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

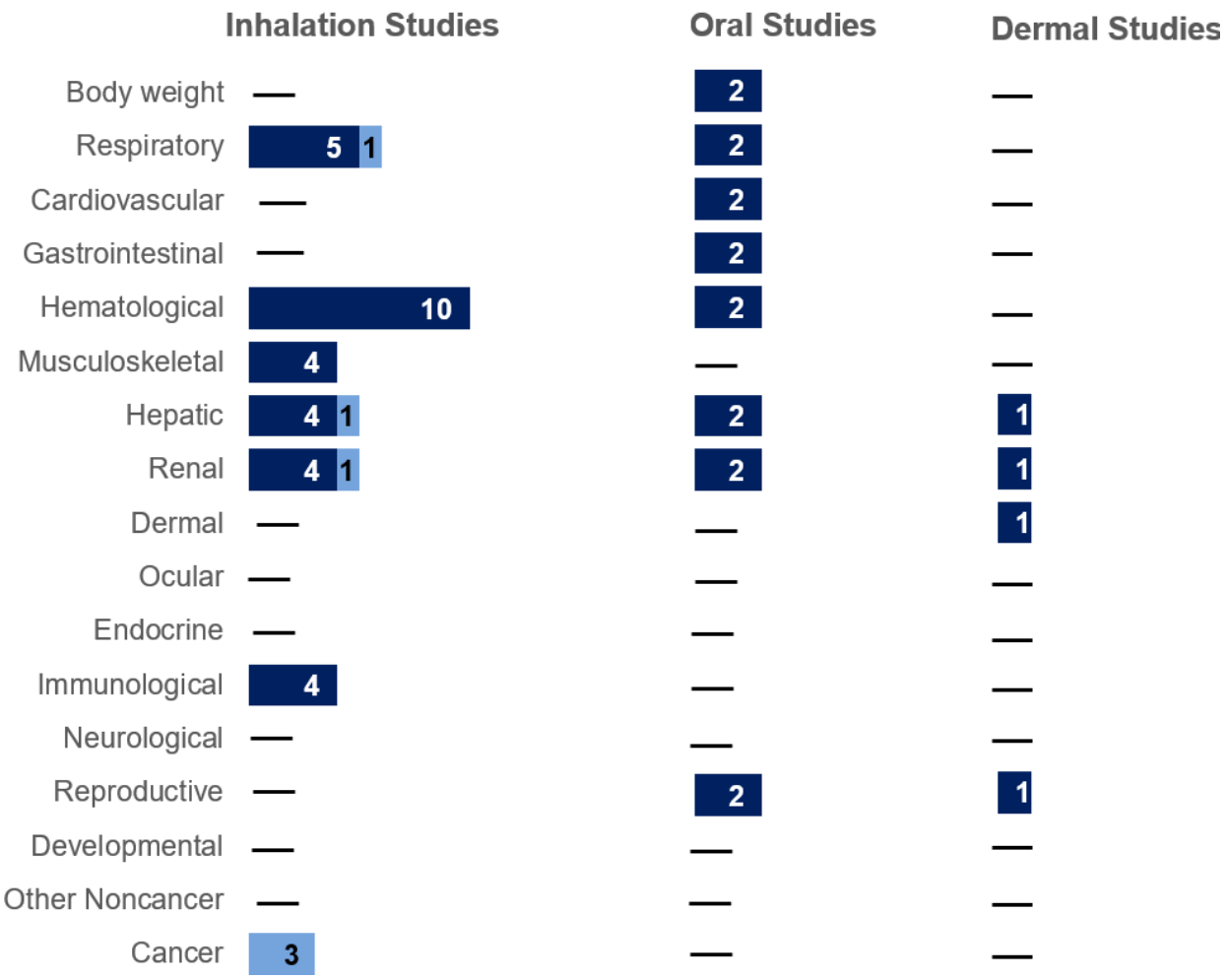
Studies evaluating the health effects of inhalation, oral, and dermal exposure of humans and animals to thorium that are discussed in Chapter 2 are summarized in Figure 6-1. The purpose of this figure is to illustrate the information concerning the health effects of thorium. The number of human and animal 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