium Compounds"[mh] AND ("endocrine system"[mh] OR "hormones, hormone substitutes, and hormone antagonists"[mh] OR "endocrine disruptors"[mh])) OR ("Thorium Compounds"[mh] AND ("computational biology"[mh] OR "medical informatics"[mh] OR genomics[mh] OR genome[mh] OR proteomics[mh] OR proteome[mh] OR metabolomics[mh] OR metabolome[mh] OR genes[mh] OR "gene expression"[mh] OR phenotype[mh] OR genetics[mh] OR genotype[mh] OR transcriptome[mh] OR ("systems biology"[mh] AND ("environmental exposure"[mh] OR "epidemiological monitoring"[mh] OR analysis[sh])) OR "transcription, genetic "[mh] OR "reverse transcription"[mh] OR "transcriptional activation"[mh] OR "transcription factors"[mh] OR ("biosynthesis"[sh] AND (RNA[mh] OR DNA[mh])) OR "RNA, messenger"[mh] OR "RNA, transfer"[mh] OR "peptide biosynthesis"[mh] OR "protein biosynthesis"[mh] OR "reverse transcriptase polymerase chain reaction"[mh] OR "base sequence"[mh] OR "trans-activators"[mh] OR "gene expression profiling"[mh])) OR ("Thorium Compounds/antagonists and inhibitors"[mh]) OR ("Thorium Compounds/metabolism"[mh] AND ("humans"[mh] OR "animals"[mh])) OR ("Thorium Compounds"[mh] AND cancer[sb]) OR ("Thorium Compounds/pharmacology"[majr])) OR ("thorium nitrate"[nm])) AND (1988/01/01 : 3000[dp] OR 1988/01/01 : 3000[mhda])) OR (("Nitric acid, thorium(4+) salt, tetrahydrate"[tw] OR "Thorium nitrate tetrahydrate"[tw] OR "Thorium fluoride (ThF4), tetrahydrate, (T-4)-"[tw] OR "Thorium fluoride"[tw] OR "Thorium tetrafluoride"[tw] OR "Thorium dicarbonate"[tw] OR "Thorium carbonate"[tw]) AND (1988/01/01 : 3000[dp] OR 1988/01/01 : 3000[crdt] OR 1988/01/01 : 3000[edat])) OR ((((("Thorium"[tw] OR "232Th"[tw] OR "228Th"[tw] OR "Thoria"[tw] OR "Thorianite"[tw] OR "Thorotrast"[tw] OR "Thortrast"[tw] OR "Umbrathor"[tw]) OR ("radiothorium"[tw]) OR ("(232)th"[tw] OR "th-232"[tw] OR "th232"[tw] OR "(226)th"[tw] OR "226th"[tw] OR "th-226"[tw] OR "th226"[tw] OR "(227)th"[tw] OR "227th"[tw] OR "th-227"[tw] OR "th227"[tw] OR "(228)th"[tw] OR "th-228"[tw] OR "th228"[tw] OR "(229)th"[tw] OR "229th"[tw] OR "th-229"[tw] OR "th229"[tw] OR "(230)th"[tw] OR "230th"[tw] OR "th-230"[tw] OR "th230"[tw] OR "(231)th"[tw] OR "231th"[tw] OR "th-231"[tw] OR "th231"[tw] OR "(234)th"[tw] OR "234th"[tw] OR "th-234"[tw] OR "th234"[tw] OR "(238)th"[tw] OR "238th"[tw] OR "th-238"[tw] OR "th238"[tw] OR

Table B-2. Database Query Strings

Database search date	Query string
	"(239)th"[tw] OR "239th"[tw] OR "th-239"[tw] OR "th239"[tw])) NOT medline[sb]) AND (1988/01/01 : 3000[dp] OR 1988/01/01 : 3000[crdt] OR 1988/01/01 : 3000[edat]))
	(("thorium"[tw] AND (1988/01/01 : 3000[dp] OR 1988/01/01 : 3000[crdt] OR 1988/01/01 : 3000[edat])) AND (to[sh] OR po[sh] OR ae[sh] OR pk[sh] OR (me[sh] AND ("humans"[mh] OR "animals"[mh])) OR ci[sh] OR bl[sh] OR cf[sh] OR ur[sh] OR "environmental exposure"[mh] OR "endocrine system"[mh] OR "hormones, hormone substitutes, and hormone antagonists"[mh] OR "endocrine disruptors"[mh] OR (("Computational biology"[mh] OR "Medical Informatics"[mh] OR Genomics[mh] OR Genome[mh] OR Proteomics[mh] OR Proteome[mh] OR Metabolomics[mh] OR Metabolome[mh] OR Genes[mh] OR "Gene expression"[mh] OR Phenotype[mh] OR genetics[mh] OR genotype[mh] OR Transcriptome[mh] OR ("Systems Biology"[mh] AND ("Environmental Exposure"[mh] OR "Epidemiological Monitoring"[mh] OR analysis[sh])) OR "Transcription, Genetic "[mh] OR "Reverse transcription"[mh] OR "Transcriptional activation"[mh] OR "Transcription factors"[mh] OR ("biosynthesis"[sh] AND (RNA[mh] OR DNA[mh])) OR "RNA, Messenger"[mh] OR "RNA, Transfer"[mh] OR "peptide biosynthesis"[mh] OR "protein biosynthesis"[mh] OR "Reverse Transcriptase Polymerase Chain Reaction"[mh] OR "Base Sequence"[mh] OR "Trans-activators"[mh] OR "Gene Expression Profiling"[mh])) OR cancer[sb] OR "pharmacology"[sh:noexp] OR thorium/ai OR thorium compounds/ai OR toxicokinetics[mh:noexp])) NOT (((((("Thorium/toxicity"[mh] OR "Thorium/adverse effects"[mh] OR "Thorium/poisoning"[mh] OR "Thorium/pharmacokinetics"[mh]) OR ("Thorium"[mh] AND ("environmental exposure"[mh] OR ci[sh])) OR ("Thorium"[mh] AND toxicokinetics[mh:noexp]) OR ("Thorium/blood"[mh] OR "Thorium/cerebrospinal fluid"[mh] OR "Thorium/urine"[mh]) OR ("Thorium"[mh] AND ("endocrine system"[mh] OR "hormones, hormone substitutes, and hormone antagonists"[mh] OR "endocrine disruptors"[mh])) OR ("Thorium"[mh] AND ("computational biology"[mh] OR "medical informatics"[mh] OR genomics[mh] OR genome[mh] OR proteomics[mh] OR proteome[mh] OR metabolomics[mh] OR metabolome[mh] OR genes[mh] OR "gene expression"[mh] OR phenotype[mh] OR genetics[mh] OR genotype[mh] OR transcriptome[mh] OR ("systems biology"[mh] AND ("environmental exposure"[mh] OR "epidemiological monitoring"[mh] OR analysis[sh])) OR "transcription, genetic "[mh] OR "reverse transcription"[mh] OR "transcriptional activation"[mh] OR "transcription factors"[mh] OR ("biosynthesis"[sh] AND (RNA[mh] OR DNA[mh])) OR "RNA, messenger"[mh] OR "RNA, transfer"[mh] OR "peptide biosynthesis"[mh] OR "protein biosynthesis"[mh] OR "reverse transcriptase polymerase chain reaction"[mh] OR "base sequence"[mh] OR "trans-activators"[mh] OR "gene expression profiling"[mh])) OR ("Thorium/antagonists and inhibitors"[mh]) OR ("Thorium/metabolism"[mh] AND ("humans"[mh] OR "animals"[mh])) OR ("Thorium"[mh] AND cancer[sb]) OR ("Thorium/pharmacology"[majr])) OR (("Thorium Compounds/toxicity"[mh] OR "Thorium Compounds/adverse effects"[mh] OR "Thorium Compounds/poisoning"[mh] OR "Thorium Compounds/pharmacokinetics"[mh]) OR ("Thorium Compounds"[mh] AND ("environmental exposure"[mh] OR ci[sh])) OR ("Thorium Compounds"[mh] AND toxicokinetics[mh:noexp]) OR ("Thorium Compounds/blood"[mh] OR "Thorium Compounds/cerebrospinal fluid"[mh] OR "Thorium Compounds/urine"[mh]) OR ("Thorium Compounds"[mh] AND ("endocrine system"[mh] OR "hormones, hormone substitutes, and hormone antagonists"[mh] OR "endocrine disruptors"[mh])) OR ("Thorium Compounds"[mh] AND ("computational biology"[mh] OR "medical informatics"[mh] OR genomics[mh] OR genome[mh] OR proteomics[mh] OR proteome[mh] OR metabolomics[mh] OR metabolome[mh] OR genes[mh] OR "gene expression"[mh] OR phenotype[mh] OR genetics[mh] OR genotype[mh] OR transcriptome[mh] OR ("systems biology"[mh] AND ("environmental exposure"[mh] OR "epidemiological monitoring"[mh] OR analysis[sh])) OR "transcription,

Table B-2. Database Query Strings

Database search date	Query string
	genetic "[mh] OR "reverse transcription"[mh] OR "transcriptional activation"[mh] OR "transcription factors"[mh] OR ("biosynthesis"[sh] AND (RNA[mh] OR DNA[mh])) OR "RNA, messenger"[mh] OR "RNA, transfer"[mh] OR "peptide biosynthesis"[mh] OR "protein biosynthesis"[mh] OR "reverse transcriptase polymerase chain reaction"[mh] OR "base sequence"[mh] OR "trans-activators"[mh] OR "gene expression profiling"[mh])) OR ("Thorium Compounds/antagonists and inhibitors"[mh]) OR ("Thorium Compounds/metabolism"[mh] AND ("humans"[mh] OR "animals"[mh])) OR ("Thorium Compounds"[mh] AND cancer[sb]) OR ("Thorium Compounds/pharmacology"[majr])) OR ("thorium nitrate"[nm])) AND (1988/01/01 : 3000[dp] OR 1988/01/01 : 3000[mhda])) OR (("Nitric acid, thorium(4+) salt, tetrahydrate"[tw] OR "Thorium nitrate tetrahydrate"[tw] OR "Thorium fluoride (ThF4), tetrahydrate, (T-4)-"[tw] OR "Thorium fluoride"[tw] OR "Thorium tetrafluoride"[tw] OR "Thorium dicarbonate"[tw] OR "Thorium carbonate"[tw]) AND (1988/01/01 : 3000[dp] OR 1988/01/01 : 3000[crdt] OR 1988/01/01 : 3000[edat])) OR ((((("Thorium"[tw] OR "232Th"[tw] OR "228Th"[tw] OR "Thoria"[tw] OR "Thorianite"[tw] OR "Thorotrast"[tw] OR "Thortrast"[tw] OR "Umbrathor"[tw]) OR ("radiothorium"[tw]) OR ("(232)th"[tw] OR "th-232"[tw] OR "th232"[tw] OR "(226)th"[tw] OR "226th"[tw] OR "th-226"[tw] OR "th226"[tw] OR "(227)th"[tw] OR "227th"[tw] OR "th-227"[tw] OR "th227"[tw] OR "(228)th"[tw] OR "th-228"[tw] OR "th228"[tw] OR "(229)th"[tw] OR "229th"[tw] OR "th-229"[tw] OR "th229"[tw] OR "(230)th"[tw] OR "230th"[tw] OR "th-230"[tw] OR "th230"[tw] OR "(231)th"[tw] OR "231th"[tw] OR "th-231"[tw] OR "th231"[tw] OR "(234)th"[tw] OR "234th"[tw] OR "th-234"[tw] OR "th234"[tw] OR "(238)th"[tw] OR "238th"[tw] OR "th-238"[tw] OR "th238"[tw] OR "(239)th"[tw] OR "239th"[tw] OR "th-239"[tw] OR "th239"[tw])) NOT medline[sb]) AND (1988/01/01 : 3000[dp] OR 1988/01/01 : 3000[crdt] OR 1988/01/01 : 3000[edat])))
Toxline	
6/2017	7440-29-1[rn] OR 1314-20-1[rn] OR 13470-07-0[rn] OR 13823-29-5[rn] OR 13453-50-4[rn] OR 13709-59-6[rn] OR 19024-62-5[rn] OR 15571-75-2[rn] OR 15623-47-9[rn] OR 14274-82-9[rn] OR 15594-54-4[rn] OR 14269-63-7[rn] OR 14932-40-2[rn] OR 15065-10-8[rn] OR 34293-72-6[rn] OR 51696-50-5[rn] "thorium" OR "232Th" OR "228Th" OR "Thoria" OR "Thorianite" OR "Thorotrast" OR "Thortrast" OR "Umbrathor" OR "radiothorium" OR "(232)th" OR "th-232" OR "th232" OR "(226)th" OR "226th" OR "th-226" OR "th226" OR "(227)th" OR "227th" OR "th-227" OR "th227" OR "(228)th" OR "th-228" OR "th228" "(229)th" OR "229th" OR "th-229" OR "th229" OR "(230)th" OR "230th" OR "th-230" OR "th230" OR "(231)th" OR "231th" OR "th-231" OR "th231" OR "(234)th" OR "234th" OR "th-234" OR "th234" OR "(238)th" OR "238th" OR "th-238" OR "th238" OR "(239)th" OR "239th" OR "th-239" OR "th239"
Toxcenter	
6/2017	FILE 'TOXCENTER' ENTERED AT 11:28:36 ON 02 JUN 2017 CHARGED TO COST=EH011.13.01.01 L3 10638 SEA FILE=TOXCENTER 7440-29-1 L4 4202 SEA FILE=TOXCENTER 1314-20-1 OR 13470-07-0 OR 13453-50-4 OR 19024-62-5 OR 15571-75-2 OR 15623-47-9 OR 14274-82-9 OR 15594-54-4 OR 14269-63-7 OR 14932-40-2 OR 15065-10-8 OR 34293-72-6 OR 51696-50-5 L5 233 SEA FILE=TOXCENTER 13823-29-5 OR 13709-59-6 L9 14008 SEA FILE=TOXCENTER L3 OR L4 OR L5 L12 14141 SEA FILE=TOXCENTER L9 NOT TSCATS/FS L14 13439 SEA FILE=TOXCENTER L12 NOT PATENT/DT

Table B-2. Database Query Strings

Database search date	Query string
	L15 9269 SEA FILE=TOXCENTER L14 AND PY>=1988 ACT TOXQUERY/Q ---
	L16 QUE (CHRONIC OR IMMUNOTOX? OR NEUROTOX? OR TOXICOKIN? OR BIOMARKER? OR NEUROLOG?)
	L17 QUE (PHARMACOKIN? OR SUBCHRONIC OR PBPK OR EPIDEMIOLOGY/ST,CT, IT)
	L18 QUE (ACUTE OR SUBACUTE OR LD50# OR LD(W)50 OR LC50# OR LC(W)50)
	L19 QUE (TOXICITY OR ADVERSE OR POISONING)/ST,CT,IT
	L20 QUE (INHAL? OR PULMON? OR NASAL? OR LUNG? OR RESPIR?)
	L21 QUE ((OCCUPATION? OR WORKPLACE? OR WORKER?) AND EXPOS?)
	L22 QUE (ORAL OR ORALLY OR INGEST? OR GAVAGE? OR DIET OR DIETS OR DIETARY OR DRINKING(W)WATER?)
	L23 QUE (MAXIMUM AND CONCENTRATION? AND (ALLOWABLE OR PERMISSIBLE))
	L24 QUE (ABORT? OR ABNORMALIT? OR EMBRYO? OR CLEFT? OR FETUS?)
	L25 QUE (FOETUS? OR FETAL? OR FOETAL? OR FERTIL? OR MALFORM? OR OVUM?)
	L26 QUE (OVA OR OVARY OR PLACENTA? OR PREGNAN? OR PRENATAL?)
	L27 QUE (PERINATAL? OR POSTNATAL? OR REPRODUC? OR STERIL? OR TERATOGEN?)
	L28 QUE (SPERM OR SPERMAC? OR SPERMAG? OR SPERMATI? OR SPERMAS? OR SPERMATOB? OR SPERMATOC? OR SPERMATOG?)
	L29 QUE (SPERMATOI? OR SPERMATOL? OR SPERMATOR? OR SPERMATOX? OR SPERMATOZ? OR SPERMATU? OR SPERMI? OR SPERMO?)
	L30 QUE (NEONAT? OR NEWBORN? OR DEVELOPMENT OR DEVELOPMENTAL?)
	L31 QUE (ENDOCRIN? AND DISRUPT?)
	L32 QUE (ZYGOTE? OR CHILD OR CHILDREN OR ADOLESCEN? OR INFANT?)
	L33 QUE (WEAN? OR OFFSPRING OR AGE(W)FACTOR?)
	L34 QUE (DERMAL? OR DERMIS OR SKIN OR EPIDERM? OR CUTANEOUS?)
	L35 QUE (CARCINOG? OR COCARCINOG? OR CANCER? OR PRECANCER? OR NEOPLAS?)
	L36 QUE (TUMOR? OR TUMOUR? OR ONCOGEN? OR LYMPHOMA? OR CARCINOM?)
	L37 QUE (GENETOX? OR GENOTOX? OR MUTAGEN? OR GENETIC(W)TOXIC?)
	L38 QUE (NEPHROTOX? OR HEPATOTOX?)
	L39 QUE (ENDOCRIN? OR ESTROGEN? OR ANDROGEN? OR HORMON?)
	L40 QUE (OCCUPATION? OR WORKER? OR WORKPLACE? OR EPIDEM?)
	L41 QUE L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR

Table B-2. Database Query Strings

Database search date	Query string
	L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33 OR L34 OR L35 OR L36 OR L37 OR L38 OR L39 OR L40
	L42 QUE (RAT OR RATS OR MOUSE OR MICE OR GUINEA(W)PIG? OR MURIDAE OR DOG OR DOGS OR RABBIT? OR HAMSTER? OR PIG OR PIGS OR SWINE OR PORCINE OR MONKEY? OR MACAQUE?)
	L43 QUE (MARMOSET? OR FERRET? OR GERBIL? OR RODENT? OR LAGOMORPHA OR BABOON? OR CANINE OR CAT OR CATS OR FELINE OR MURINE)
	L44 QUE L41 OR L42 OR L43
	L45 QUE (HUMAN OR HUMANS OR HOMINIDAE OR MAMMALS OR MAMMAL? OR PRIMATES OR PRIMATE?)
	L46 QUE L44 OR L45

	L48 3483 SEA FILE=TOXCENTER L15 AND L46 AND L9
	L51 722 SEA FILE=TOXCENTER L48 AND MEDLINE/FS
	L52 439 SEA FILE=TOXCENTER L48 AND BIOSIS/FS
	L53 2310 SEA FILE=TOXCENTER L48 AND CAPLUS/FS
	L54 12 SEA FILE=TOXCENTER L48 NOT (MEDLINE/FS OR BIOSIS/FS OR CAPLUS/FS)
	L55 3010 DUP REM L51 L52 L54 L53 (473 DUPLICATES REMOVED)
	ANSWERS '1-3010' FROM FILE TOXCENTER
	L*** DEL 722 S L48 AND MEDLINE/FS
	L*** DEL 722 S L48 AND MEDLINE/FS
	L56 722 SEA FILE=TOXCENTER L55
	L*** DEL 439 S L48 AND BIOSIS/FS
	L*** DEL 439 S L48 AND BIOSIS/FS
	L57 301 SEA FILE=TOXCENTER L55
	L*** DEL 2310 S L48 AND CAPLUS/FS
	L*** DEL 2310 S L48 AND CAPLUS/FS
	L58 1981 SEA FILE=TOXCENTER L55
	L*** DEL 12 S L48 NOT (MEDLINE/FS OR BIOSIS/FS OR CAPLUS/FS)
	L*** DEL 12 S L48 NOT (MEDLINE/FS OR BIOSIS/FS OR CAPLUS/FS)
	L59 6 SEA FILE=TOXCENTER L55
	L60 2288 SEA FILE=TOXCENTER (L56 OR L57 OR L58 OR L59) NOT MEDLINE/FS
	D SCAN L60

Table B-3. Strategies to Augment the Literature Search

Source	Query and number screened when available
TSCATS[a]	
6/2017	Compounds searched: 7440-29-1; 1314-20-1; 13470-07-0; 13823-29-5; 13453-50-4; 13709-59-6; 19024-62-5; 15571-75-2; 15623-47-9; 14274-82-9; 15594-54-4; 14269-63-7; 14932-40-2; 15065-10-8; 34293-72-6; 51696-50-5
NTP	
6/2017	Terms searched separately: 7440-29-1; 1314-20-1; 13470-07-0; 13823-29-5; 13453-50-4; 13709-59-6; 19024-62-5; 15571-75-2; 15623-47-9; 14274-82-9; 15594-54-4; 14269-63-7; 14932-40-2; 15065-10-8; 34293-72-6; 51696-50-5; thorium; 232Th; 228Th; Thoria; Thorianite; Thorotrast; Thortrast; Umbrathor; radiothorium; (232)th; th-232; th232; (226)th; 226th; th-226; th226; (227)th; 227th; th-227; th227; (228)th; th-228; th228; (229)th; 229th; th-229; th229; (230)th; 230th; th-230; th230; (231)th; 231th; th-231; th231; (234)th; 234th; th-234; th234; (238)th; 238th; th-238; th238; (239)th; 239th; th-239; th239
NIH RePORTER	
10/2017	Search Criteria: Text Search: "thorium" OR "thoria" OR "thorianite" OR "thorotrast" OR "thortrast" OR "umbrathor" OR "radiothorium" OR "232th" OR "(232)th" OR "th-232" OR "th232" OR "(226)th" OR "226th" OR "th-226" OR "th226" OR "(227)th" OR "227th" OR "th-227" OR "th227" OR "228th" OR "(228)th" OR "th-228" OR "th228" OR "(229)th" OR "229th" OR "th-229" OR "th229" OR "(230)th" OR "230th" OR "th-230" OR "th230" OR "(231)th" OR "231th" OR "th-231" OR "th231" OR "(234)th" OR "234th" OR "th-234" OR "th234" OR "(238)th" OR "238th" OR "th-238" OR "th238" OR "(239)th" OR "239th" OR "th-239" OR "th239" Search in: Projects AdminIC: All, Fiscal Year: Active Projects
Other	Identified throughout the assessment process

[a]Several versions of the TSCATS database were searched, as needed, by CASRN including TSCATS1 via Toxline (no date limit), TSCATS2 via https://yosemite.epa.gov/oppts/epatscat8.nsf/ReportSearch?OpenForm (date restricted by EPA receipt date), and TSCATS via CDAT (date restricted by 'Mail Received Date Range'), as well as google for recent TSCA submissions.

The 2017 results were:

- Number of records identified from PubMed, TOXLINE, and TOXCENTER (after duplicate removal): 5,166
- Number of records identified from other strategies: 53
- Total number of records to undergo literature screening: 5,219

B.1.2 Literature Screening

A two-step process was used to screen the literature search to identify relevant studies on thorium:

- Title and abstract screen
- Full text screen

Title and Abstract Screen. Within the reference library, titles and abstracts were screened manually for relevance. Studies that were considered relevant (see Table B-1 for inclusion criteria) were moved to the second step of the literature screening process. Studies were excluded when the title and abstract clearly indicated that the study was not relevant to the toxicological profile.

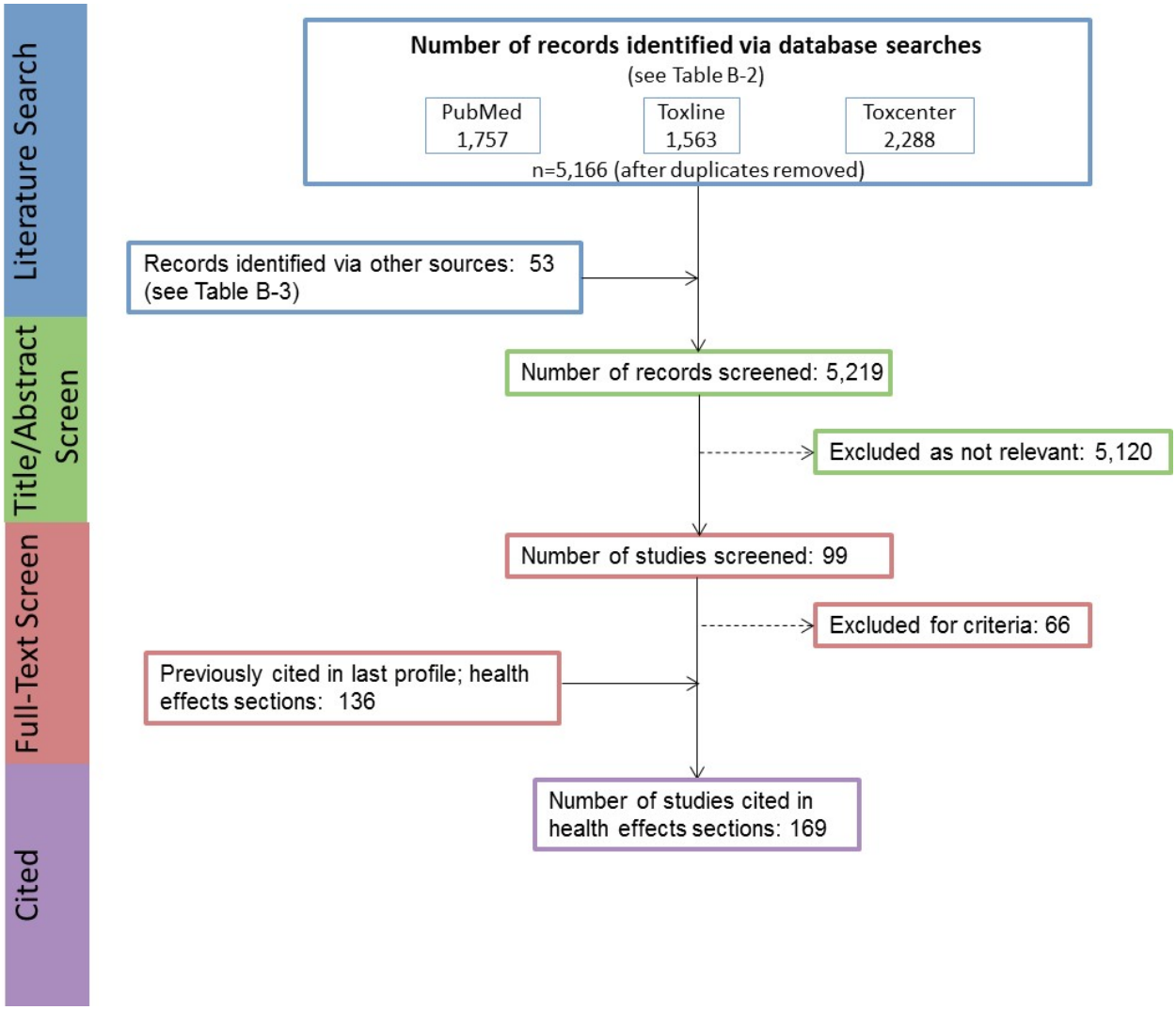
- Number of titles and abstracts screened: 5,219
- Number of health effects studies considered relevant and moved to the next step: 99

Full Text Screen. The second step in the literature screening process was a full text review of individual studies considered relevant in the title and abstract screen step. Each study was reviewed to determine whether it was relevant for inclusion in the toxicological profile.

- Number of studies undergoing full text review: 99
- Number of health effect studies cited in the health effects section of the 1990 toxicological profile: 136
- Total number of health effect studies cited in the health effects sections of the updated profile: 169
- Number of new studies cited in the updated profile: 33

A summary of the results of the literature search and screening is presented in Figure B-1.

Figure B-1. June 2017 Literature Search Results and Screen for Thorium



APPENDIX C. USER'S GUIDE

Chapter 1. Relevance to Public Health

This chapter provides an overview of U.S. exposures, a summary of health effects based on evaluations of existing toxicologic, epidemiologic, and toxicokinetic information, and an overview of the minimal risk levels. This is designed to present interpretive, weight-of-evidence discussions for human health endpoints 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?

Minimal Risk Levels (MRLs)

Where sufficient toxicologic information is available, ATSDR derives 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 hazardous substance 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. Section 1.2, Summary of Health Effects, contains basic information known about the substance. Other sections, such as Section 3.2 Children and Other Populations that are Unusually Susceptible and Section 3.4 Interactions with Other Substances, 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 endpoint 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 endpoint 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 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 that are provided in Chapter 2. Detailed discussions of the MRLs are presented in Appendix A.

Chapter 2. 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 and MRLs to humans for noncancer endpoints. The LSE tables and figures can be used for a quick review of the health effects and to locate data for a specific exposure scenario. The LSE tables and figures should always be used in conjunction with the text. 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 tables and figures follow. The numbers in the left column of the legends correspond to the numbers in the example table and figure.

TABLE LEGEND

See Sample LSE Table (page C-5)

(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 figures are limited to the inhalation and oral routes. Not all substances will have data on each route of exposure and will not, therefore, have all five of the tables and figures. Profiles with more than one chemical may have more LSE tables and figures.

(2) Exposure period. Three exposure periods—acute (<15 days), intermediate (15–364 days), and chronic (≥365 days)—are presented within each relevant route of exposure. In this example, two oral studies of chronic-duration exposure are 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) Figure key. 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 51 identified NOAELs and less serious LOAELs (also see the three "51R" data points in sample LSE Figure 2-X).

(4) Species (strain) No./group. The test species (and strain), whether animal or human, are identified in this column. The column also contains information on the number of subjects and sex per group. Chapter 1, Relevance to Public Health, covers the relevance of animal data to human toxicity and Section 3.1, 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.

(5) Exposure parameters/doses. The duration of the study and exposure regimens are provided in these columns. This permits comparison of NOAELs and LOAELs from different studies. In this case (key number 51), rats were orally exposed to “Chemical X” via feed for 2 years. For a

more complete review of the dosing regimen, refer to the appropriate sections of the text or the original reference paper (i.e., Aida et al. 1992).

(6) Parameters monitored. This column lists the parameters used to assess health effects. Parameters monitored could include serum (blood) chemistry (BC), behavioral (BH), biochemical changes (BI), body weight (BW), clinical signs (CS), developmental toxicity (DX), enzyme activity (EA), food intake (FI), fetal toxicity (FX), gross necropsy (GN), hematology (HE), histopathology (HP), lethality (LE), maternal toxicity (MX), organ function (OF), ophthalmology (OP), organ weight (OW), teratogenicity (TG), urinalysis (UR), and water intake (WI).

(7) Endpoint. This column lists the endpoint examined. The major categories of health endpoints included in LSE tables and figures are death, body weight, respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, dermal, ocular, endocrine, immunological, neurological, reproductive, developmental, other noncancer, and cancer. "Other noncancer" refers to any effect (e.g., alterations in blood glucose levels) not covered in these systems. In the example of key number 51, three endpoints (body weight, hematological, and hepatic) were investigated.

(8) NOAEL. A NOAEL is the highest exposure level at which no adverse effects were seen in the organ system studied. The body weight effect reported in key number 51 is a NOAEL at 25.5 mg/kg/day. NOAELs are not reported for cancer and death; with the exception of these two endpoints, this field is left blank if no NOAEL was identified in the study.

(9) LOAEL. A LOAEL is the lowest dose used in the study that caused an adverse 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 endpoint used to quantify the adverse effect accompanies the LOAEL. Key number 51 reports a less serious LOAEL of 6.1 mg/kg/day for the hepatic system, which was used to derive a chronic exposure, oral MRL of 0.008 mg/kg/day (see footnote "c"). MRLs are not derived from serious LOAELs. A cancer effect level (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. If no LOAEL/CEL values were identified in the study, this field is left blank.

(10) Reference. The complete reference citation is provided in Chapter 8 of the profile.

(11) Footnotes. Explanations of abbreviations or reference notes for data in the LSE tables are found in the footnotes. For example, footnote "c" indicates that the LOAEL of 6.1 mg/kg/day in key number 51 was used to derive an oral MRL of 0.008 mg/kg/day.

FIGURE LEGEND

See Sample LSE Figure (page C-6)

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 chronic exposure period are illustrated.

(14) Endpoint. These are the categories of health effects for which reliable quantitative data exist. The same health effect endpoints 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) LOAEL. In this example, the half-shaded circle that is designated 51R identifies a LOAEL critical endpoint in the rat upon which a chronic oral exposure MRL is based. The key number 51 corresponds to the entry in the LSE table. The dashed descending arrow indicates the extrapolation from the exposure level of 6.1 mg/kg/day (see entry 51 in the sample LSE table) to the MRL of 0.008 mg/kg/day (see footnote "c" in the sample LSE table).

(17) CEL. Key number 59R is one of studies for which CELs were derived. The diamond symbol refers to a CEL for the test species (rat). The number 59 corresponds to the entry in the LSE table.

(18) Key to LSE figure. The key provides the abbreviations and symbols used in the figure.

Table 2-X. Levels of Significant Exposure to [Chemical X] – Oral (1)

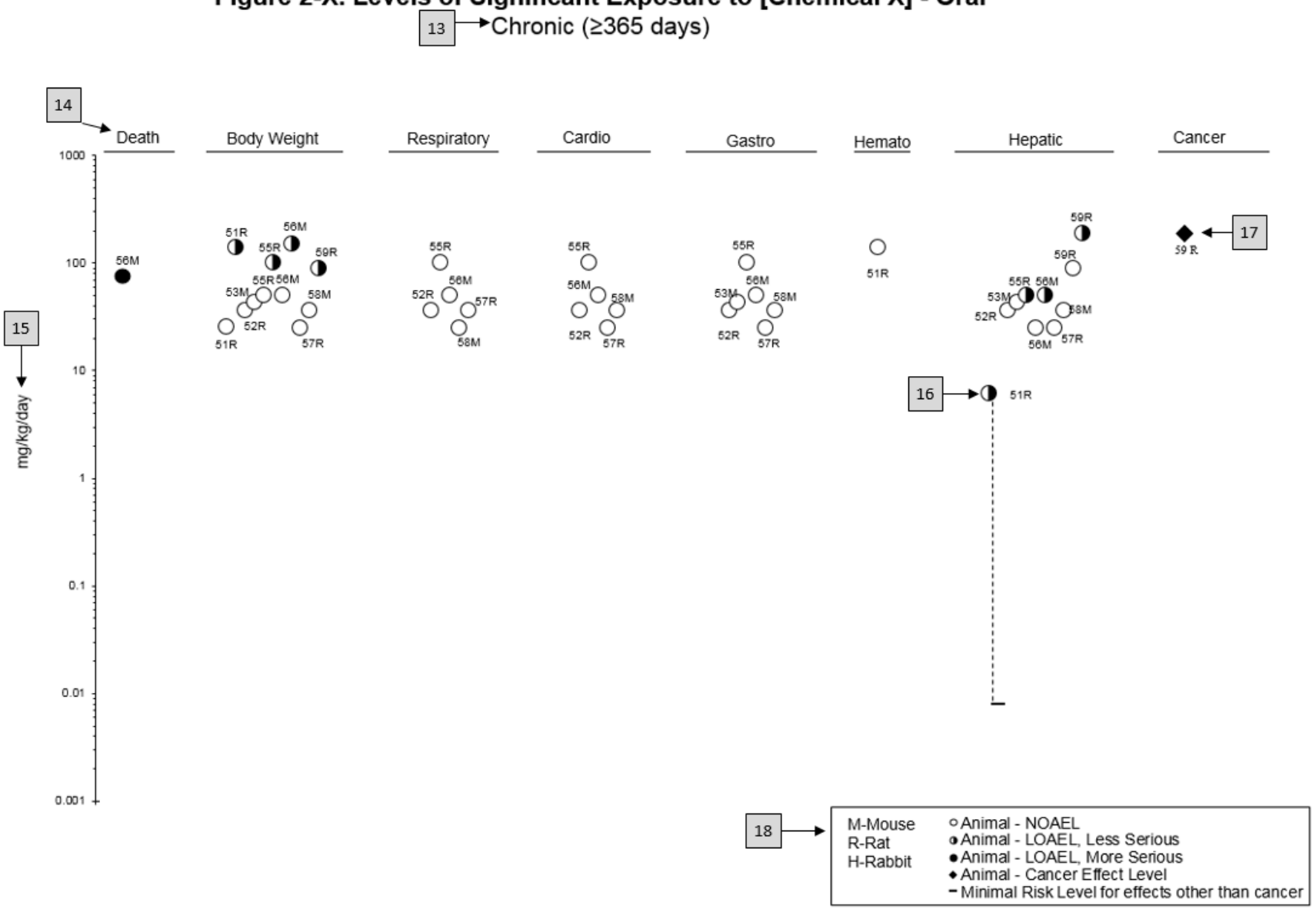
Figure key[a] (3)	Species (strain) No./group (4)	Exposure parameters (5)	Doses (mg/kg/day) (5)	Parameters monitored (6)	Endpoint (7)	NOAEL (mg/kg/day) (8)	Less serious LOAEL (mg/kg/day) (9)	Serious LOAEL (mg/kg/day) (9)	Effect
CHRONIC EXPOSURE (2)									
51	Rat (Wistar) 40 M, 40 F	2 years (F)	M: 0, 6.1, 25.5, 138.0 F: 0, 8.0, 31.7, 168.4	CS, WI, BW, OW, HE, BC, HP	Bd wt	25.5	138.0		Decreased body weight gain in males (23–25%) and females (31–39%)
					Hemato	138.0			
					Hepatic		6.1[c]		Increases in absolute and relative weights at ≥6.1/8.0 mg/kg/day after 12 months of exposure; fatty generation at ≥6.1 mg/kg/day in males and at ≥31.7 mg/kg/day in females, and granulomas in females at 31.7 and 168.4 mg/kg/day after 12, 18, or 24 months of exposure and in males at ≥6.1 mg/kg/day only after 24 months of exposure
Aida et al. 1992 (10)									
52	Rat (F344) 78 M	104 weeks (W)	0, 3.9, 20.6, 36.3	CS, BW, FI, BC, OW, HP	Hepatic	36.3			
					Renal	20.6	36.3		Increased incidence of renal tubular cell hyperplasia
					Endocr	36.3			
George et al. 2002									
59	Rat (Wistar) 58M, 58F	Lifetime (W)	M: 0, 90 F: 0, 190	BW, HP	Cancer		190 F		Increased incidence of hepatic neoplastic nodules in females only; no additional description of the tumors was provided
Tumasonis et al. 1985									

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

(11) [b]Used to derive an acute-duration oral minimal risk level (MRL) of 0.1 mg/kg/day based on the $BMDL_{05}$ of 10 mg/kg/day and an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

[c]Used to derive a chronic-duration oral MRL of 0.008 mg/kg/day based on the $BMDL_{10}$ of 0.78 mg/kg/day and an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

Figure 2-X. Levels of Significant Exposure to [Chemical X] - Oral



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 this material 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 (^{14}C) and tritium (^{3}H) 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 humans 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 depends on the balance of forces within 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) = 3.7×10^{10} disintegrations (transformations)/second (dps) or
= 2.22×10^{12} disintegrations (transformations)/minute (dpm).

The SI unit of activity is the becquerel (Bq); 1 Bq = that quantity of radioactive material in which there is 1 transformation/second. Since activity is proportional to the number of atoms of the radioactive material, the quantity of any radioactive material is usually expressed in curies, regardless of its purity or concentration. The transformation of radioactive nuclei is a random process, and the number of transformations is directly proportional to the number of radioactive atoms present. For any pure radioactive substance, the rate of decay is usually described by its radiological half-life ($t_{½}$, 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.

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 (π) (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
Thorium 232	Liver, bone	14,000,000,000 y	2.6 y	2.6 y
Hydrogen 3 (Tritium)[b]	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	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, which may then react with and transfer energy to a target molecule. This particle is called a primary ionizing particle. Charged particles, in contrast, strike tissue or media 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 by two, thereby changing the parent to a different element. The alpha particle is identical to a helium nucleus consisting of two neutrons and two protons. It results from the radioactive decay of some heavy elements such as uranium, plutonium, radium, thorium, and radon. 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 size, alpha particles have great ionizing power and, thus, lose their kinetic energy quickly. This results in very little penetrating power.

In fact, an alpha particle cannot penetrate a sheet of paper. The range of an alpha particle (the distance the charged particle travels from the point of origin to its resting point) is about 4 cm in air, which decreases considerably to a few micrometers in tissue. These properties cause alpha emitters to be hazardous only if there is internal contamination (i.e., if the radionuclide is inside the body).

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

D.2.4.2.1 Beta Negative Emission. Beta particle (β^-) emission is another process by which a radionuclide, with a neutron excess achieves stability. Beta particle emission decreases the number of neutrons by one and increases the number of protons by one, while the atomic mass number remains unchanged.[1] This transformation results in the formation of a different element. The energy spectrum of beta particle emission ranges from a certain maximum down to zero with the mean energy of the spectrum being about one-third of the maximum. The range 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^+) 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 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 air. In general, external exposures are from material emitting gamma radiation, which readily penetrate the skin and internal organs. Beta and alpha radiation from external sources are far less penetrating and deposit their energy primarily on the skin's outer layer. Consequently, their contribution to the absorbed dose of the total body dose, compared to that deposited by gamma rays, may be negligible.

Characterizing the radiation dose to persons as a result of exposure to radiation is a complex issue. It is difficult to: (1) measure internally the amount of energy actually transferred to an organic material and to correlate any observed effects with this energy deposition; and (2) account for and predict secondary processes, such as collision effects or biologically-triggered effects, that are an indirect consequence of the primary interaction event. Radiation exposure

[1] Neutrinos accompany negative beta particle emissions; anti-neutrinos accompany positron emissions

(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 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 rays, 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-ray 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 healthy 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 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 = radiation 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 have published 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 (ω_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.

Radiation weighting factors for neutrons are based on particle energy according to the following formulas (ICRP 2007):

$$\omega_R = \begin{cases} 2.5 + 18.2e^{\frac{-\ln(E^2 n)}{6}} & , En < 1\ MeV \\ 5.0 + 17.0e^{\frac{-\ln(2E^2 n)}{6}} & , 1\ MeV \leq En \leq 50\ MeV \\ 2.5 + 3.25e^{\frac{-\ln(0.04E^2 n)}{6}} & , En > 50\ MeV \end{cases}$$

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) to tissue T,
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})	1.602×10^{-10} Jm^{-1}	kiloelectron volts per micrometer (keV μm^{-1})	1.602×10^{-10} Jm^{-1}

Jkg^{-1} = Joules per kilogram; $Jkg^{-1}s^{-1}$ = Joules per kilogram per second; Jm^{-1} = Joules per meter; s^{-1} = per second

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 1.3×10^5 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 (^{220}Rn). In this case, 1.3×10^5 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 inhaling a concentration of 1 WL for the reference period of 170 hours, or more generally

WLM = concentration (WL) x exposure time (months) / (one “month” = 170 working hours).

D.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 particles 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

According to Mettler and Moseley (1985), at acute doses up to 10 rad (100 mGy), single strand breaks in DNA may be produced. These single strand breaks may be repaired rapidly. With doses in the range of 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, 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, such as the breast, lung, stomach, and thyroid, appear to be more common than others.

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 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 cholesterol, diabetes, and infection.

REFERENCES FOR APPENDIX D

ATSDR. 1990a. Toxicological profile for thorium. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. Atlanta, GA.

ATSDR. 1990. Toxicological profile for radium. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. Atlanta, GA.

ATSDR. 2012. Toxicological profile for radon. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. Atlanta, GA.

ATSDR. 2013. Toxicological profile for uranium. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. Atlanta, GA.

BEIR III. 1980. The effects on populations of exposure to low levels of ionizing radiation. Committee on the Biological Effects of Ionizing Radiations, National Research Council. Washington, DC: National Academy Press.

BEIR IV. 1988. Health risks of radon and other internally deposited alpha emitters. Committee on the Biological Effects of Ionizing Radiations, National Research Council. Washington, DC: National Academy Press.

BEIR V. 1988. Health effects of exposure to low levels of ionizing radiation. Committee on the Biological Effects of Ionizing Radiations, National Research Council. Washington, DC: National Academy Press.

Brodsky A. 1996. Review of radiation risks and uranium toxicity with application to decisions associated with decommissioning clean-up criteria. Hebron, Connecticut: RSA Publications.

Cember H. 1996. Introduction to health physics. New York, NY: McGraw Hill.

Cember H and Johnson T. 2007.

Early P, Razzak M, Sodee D. 1979. Nuclear medicine technology. 2nd ed. St. Louis: C.V. Mosby Company.

Eichholz G. 1982. Environmental aspects of nuclear power. Ann Arbor, MI: Ann Arbor Science.

Hendee W. 1973. Radioactive isotopes in biological research. New York, NY: John Wiley and Sons.

Hobbs C, McClellan R. 1986. Radiation and radioactive materials. In: Doull J, et al., eds. Casarett and Doull's Toxicology. 3rd ed. New York, NY: Macmillan Publishing Co., Inc., 497-530.

ICRP. 1977. International Commission on Radiological Protection. Recommendations of the International Commission on Radiological Protection. ICRP Publication 26. Vol 1. No. 3. Oxford: Pergamon Press.

ICRP. 1979. International Commission on Radiological Protection. Limits for intakes of radionuclides by workers. ICRP Publication 20. Vol. 3. No. 1-4. Oxford: Pergamon Press.

ICRP. 1979. Limits for Intakes of Radionuclides by Workers. Publication 30. International Commission on Radiological Protection. Pergamon Press.

ICRP. 1984. International Commission on Radiological Protection. A compilation of the major concepts and quantities in use by ICRP. ICRP Publication 42. Oxford: Pergamon Press.

ICRP. 1990. International Commission on Radiological Protection 1990 Recommendations of the ICRP

ICRP. 2007. Publication No. 103, The 2007 Recommendations of the International Commission on Radiological Protection. ICRP 37(2-4):1-332.

ICRU. 1980. International Commission on Radiation Units and Measurements. ICRU Report No. 33. Washington, DC.

James A. 1987. A reconsideration of cells at risk and other key factors in radon daughter dosimetry. In: Hopke P, ed. Radon and its decay products: Occurrence, properties and health effects. ACS Symposium Series 331. Washington, DC: American Chemical Society, 400-418.

James A, Roy M. 1987. Dosimetric lung models. In: Gerber G, et al., ed. Age-related factors in radionuclide metabolism and dosimetry. Boston: Martinus Nijhoff Publishers, 95-108.

Kondo S. 1993. Health effects of low-level radiation. Kinki University Press, Osaka, Japan (available from Medical Physics Publishing, Madison, Wisconsin).

Kato H, Schull W. 1982. Studies of the mortality of A-bomb survivors. Report 7 Part 8, Cancer mortality among atomic bomb survivors, 1950-78. Radiat Res 90;395-432.

Klaassen. 2001. Casarett and Doull's toxicology: The basic science of poisons. McGraw-Hill.

LBL. 2011. Atomic and nuclear properties of materials: Neutron (n). Lawrence Berkeley Laboratory. http://pdg.lbl.gov/2011/AtomicNuclearProperties/neutron.html. (December 7, 2011).

Mettler F, Moseley R. 1985. Medical effects of ionizing radiation. New York: Grune and Stratton.

Nakamura. Particle data group. 2012. The review of particle physics and 2011 partial update. J Phys G 37:075021. http://pdg.lbl.gov/. (December 7, 2011).

NCRP. 1971. Basic radiation protection criteria. National Council on Radiation Protection and Measurements. Report No. 39. Washington, DC.

NCRP. 1985. A handbook of radioactivity measurements procedures. 2nd ed. National Council on Radiation Protection and Measurements. Report No. 58. Bethesda, MD:

NCRP. 1993. Risk estimates for radiation protection. National Council on Radiation Protection and Measurements. Report 115. Bethesda, Maryland

NRC. 2012a. Electronic Code of Federal Regulations. Title 10: Energy. Part 20-Standards for protection against radon. Subpart A-General provisions. § 20.1003 Definitions. http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&sid=48e22c6aa171831075552dcbea1a5939&rgn=div8&view=text&node=10:1.0.1.1.16.1.76.3&idno=10. (January 27, 2012)

NRC. 2012b. Electronic Code of Federal Regulations. Title 10: Energy. Part 20-Standards for protection against radon. Subpart A-General provisions. § 20.1004 Units of radiation dose. http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr;sid=1f508d141b96be7c2a197d0724844aa5;rgn=div5;view=text;node=10%3A1.0.1.1.16;idno=10;cc=ecfr#10:1.0.1.1.16.1.76.4. (January 27, 2012)

Oganessian YT, Abdullin FS, Bailey PD, et al. 2010. Synthesis of a new element with atomic number Z = 117. Phys Rev Lett 104(14):142502-1 to 142402-4

Otake M, Schull W. 1984. Mental retardation in children exposed in utero to the atomic bombs: A reassessment. Technical Report RERF TR 1-83, Radiation Effects Research Foundation, Japan.

Raabe OG. 2010. Concerning the health effects of internally deposited radionuclides. Health Phys 98(3):515-536.

Rubin P, Casarett G. 1968. Clinical radiation pathology. Philadelphia: W.B. Sanders Company, 33.

Schull WJ. 1988. Effect on intelligence test score of prenatal exposure to ionizing radiation in Hiroshima and Nagasaki: A comparison of the T65DR and DS86 dosimetry systems. Radiation Effects Research Foundation. Japan.

Shimizu Y, Kodama K, Nishi, N, et al. 2010. Radiation exposure and circulatory disease risk: Hiroshima and Nagasaik atomic bomb survivor data, 1950-2003. Brit Med J. 340:b5349.

Thisgaard H, Jensen M, Elema DR. 2001. Medium to large scale radioisotope production for targeted radiotherapy using a small PET cyclotron. Appl Radiat Isot 69(1):1-7.

UNSCEAR. 1977. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources and effects of ionizing radiation. New York: United Nations.

UNSCEAR. 1982. United Nations Scientific Committee on the Effects of Atomic Radiation. Ionizing radiation: Sources and biological effects. New York: United Nations.

UNSCEAR. 1986. United Nations Scientific Committee on the Effects of Atomic Radiation. Genetic and somatic effects of ionizing radiation. New York: United Nations.

UNSCEAR. 1988. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources, effects and risks of ionization radiation. New York: United Nations.

UNSCEAR. 1993. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources and effects of ionizing radiation. New York: United Nations.

USNRC. 2011a. Title 10, Code of Federal Regulations Part 20.1003, U.S. Nuclear Regulatory Commission, Washington, DC. http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&sid=a0927f5dead51eb92d3892fad0f1ac42&rgn=div8&view=text&node=10:1.0.1.1.16.1.76.3&idno=10. (December 9, 2011)

USNRC. 2011. Title 10 Code of Federal Regulations Part 20, Table 1004(b).1. U.S. Nuclear Regulatory Commission, Washington, D.C. http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&sid=a0927f5dead51eb92d3892fad0f1ac42&rgn=div8&view=text&node=10:1.0.1.1.16.1.76.4&idno=10. (December 9, 2011)

APPENDIX E. 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 may find the following information helpful for fast answers to often-asked questions.

Primary Chapters/Sections of Interest

Chapter 1: Relevance to Public Health: The Relevance to Public Health Section provides an overview of exposure and health effects and evaluates, interprets, and assesses the significance of toxicity data to human health. A table listing minimal risk levels (MRLs) is also included in this chapter.

Chapter 2: Health Effects: Specific health effects identified in both human and animal studies are reported by type of health effect (e.g., death, hepatic, renal, immune, reproductive), route of exposure (e.g., inhalation, oral, dermal), and length of exposure (e.g., acute, intermediate, and chronic).
NOTE: Not all health effects reported in this section are necessarily observed in the clinical setting.

Pediatrics:

Section 3.2 Children and Other Populations that are Unusually Susceptible
Section 3.3 Biomarkers of Exposure and Effect

ATSDR Information Center

Phone: 1-800-CDC-INFO (800-232-4636) or 1-888-232-6348 (TTY)
Internet: http://www.atsdr.cdc.gov

The following additional materials are available online:

Case Studies in Environmental Medicine are self-instructional publications designed to increase primary health care providers' knowledge of a hazardous substance in the environment and to aid in the evaluation of potentially exposed patients (see https://www.atsdr.cdc.gov/csem/csem.html).

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 (see https://www.atsdr.cdc.gov/MHMI/index.asp). 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 (see https://www.atsdr.cdc.gov/toxfaqs/Index.asp).

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 • Web Page: https://www.cdc.gov/nceh/.

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, 395 E Street, S.W., Suite 9200, Patriots Plaza Building, Washington, DC 20201 • Phone: 202-245-0625 or 1-800-CDC-INFO (800-232-4636) • Web Page: https://www.cdc.gov/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 • Web Page: https://www.niehs.nih.gov/.

Clinical Resources (Publicly Available Information)

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 • Web Page: http://www.acoem.org/.

The American College of Medical Toxicology (ACMT) is a nonprofit association of physicians with recognized expertise in medical toxicology. Contact: ACMT, 10645 North Tatum Boulevard, Suite 200-111, Phoenix AZ 85028 • Phone: 844-226-8333 • FAX: 844-226-8333 • Web Page: http://www.acmt.net.

The Pediatric Environmental Health Specialty Units (PEHSUs) is an interconnected system of specialists who respond to questions from public health professionals, clinicians, policy makers, and the public about the impact of environmental factors on the health of children and reproductive-aged adults. Contact information for regional centers can be found at http://pehsu.net/findhelp.html.

The American Association of Poison Control Centers (AAPCC) provide support on the prevention and treatment of poison exposures. Contact: AAPCC, 515 King Street, Suite 510, Alexandria VA 22314 • Phone: 701-894-1858 • Poison Help Line: 1-800-222-1222 • Web Page: http://www.aapcc.org/.

APPENDIX F. GLOSSARY

Absorption—The process by which a substance crosses biological membranes and enters systemic circulation. Absorption can also refer to the taking up of liquids by solids, or of gases by solids or liquids.

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

Adsorption—The adhesion in an extremely thin layer of molecules (as of gases, solutes, or liquids) to the surfaces of solid bodies or liquids with which they are in contact.

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

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

Benchmark Dose (BMD) or Benchmark Concentration (BMC)—is the dose/concentration corresponding to a specific response level estimate using a statistical dose-response model applied to either experimental toxicology or epidemiology data. For example, a BMD_{10} would be the dose corresponding to a 10% benchmark response (BMR). The BMD is determined by modeling the dose-response curve in the region of the dose-response relationship where biologically observable data are feasible. The BMDL or BMCL is the 95% lower confidence limit on the BMD or BMC.

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.

Biomarkers—Indicators signaling events in biologic systems or samples, typically classified as markers of exposure, effect, and susceptibility.

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

Carcinogen—A chemical capable of inducing cancer.

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

Case Report—A report that describes a single individual with a particular disease or exposure. These reports may suggest some potential topics for scientific research, but are not actual research studies.

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

Ceiling Value—A concentration that must not be exceeded.

Chronic Exposure—Exposure to a chemical for ≥365 days, as specified in the Toxicological Profiles.

Clastogen—A substance that causes breaks in chromosomes resulting in addition, deletion, or rearrangement of parts of the chromosome.

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, and who are disease-free at start of follow-up. Often, at least one exposed group is compared to one unexposed group, while in other cohorts, exposure is a continuous variable and analyses are directed towards analyzing an exposure-response coefficient.

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

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

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

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

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 effect occurs. Effects include malformations and variations, altered growth, and *in utero* death.

Epidemiology—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.

Excretion—The process by which metabolic waste products are removed from the body.

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.

Half-life—A measure of rate for the time required to eliminate one-half of a quantity of a chemical from the body or environmental media.

Health Advisory—An estimate of acceptable drinking water levels for a chemical substance derived by EPA and 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.

Immediately Dangerous to Life or Health (IDLH)—A condition that poses a threat of life or health, or conditions that pose an immediate threat of severe exposure to contaminants that are likely to have adverse cumulative or delayed effects on health.

Immunotoxicity—Adverse effect on the functioning of the immune system that may result from exposure to chemical substances.

Incidence—The ratio of new cases 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.

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

***In Vitro*—**Isolated from the living organism and artificially maintained, as in a test tube.

***In Vivo*—**Occurring within the living organism.

Lethal Concentration$_{(LO)}$ (LC_{LO})—The lowest concentration of a chemical in air 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.

Lethal Dose$_{(LO)}$ (LD_{Lo})—The lowest dose of a chemical introduced by a route other than inhalation that has been reported to have caused death in humans or animals.

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

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

Lowest-Observed-Adverse-Effect Level (LOAEL)—The lowest exposure level 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.

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.

Metabolism—Process in which chemical substances are biotransformed in the body that could result in less toxic and/or readily excreted compounds or produce a biologically active intermediate.

Minimal Risk Level (MRL)—An estimate of daily human exposure to a hazardous substance that is likely to be without an appreciable risk of adverse noncancer health effects over a specified route and 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—The state of being diseased; the morbidity rate is the incidence or prevalence of a disease in a specific population.

Mortality—Death; the mortality rate is a measure of the number of deaths in a population during a specified interval of time.

Mutagen—A substance that causes mutations, which are changes in the DNA sequence of a cell's DNA. 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 hazardous substance.

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

Octanol-Water Partition Coefficient (K_{ow})—The equilibrium ratio of the concentrations of a chemical in *n*-octanol and water, in dilute solution.

Odds Ratio (OR)—A means of measuring the association between an exposure (such as toxic substances and a disease or condition) that represents the best estimate of relative risk (risk as a ratio of the incidence among subjects exposed to a particular risk factor divided by the incidence among subjects who were not exposed to the risk factor). An odds ratio that is greater than 1 is considered to indicate greater risk of disease in the exposed group compared to the unexposed group.

Permissible Exposure Limit (PEL)—An Occupational Safety and Health Administration (OSHA) regulatory limit on the amount or concentration of a substance not to be exceeded in workplace air averaged over any 8-hour work shift of a 40-hour workweek.

Pesticide—General classification of chemicals specifically developed and produced for use in the control of agricultural and public health pests (insects or other organisms harmful to cultivated plants or animals).

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.

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.

Physiologically Based Pharmacodynamic (PBPD) Model—A type of physiologically based dose-response model that quantitatively describes the relationship between target tissue dose and toxic endpoints. 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 type of physiologically based dose-response model that is comprised of a series of compartments representing organs or tissue groups with realistic weights and blood flows. These models require a variety of physiological information, including tissue volumes, blood flow rates to tissues, cardiac output, alveolar ventilation rates, and possibly membrane permeabilities. The models also utilize biochemical information, such as blood:air partition coefficients, and metabolic parameters. PBPK models are also called biologically based tissue dosimetry models.

Prevalence—The number of cases of a disease or condition in a population at one point in time.

Prospective Study—A type of cohort study in which a group is followed over time and the pertinent observations are made on events occurring after the start of the study.

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 RfC is expressed in units of mg/m^3 or ppm.

Reference Dose (RfD)—An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily oral exposure of the human population to a potential hazard that is likely to be without risk of deleterious noncancer health effects during a lifetime. The oral RfD is expressed in units of mg/kg/day.

Reportable Quantity (RQ)—The quantity of a hazardous substance that is considered reportable under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). RQs are (1) ≥1 pound or (2) for selected substances, an amount established by regulation either under CERCLA or under Section 311 of the Clean Water Act. Quantities are measured over a 24-hour period.

Reproductive Toxicity—The occurrence of adverse effects on the reproductive system that may result from exposure to a hazardous substance. 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.

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 hazardous substance.

Risk Factor—An aspect of personal behavior or lifestyle, an environmental exposure, existing health condition, or an inborn or inherited characteristic that is associated with an increased occurrence of disease or other health-related event or condition.

Risk Ratio/Relative Risk—The ratio of the risk among persons with specific risk factors compared to the risk among persons without risk factors. A risk ratio that is greater than 1 indicates greater risk of disease in the exposed group compared to the unexposed group.

Short-Term Exposure Limit (STEL)—A STEL is a 15-minute TWA exposure that should not be exceeded at any time during a workday.

Standardized Mortality Ratio (SMR)—A ratio of the observed number of deaths and the expected number of deaths in a specific standard population.

Target Organ Toxicity—This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

Teratogen—A chemical that causes structural defects that affect the development of an organism.

Threshold Limit Value (TLV)—An American Conference of Governmental Industrial Hygienists (ACGIH) concentration of a substance to which it is believed that nearly all workers may be repeatedly exposed, day after day, for a working lifetime without adverse effect. The TLV may be expressed as a Time-Weighted Average (TLV-TWA), as a Short-Term Exposure Limit (TLV-STEL), or as a ceiling limit (TLV-C).

Time-Weighted Average (TWA)—An average exposure within a given time period.

Toxicokinetic—The absorption, distribution, metabolism, and elimination of toxic compounds in the living organism.

Toxics Release Inventory (TRI)—The TRI is an EPA program that tracks toxic chemical releases and pollution prevention activities reported by industrial and federal facilities.

Uncertainty Factor (UF)—A factor used in operationally deriving the Minimal Risk Level (MRL), Reference Dose (RfD), or Reference Concentration (RfC) 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 lowest-observed-adverse-effect level (LOAEL) data rather than no-observed-adverse-effect level (NOAEL) data. A default for each individual UF is 10; if complete certainty in data exists, a value of 1 can be used; however, a reduced UF of 3 may be used on a case-by-case basis (3 being the approximate logarithmic average of 10 and 1).

Xenobiotic—Any substance that is foreign to the biological system.

APPENDIX G. ACRONYMS, ABBREVIATIONS, AND SYMBOLS

AAPCC	American Association of Poison Control Centers
ACGIH	American Conference of Governmental Industrial Hygienists
ACOEM	American College of Occupational and Environmental Medicine
ACMT	American College of Medical Toxicology
ADI	acceptable daily intake
ADME	absorption, distribution, metabolism, and excretion
AEGL	Acute Exposure Guideline Level
AIC	Akaike's information criterion
AIHA	American Industrial Hygiene Association
ALT	alanine aminotransferase
AOEC	Association of Occupational and Environmental Clinics
AP	alkaline phosphatase
AST	aspartate aminotransferase
atm	atmosphere
ATSDR	Agency for Toxic Substances and Disease Registry
AWQC	Ambient Water Quality Criteria
BCF	bioconcentration factor
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
BMR	benchmark response
BUN	blood urea nitrogen
C	centigrade
CAA	Clean Air Act
CAS	Chemical Abstract Services
CDC	Centers for Disease Control and Prevention
CEL	cancer effect level
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
Ci	curie
CI	confidence interval
cm	centimeter
CPSC	Consumer Products Safety Commission
CWA	Clean Water Act
DNA	deoxyribonucleic acid
DOD	Department of Defense
DOE	Department of Energy
DWEL	drinking water exposure level
EAFUS	Everything Added to Food in the United States
ECG/EKG	electrocardiogram
EEG	electroencephalogram
EPA	Environmental Protection Agency
ERPG	emergency response planning guidelines
F	Fahrenheit
F1	first-filial generation
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FR	Federal Register

FSH	follicle stimulating hormone
g	gram
GC	gas chromatography
gd	gestational day
GGT	γ-glutamyl transferase
GRAS	generally recognized as safe
HEC	human equivalent concentration
HED	human equivalent dose
HHS	Department of Health and Human Services
HPLC	high-performance liquid chromatography
HSDB	Hazardous Substance Data Bank
IARC	International Agency for Research on Cancer
IDLH	immediately dangerous to life and health
IRIS	Integrated Risk Information System
Kd	adsorption ratio
kg	kilogram
kkg	kilokilogram; 1 kilokilogram is equivalent to 1,000 kilograms and 1 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	Level of Significant Exposure
LT_{50}	lethal time, 50% kill
m	meter
mCi	millicurie
MCL	maximum contaminant level
MCLG	maximum contaminant level goal
MF	modifying factor
mg	milligram
mL	milliliter
mm	millimeter
mmHg	millimeters of mercury
mmol	millimole
MRL	Minimal Risk Level
MS	mass spectrometry
MSHA	Mine Safety and Health Administration
Mt	metric ton
NAAQS	National Ambient Air Quality Standard
NAS	National Academy of Science
NCEH	National Center for Environmental Health
ND	not detected
ng	nanogram
NHANES	National Health and Nutrition Examination Survey
NIEHS	National Institute of Environmental Health Sciences

NIOSH	National Institute for Occupational Safety and Health
NLM	National Library of Medicine
nm	nanometer
nmol	nanomole
NOAEL	no-observed-adverse-effect level
NPL	National Priorities List
NR	not reported
NRC	National Research Council
NS	not specified
NTP	National Toxicology Program
OR	odds ratio
OSHA	Occupational Safety and Health Administration
PAC	Protective Action Criteria
PAH	polycyclic aromatic hydrocarbon
PBPD	physiologically based pharmacodynamic
PBPK	physiologically based pharmacokinetic
PEHSU	Pediatric Environmental Health Specialty Unit
PEL	permissible exposure limit
PEL-C	permissible exposure limit-ceiling value
pg	picogram
PND	postnatal day
POD	point of departure
ppb	parts per billion
ppbv	parts per billion by volume
ppm	parts per million
ppt	parts per trillion
REL	recommended exposure level/limit
REL-C	recommended exposure level-ceiling value
RfC	reference concentration
RfD	reference dose
RNA	ribonucleic acid
SARA	Superfund Amendments and Reauthorization Act
SCE	sister chromatid exchange
SD	standard deviation
SE	standard error
SGOT	serum glutamic oxaloacetic transaminase (same as aspartate aminotransferase or AST)
SGPT	serum glutamic pyruvic transaminase (same as alanine aminotransferase or ALT)
SIC	standard industrial classification
SMR	standardized mortality ratio
sRBC	sheep red blood cell
STEL	short term exposure limit
TLV	threshold limit value
TLV-C	threshold limit value-ceiling value
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
TWA	time-weighted average
UF	uncertainty factor
U.S.	United States
USDA	United States Department of Agriculture
USGS	United States Geological Survey
USNRC	U.S. Nuclear Regulatory Commission

VOC	volatile organic compound
WBC	white blood cell
WHO	World Health Organization
>	greater than
≥	greater than or equal to
=	equal to
<	less than
≤	less than or equal to
%	percent
α	alpha
β	beta
γ	gamma
δ	delta
μm	micrometer
μg	microgram
q_1^*	cancer slope factor
–	negative
+	positive
(+)	weakly positive result
(–)	weakly negative result