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 mercury is available. Where adequate information is not available, ATSDR, in conjunction with NTP, is required to ensure the initiation of a program of research designed to determine the adverse health effects (and techniques for developing methods to determine such health effects) from exposure to mercury.

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 mercury that are discussed in Chapter 2 are summarized in Figure 6-1 for elemental mercury, Figure 6-2 for inorganic mercury, Figure 6-3 for organic mercury, and Figure 6-4 for predominant form of mercury exposure unknown in general populations. The purpose of these figures is to illustrate the information concerning the health effects of mercury compounds. 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.

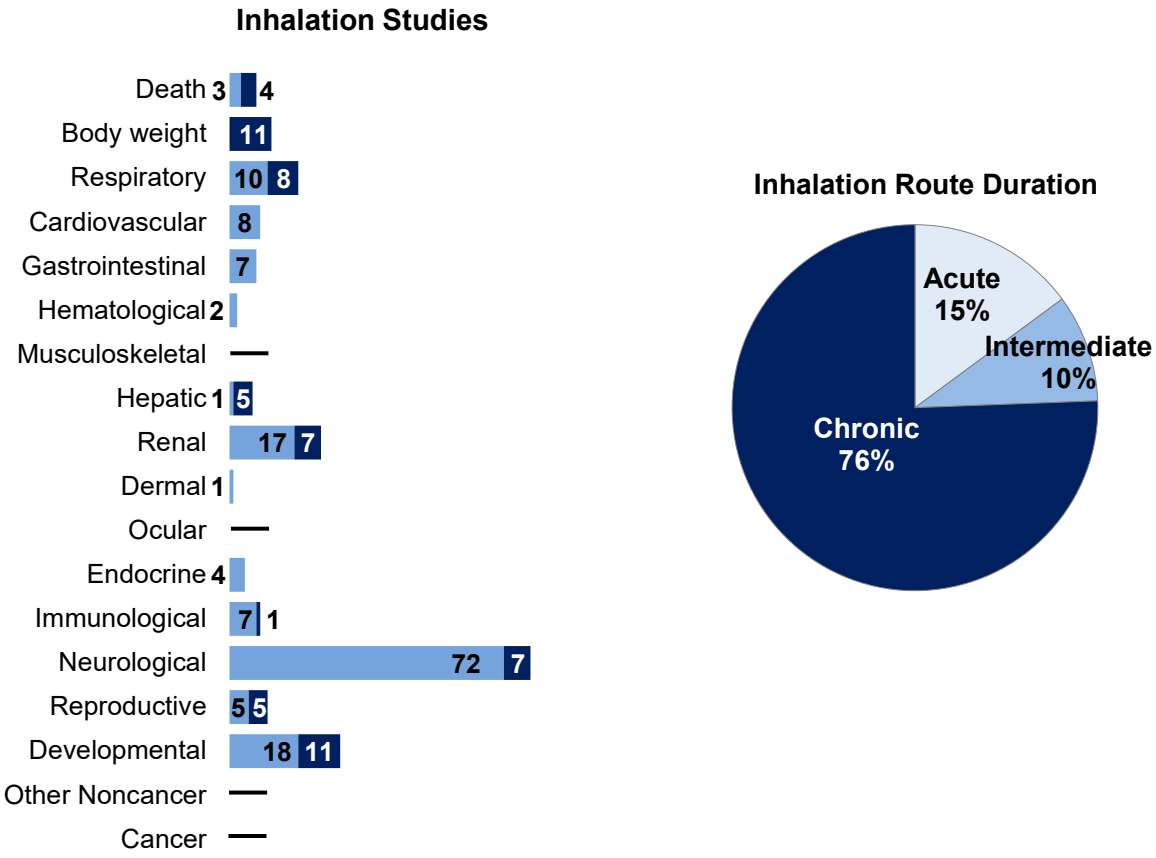
6.2 IDENTIFICATION OF DATA NEEDS

Missing information in Figures 6-1, 6-2, 6-3, and 6-4 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 Elemental Mercury by Route and Endpoint*

The most studied endpoints (in humans & animals) were potential neurological, developmental, and renal effects resulting from inhalation exposure

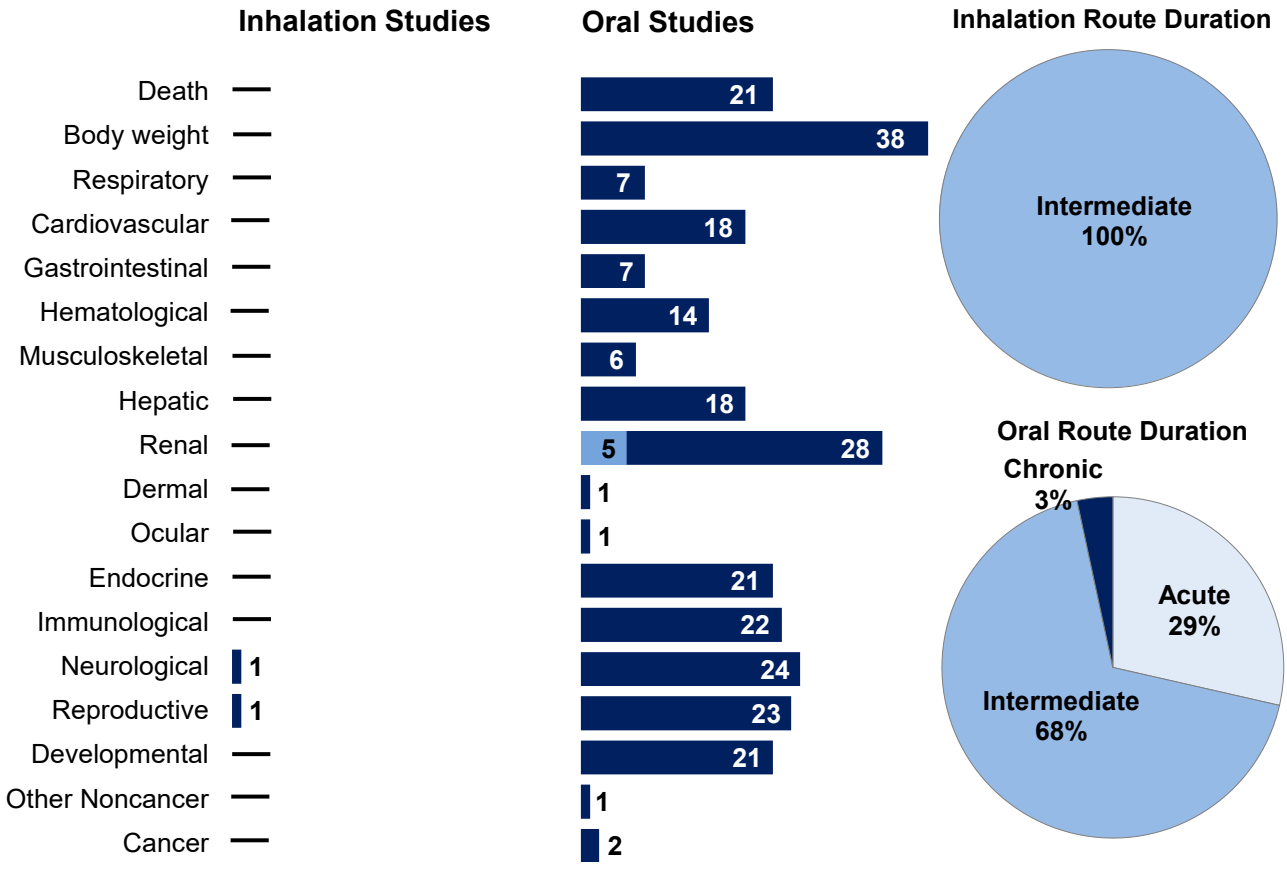
Inhalation exposure studies in humans comprised the majority of elemental mercury health effects research



*Includes studies discussed in Chapter 2; the number of studies include those finding no effect. Most studies examined multiple endpoints. No oral or dermal studies in humans or animals were located.

Figure 6-2. Summary of Existing Health Effects Studies on Inorganic Mercuric Salts by Route and Endpoint*

The most studied endpoints (in humans & animals) were potential hematological, immune, neurological, renal, and cardiac system effects resulting from oral exposure in animals
Oral exposure studies in animals comprised the majority of inorganic mercury health effects research

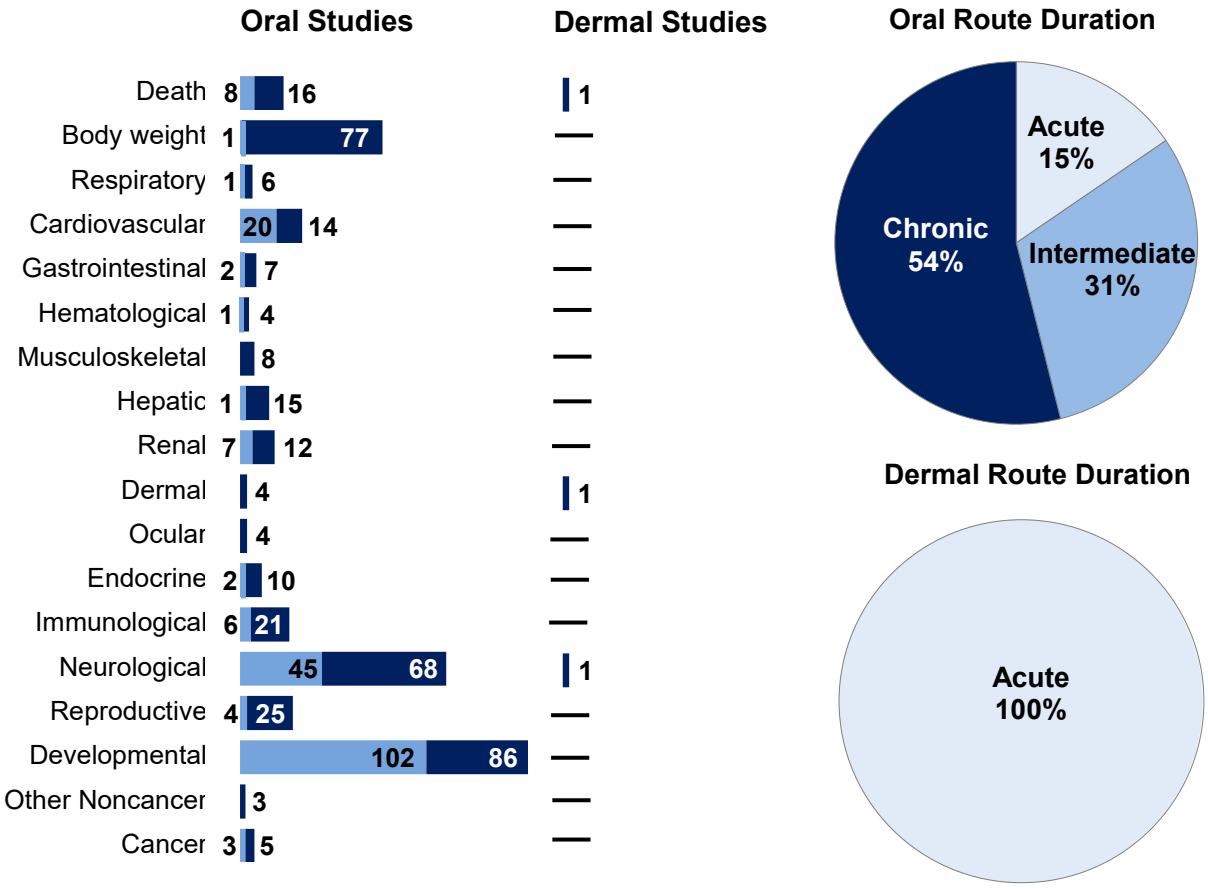


*Includes studies discussed in Chapter 2; the number of studies include those finding no effect. Most studies examined multiple endpoints. No dermal studies in humans or animals were located.

Figure 6-3. Summary of Existing Health Effects Studies on Organic Mercury by Route and Endpoint*

The most studied endpoints (in humans & animals) were potential developmental, neurological, and body weight effects resulting from oral exposure

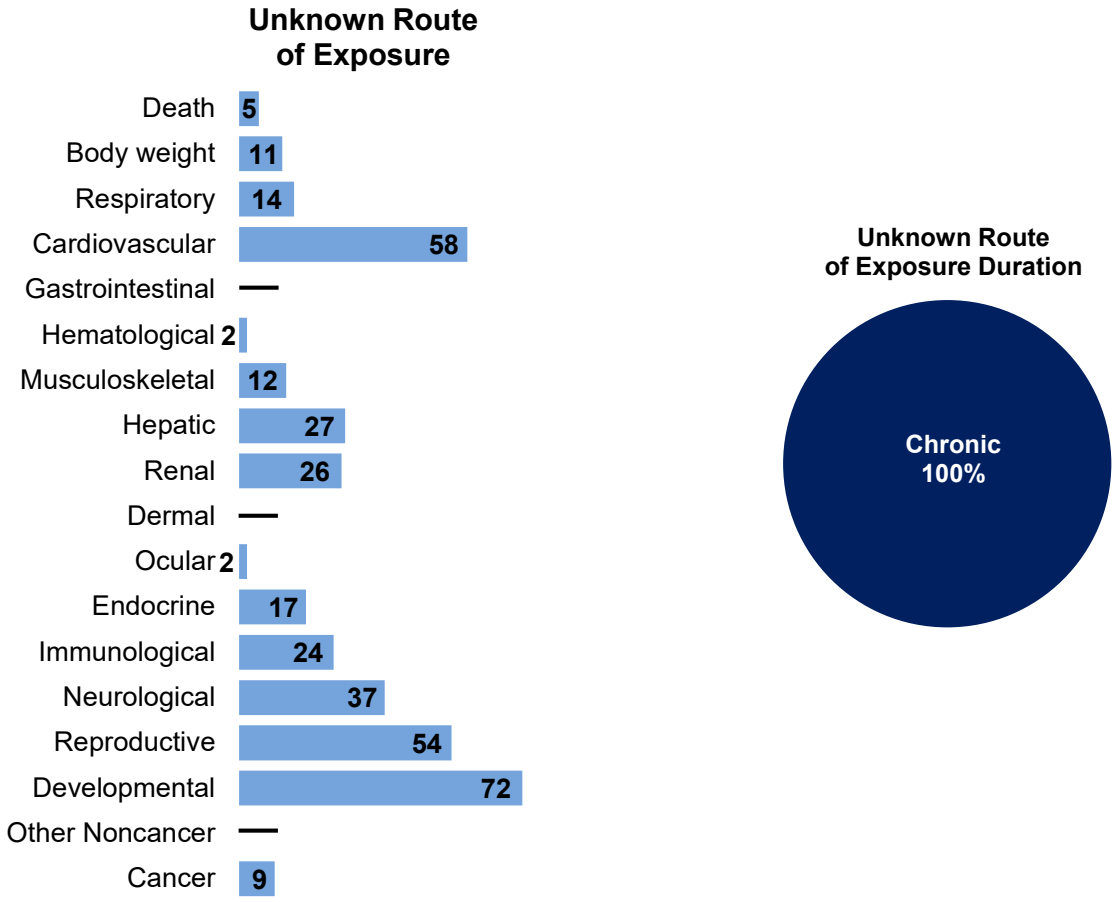
Oral exposure studies in humans and animals comprised the majority of inorganic mercury health effects research



*Includes studies discussed in Chapter 2; the number of studies include those finding no effect. Most studies examined multiple endpoints. No inhalation studies in humans or animals were located.

Figure 6-4. Summary of Existing Health Effects Studies on General Population Exposure to Mercury (Unspecified Route and Form)*

The most studied endpoints (in humans) were potential developmental, cardiovascular, and reproductive effects resulting from unknown exposure sources



*Includes studies discussed in Chapter 2; the number of studies include those finding no effect. Most studies examined multiple endpoints.

Elemental Mercury Inhalation MRLs. A chronic-duration inhalation MRL was developed for elemental mercury based on neurological effects (tremor) in mercury workers. Additional data may provide further definition of the NOAEL-LOAEL boundary.

The acute-duration animal inhalation database identified neurodevelopmental effects as the critical effect in animals. However, the database was not considered adequate for identification of a point of departure. The studies that identified the lowest LOAEL values involved whole-body exposure for relative short daily durations (1 or 4 hours/day) and did not control for potential oral exposure from preening or volatilization of mercury deposited on the skin/fur. Studies limiting the inhalation exposure to nose-only that examine neurodevelopmental endpoints, test multiple concentrations, and are for longer daily durations would be useful for establishing an acute-duration inhalation MRL for elemental mercury.

The available data from animal intermediate-duration inhalation studies suggest that neurodevelopmental toxicity is the most sensitive target of toxicity. However, most of the studies in the database only tested one concentration and were not considered adequate for establishing concentration-response relationships. Additional studies evaluating neurodevelopmental endpoints and testing several concentrations would be useful for developing an intermediate-duration inhalation MRL for elemental mercury.

Elemental Mercury Oral MRLs. No oral MRLs for elemental mercury have been derived for any exposure duration due to lack of data. The primary route of exposure to elemental mercury is inhalation. Oral exposure to elemental mercury is not considered an important route of environmental exposure. Therefore, there is not a data need for elemental mercury and oral exposure.

Inorganic Mercury Salts Inhalation MRLs. No inhalation MRLs for inorganic mercury salts have been derived for any exposure duration due to lack of data. The primary route of exposure to inorganic mercury salts is oral. While inorganic salts can release mercury vapor into the air, inhalation exposure to inorganic mercury compounds is not currently considered an important route of environmental exposure. Therefore, there is not a data need for inorganic mercury compounds and inhalation exposure.

Inorganic Mercury Salts Oral MRLs. Acute- and immediate-duration oral MRLs were derived for inorganic mercury salts based on renal effects in rats (Apaydin et al. 2016; Dieter et al. 1992; NTP 1993). However, data for chronic-duration exposure are insufficient to derive an MRL. For chronic-duration exposure, the lowest LOAEL identified is 0.66 mg Hg/kg/day for increased systolic blood pressure in rats

exposed to mercuric chloride in drinking water for 1 year, with a NOAEL of 0.33 mg Hg/kg/day (Perry and Erlanger 1974). Thus, the lowest chronic-duration LOAEL is 44-fold higher than the lowest intermediate-duration LOAEL of 0.015 mg Hg/kg/day, which was identified in the study used in development of the intermediate-duration oral MRL. Studies examining effects of chronic-duration oral exposure at lower levels, particularly ones evaluating sensitive systems identified in Section 1.2 (neurological and neurodevelopmental, renal, cardiovascular, hematological, immunological, and male reproductive), may provide sufficient data to derive a chronic-duration oral MRL.

Organic Mercury Inhalation MRLs. No inhalation MRLs for organic mercury have been derived for any exposure duration due to lack of data. The primary route of exposure to organic mercury compounds is oral. Inhalation exposure to organic mercury is not considered an important route of environmental exposure. Therefore, there is not a data need for organic mercury compounds and inhalation exposure.

Organic Mercury Oral MRLs. A chronic-duration oral MRL for methylmercury was derived based on a meta-analysis of three epidemiological studies for neurodevelopmental effects. Additional data may lead to more accurate definition of the NOAEL-LOAEL boundary.

No acute- or intermediate-duration oral MRLs were derived for organic mercury compounds. The human database is limited to dietary exposure for chronic-durations. The animal database provides data for acute- and intermediate-duration oral exposure. However, if MRLs were based on available animal data, the acute- and intermediate-duration oral MRLs would be lower than the chronic-duration oral MRLs based on data in humans. Additional studies in animals would provide important information regarding effects of organic mercury at low levels of exposure, but additional animal data would not be useful to derive acute- and intermediate-duration oral MRLs for organic mercury.

Health Effects.

Neurological and Neurodevelopmental. The nervous system, including the developing nervous system, is well-established as a sensitive target for all forms of mercury. Epidemiological studies have identified associations between exposure to elemental mercury and neurological effects and between methylmercury exposure and neurodevelopmental effects. Additional studies evaluating neurological and neurodevelopmental effects at low exposures would provide additional data to better define population NOAELs.

The oral database evaluating neurological effects in animals following exposure to inorganic or organic mercury compounds clearly identifies the developing and the adult nervous system as a sensitive target of mercury toxicity. Additional studies conducted at low doses for inorganic mercury compounds would provide additional information to define NOAELs and LOAELs at the low end of the dose-response curve. Evidence for neurological effects in animals following inhalation exposure to elemental mercury is less robust, particularly regarding neuro-developmental effects. Additional inhalation studies in adult and developing animals may better inform dose-response relationships following exposure to mercury vapor.

Renal. The kidney is a well-established target of mercury in humans and animals. Additional epidemiological studies for elemental mercury and organic mercury would provide additional data to define the low end of the dose-response curve for these mercury classes. The renal toxicity of inorganic mercury salts has been well-characterized in animal studies. Additional low-dose, oral studies on inorganic mercury salts in animals would provide important information to define NOAEL and LOAEL values for renal effects.

Cardiovascular. Results of epidemiological studies on populations exposed to elemental mercury and methylmercury do not provide conclusive evidence that the cardiovascular system is a sensitive target in humans exposed to mercury.

Epidemiological studies are inconsistent, with some studies showing an association between biomarkers and cardiovascular effects and other studies showing no associations. Additional study populations exposed to elemental mercury and methylmercury would provide important information to determine if the cardiovascular system is a target of mercury at occupational (elemental mercury) and environmental (general populations and populations with high fish diets) exposure levels.

The majority of animal studies show that oral exposure to mercuric chloride or methylmercury is associated with altered cardiovascular function (increased blood pressure, positive cardiac inotropism, decreased baroreflex sensitivity). Mechanistic studies would help to determine mechanisms of action and human relevance of cardiovascular findings in animals.

Hematological. Few epidemiological studies have evaluated hematological effects of mercury compounds. Although there are plausible mechanisms for mercury to adversely affect

erythrocytes, data from epidemiological studies are insufficient to determine if exposure to mercury produces adverse hematological effects in humans. Additional epidemiological studies on elemental and methylmercury would provide important information to determine if the hematological system is a target of occupational or environmental exposure to mercury.

There is limited evidence of impaired clotting, decreases in RBC parameters, and increases in WBC counts in animals following oral exposure to inorganic mercury salts. However, biological relevance of available findings is unclear due to limited data, small magnitude of effect, and/or inconsistent findings. Additional multi-dose studies of various durations in multiple species are needed to better define potential hematological effects and inform dose-response relationships for inorganic mercury salts. Additional animal studies on hematological effects of elemental and organic mercury compounds could provide information on the potential for hematological effects.

Immunological. Immunological effects of mercury compounds have not been well-investigated in epidemiological studies, and there is currently no clear evidence that elemental or methylmercury is associated with altered immune function. Epidemiological studies of populations exposed to elemental and organic mercury could provide information on potential associations between exposure and immune system function.

Mercury-induced autoimmunity has been reported in autoimmune-susceptible mice following oral exposure to mercuric chloride or methylmercury, including autoimmune-susceptible mice exposed during development. Data in non-susceptible animal strains exposed to methylmercury generally report immune suppression following oral exposure; however, there are limited data suggesting that very low exposure levels may stimulate the immune system. Additional low-dose studies of mercuric chloride or methylmercury in non-susceptible strains may help elucidate potential non-monotonic immune responses associated with mercury exposure. Mechanistic studies would help determine mechanisms of action and human relevance of findings in autoimmune susceptible mice.

Reproductive. Epidemiological studies are available for workers exposed to elemental mercury, populations with high fish diets, and general populations. Few studies have examined the same reproductive endpoints, and those that did often reported conflicting results. The available epidemiological studies do not provide convincing evidence that the reproductive system is a sensitive target of mercury exposure in males or females. Additional epidemiological

studies could provide evidence to determine if reproductive effects are associated with environmental exposures in humans.

Laboratory animal studies evaluating reproductive endpoints following oral exposure to mercuric chloride or methylmercury consistently reported dose-related impairments in fertility. A few inorganic mercuric chloride studies suggest that the male reproductive system may be a sensitive target of toxicity at very low oral doses; however, findings from these studies need to be confirmed with additional low-exposure, multi-dose oral studies reporting quantitative endpoints to better define potential male reproductive effects and inform dose-response relationships.

Developmental. Epidemiological studies have assessed effects in workers exposed to elemental mercury, populations with high fish diets, and general populations. These studies examined mercury exposure and anthropometric measures in newborns (e.g., birth weight and size) and postnatal growth in children. Results are conflicting, with no strong evidence of associations between mercury exposure and *in utero* or postnatal growth. Additional epidemiological studies would provide important information to determine if gestational exposure to elemental or organic mercury alters the developing fetus.

Laboratory animal studies evaluating developmental endpoints following oral exposure to methylmercury reported adverse effects (decreased offspring weight and survival, increased fetal malformations and variations) at concentrations 3–4-fold higher than the lowest LOAELs associated with neurodevelopmental or immunodevelopmental effects. Since the nervous and immune systems appear to be the most sensitive targets during development, additional studies evaluating standard developmental effects are not a high priority.

Epidemiology and Human Dosimetry Studies. Most epidemiology studies of associations between exposure to mercury and health outcomes have relied on biomarkers (blood, hair, urine) as exposure metrics. Use of these studies for estimating risks from exposures to mercury require applications of dosimetry models for converting biomarkers into equivalent exposures. Steady-state mass balance models have been used to convert BHg or HHg levels into equivalent daily average intakes of methylmercury (ATSDR 1997; IRIS 2001). Additional studies would be helpful for addressing uncertainties in key parameters in these models. These include central estimates of population variability for the following parameters, including during pregnancy: (1) fraction of ingested methylmercury absorbed; (2) fraction of mercury body burden in blood; (3) terminal elimination half-time of mercury

from blood; and (4) hair-blood mercury ratio. Steady-state mass-balance models can also be used to convert urinary mercury levels to equivalent exposure concentrations of elemental mercury vapor in air. Additional studies would be helpful for addressing uncertainties in key parameters of these models. These include central estimates and population variability for the following parameters: (1) fraction of inhaled mercury absorbed; (2) fraction of absorbed dose excreted in urine; and (3) relationship between steady-state urinary mercury (μg/g creatinine or μg/L) and urinary excretion rate (μg/day).

Steady-state models can be used for dosimetry extrapolations of exposures that are constant for a period of approximately 1 year, the exposure duration needed to achieve >95% of steady state (Section 3.1). Dosimetry extrapolations for exposures of shorter duration (e.g., acute-duration MRLs) require PBPK models that can reliably predict the kinetics of change in BHg levels prior to achieving steady state. Several pharmacokinetics models of inorganic mercury (mercury vapor, mercuric) in humans have been published (Abass et al. 2018; Farris et al. 2008; Jonsson et al. 1999; Leggett et al. 2001 (Section 3.1.5). Pharmacokinetics models of methylmercury have been developed for humans (Byczkowski and Lipscomb 2001; Carrier et al. 2001a; Gearhart et al. 1995; Young et al. 2001) and a variety of other animal species (Carrier et al. 2001b; Farris et al. 1993; Young et al. 2001). The developing fetus and neonate are highly sensitive to exposures to methylmercury; therefore, predictions of exposures during fetal and postnatal development are potentially valuable for improving dosimetry extrapolations (Byczkowski and Lipscomb 2001; Gearhart et al. 1995). Additional studies that evaluate performance of these models for predicting maternal BHg and HHg levels during pregnancy and fetal (cord) blood levels would be helpful for assessing uncertainty in application of these models to human dosimetry extrapolation.

PBPK models for inorganic mercuric mercury in humans have been developed (Abass et al. 2018; Farris et al. 2008); however, no models are available for use in interspecies dosimetry extrapolation. PBPK models of inorganic mercuric mercury in monkeys, mice, and rats would be helpful for extrapolating external dose-response relationships (e.g., NOAELs, LOAELs) observed in these species to equivalent external doses in humans.

Biomarkers of Exposure and Effect. Epidemiology studies of health effects of mercury have relied on mercury levels in blood and hair as biomarkers of exposure to methylmercury and mercury in urine as a biomarker of exposure to inorganic (elemental or mercuric) mercury (Section 3.3.1, Biomarkers of Exposure). These biomarkers are most useful in studies of populations in which the dominant exposures are to methylmercury (e.g., high fish consumers) or inorganic mercury (e.g., workers exposed to relatively

high levels of mercury vapor). In high fish consumers, most of the mercury in hair and blood will derive from methylmercury, whereas in workers exposed to high levels of mercury vapor, most of the mercury in urine will derive from exposure to mercury vapor. Interpretation of biomarkers measured in general populations that experience relatively low exposures to all forms of mercury is more uncertain because exposure to any form of mercury will contribute mercury to blood, hair, and urine. Additional studies would be helpful for identifying biomarkers of exposure to methylmercury and inorganic mercury (elemental and mercuric) in general populations, to facilitate studies of dose-response relationships at the lower exposure levels expected in these populations.

No biomarkers specific for the health effects of mercury are available. Exposure biomarkers that reflect mercury body burden (mercury levels in blood, hair, urine) are used to attribute signs and symptoms to mercury exposure.

Absorption, Distribution, Metabolism, and Excretion. Mercury toxicokinetics have been extensively studied in humans and animals (Section 3.1, Toxicokinetics). However, additional studies would be helpful for increasing confidence in estimates of certain toxicokinetics parameters that are important in dosimetry models, in particular, conversion of biomarker measurements, such as mercury in blood, hair, or urine, to equivalent exposures (see Epidemiology and Human Dosimetry Studies section above). These include, for all forms of mercury, the absorption fractions for oral and inhalation exposure, fractions of absorbed mercury distributed to blood, and half-time for elimination of mercury from blood.

Comparative Toxicokinetics. Mercury toxicokinetics have been studied in the animal models used to estimate dose-response relationships for methylmercury, elemental mercury vapor, and inorganic mercury compounds (humans, monkeys, mice, rats). Toxicokinetics models of methylmercury for a variety of animal species have been developed (Section 3.1.5). Models of mercury vapor and inorganic mercuric mercury in monkeys, mice, and rats would be helpful for extrapolating external dose-response relationships (e.g., NOAELs, LOAELs) observed in these species to equivalent external doses in humans.

Children's Susceptibility. All forms of mercury are toxic to the developing nervous system and studies conducted in humans and animals suggest that the developing nervous system is more vulnerable than the fully-developed nervous system. Additional epidemiological studies of neurodevelopmental outcomes in populations exposed to low levels of methylmercury (levels experienced in general populations) would be helpful for establishing toxicity thresholds, if they exist. Outcomes of particular interest are attainment of language proficiency, which was found to be inversely associated with mercury

intake from dietary fish in a large general population prospective study (Vejrup et al. 2016, 2018), but was not studied in two other important prospective studies of high fish consumers who experienced higher exposures to methylmercury (Faroe Islands, Seychelle Islands).

Physical and Chemical Properties. The physical and chemical properties of metallic mercury and its inorganic and organic compounds have been well characterized to permit estimation of their environmental fate (Budavari 1989; Lewis 1993; Osol 1980; Spencer and Voigt 1968; Verschueren 1983; Weast 1988; Weiss 1986). Most values are available for the log K_{ow}, log K_{oc}, Henry's law constant, vapor pressure, and solubility in water. Experimental data exist that allow characterization of the environmental fate of metallic mercury and inorganic and organic mercury compounds in a variety of environmental media. No data needs are identified.

Production, Import/Export, Use, Release, and Disposal. Information on mercury production, import/export, and use are well documented (EPA 2020b, 2023; USGS 2020, 2023a).

Information on disposal methods and recycling of mercury and mercury containing wastes are available (DOI 1985, 1989, 1993).

One area that requires additional study is the use of elemental mercury by members of specific religious or cultural groups in their ceremonies, rituals, and practices so an assessment of the magnitude of these activities can be made. In addition, information on how mercury is used in these ceremonies and rituals, as well as the methods of mercury disposal used, would be helpful in assessing the potential pathways for human exposure and environmental releases.

Environmental Fate. Mercury released to the atmosphere may be transported long distances before being removed by wet or dry deposition. Residence time in the atmosphere has been estimated to range from 60–90 days to 0.3–2 years (EPA 1984; Glass et al. 1991). Volatile forms of mercury released in water or soil can enter the atmosphere, but most mercury is adsorbed to soil and sediment (EPA 1984; Meili et al. 1991). Sorbed mercury may be reduced to elemental mercury or bioconverted to volatile organic forms (EPA 1984). The major transport and transformation processes involved in the environmental fate of mercury have been fairly well defined; the most important fate process for human exposure, bioaccumulation of methylmercury in aquatic food chains is also well defined (EPA 1979, 1984; Stein et al. 1996; UNEP 2018). Additional information on mercury transport and flux in waterbodies and in tropical environments, in general, would be helpful.

Bioavailability from Environmental Media. Metallic mercury vapors in the air are readily absorbed through the lungs following inhalation exposure, while inorganic and organic mercury compounds are poorly absorbed via this route (Berlin et al. 1969a). Gastrointestinal absorption of methylmercury is nearly 100%, while gastrointestinal absorption of inorganic mercury is low (typically <10%) (Clarkson 1989; Friberg and Nordberg 1973). Metallic mercury vapor can be absorbed following dermal exposure; however, dermal absorption of the vapor accounts for a much smaller percentage (2.6% of the total absorbed through the lungs) than absorption through the inhalation route (Hursh et al. 1989). Toxicokinetic data indicate that inorganic mercury salts and organomercury compounds are dermally absorbed to some extent (Friberg et al. 1961; Moody et al. 2009; Sartorelli et al. 2003; Skowronski et al. 2000); however, certain organomercury compounds (dimethylmercury, phenylmercury) are readily absorbed through the skin (Blayney et al. 1997; Gotelli et al. 1985; Nierenberg et al. 1998; Siegler et al. 1999; Toribara et al. 1997). Data are needed regarding the bioavailability of elemental, inorganic, and organic mercury forms from contaminated surface water, groundwater, soil, or plant material. Data are also needed regarding the bioavailability of mercuric chloride in air because of the possibility of inhalation of volatilized mercuric chloride near emission sources. Additional data on the bioavailability of elemental mercury, inorganic mercury compounds, and organic mercury compounds (specifically, methylmercury) in soil would also be useful in assessing the risks from dermal and oral exposures at mining, industrial, or hazardous waste sites.

Food Chain Bioaccumulation. Mercury is known to bioconcentrate in aquatic organisms and biomagnify in aquatic food chains (ASTER 1997; EPA 1984; Kohler et al. 1990; Watras and Bloom 1992; UNEP 2018). While bioconcentration in the aquatic food chain is well studied, little is known about the bioaccumulation potential for terrestrial food chains, although it appears to be smaller than in aquatic systems (Lindqvist et al. 1991). Additional information on the potential for terrestrial food chain biomagnification would be useful since mercury binds to organic matter in soils and sediment. Information on foliar uptake of mercury and of plant/mercury chemistry is needed to determine whether plants convert elemental or divalent mercury into other forms of mercury that are more readily bioaccumulated and whether plants are able to emit these different forms to the air. Additional information is also needed to improve biotransfer factors for mercury from soil to plants to animals.

Exposure Levels in Environmental Media. Environmental monitoring data are available for mercury in ambient air, surface water, groundwater, drinking water, soils, sediments, and foodstuffs

(Section 3.3.1 for citations); however, additional monitoring data on mercury levels in all environmental media, particularly drinking water, would be helpful in determining current exposure levels.

Estimates of human intake from inhalation of ambient air and ingestion of contaminated foods and drinking water are available (Burger et al. 1992), although the estimates may be based on specific intake scenarios (e.g., information is most extensive for fish and other seafood products). Better estimates of fish consumption rates for high-volume consumers (subsistence fishers) and recreational fishers are needed, as is information on fish-specific consumption rates by these populations.

Additional information on the levels of mercury in foods other than fish and seafood would be very useful in determining total dietary intakes. Additional research is needed to characterize mercury exposures via consumption of marine mammal species. Available data indicate that the ratio of methylmercury to total mercury varies within tissues, and that only a small portion of mercury is methylated in the marine mammal liver. Also, other trace metal constituents of marine mammal tissues such as selenium, cadmium, and other metals may interact with and influence the bioavailability of mercury. Additional studies are needed to understand why the relatively high concentrations of mercury measured in marine mammal tissues do not appear to result in elevation of HHg levels among Alaskan natives that consume marine mammal tissues.

Reliable monitoring data for the levels of mercury in contaminated media at hazardous waste sites are needed so that the information obtained on levels of mercury in the environment can be used in combination with the known body burden of mercury to assess the potential risk of adverse health effects in populations living in the vicinity of hazardous waste sites.

Exposure Levels in Humans. Mercury has been measured in human blood, hair, breast milk, urine, feces, and saliva (Section 3.3.1). Continued biomonitoring data are needed to determine the temporal trends of mercury exposure to the U.S. population and for integrating these data into existing health information systems.

Exposures of Children. Children are exposed to mercury by a variety of exposure pathways depending on their age. The most important pathways appear to be ingestion of methylmercury in foods, primarily fish and shellfish (FDA 2017a), intake of inorganic mercury associated with dental amalgams in children up to 18 years old, and inhalation of metallic mercury vapors. These are the same important pathways of exposure for adults as well. Nursing infants can also be exposed to mercury in breastmilk.

More data are needed on the levels of mercury exposure in nursing women from inhalation of metallic mercury in occupational or domestic situations, including religious and ethnic uses (ATSDR 1997; Riley et al. 2006; Wendroff 1990, 1991; Zayas and Ozuah 1996); from use of commercial or hobby arts and crafts (Grabo 1997; Rastogi and Pritzl 1996); from mercury-containing herbal remedies, cosmetics, and prescription drugs (Al-Saleh and Al-Doush 1997; Espinoza et al. 1996; Lauwerys et al. 1987; Perharic et al. 1994; Washam 2011); and from consumption of mercury-contaminated fish and wildlife, including marine mammals (ADPH 1998; CRITFC 1994; Oskarsson et al. 1996).

6.3 ONGOING STUDIES

There are numerous ongoing studies supported by the National Institutes of Health (NIH) evaluating the potential adverse effects of mercury exposure in humans and laboratory animals, as well as underlying mechanisms of toxicity (Table 6-1) (RePORTER 2024). Most ongoing human studies are focused on neurodevelopmental endpoints, while most ongoing animal studies are focused on autoimmune effects.

Table 6-1. Ongoing Studies on Mercury Sponsored by the National Institutes of Health (NIH)

Investigator	Affiliation	Research description	Sponsor
Human studies			
Andres Cardenas	University of California Berkeley	Prenatal and postnatal exposure to environmental mixtures: neurodevelopment and DNA methylation biomarkers	NIEHS
Celia Chen	Dartmouth College	Sources and protracted effects of early life exposure to arsenic and mercury	NIEHS
Danielle Fallin	Johns Hopkins University	Prenatal exposure to metals and risk for autism spectrum disorder in MARBLES and EARLI	NIEHS
Ka He	Columbia University Health Sciences	Trace mineral levels, metabolomics, and diabetes risk	NIDDK
Irva Hertz-Picciotto	University of California at Davis	The CHARGE Study: Childhood Autism Risks from Genetics and the Environment	NIEHS
Sek Won Kong	Boston Children's Hospital	An environment-wide association study in autism spectrum disorders using novel bioinformatics methods and metabolomics via mass spectrometry	NIMH
Jonathan Levy	Boston University Medical Campus	Assessing the relation of chemical and non-chemical stressors with risk-taking behavior and related outcomes among adolescents living near the New Bedford Harbor Superfund Site	NIEHS
Simin Liu	Brown University	Environmental heavy metals and risk of ischemic heart disease and stroke in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil)	NIEHS

Table 6-1. Ongoing Studies on Mercury Sponsored by the National Institutes of Health (NIH)

Investigator	Affiliation	Research description	Sponsor
Mohammad Rahbar	University of Texas Health Science Center Houston	Epidemiological research on autism in Jamaica, Phase II	NIEHS
Sarah Rothenberg	Oregon State University	Exploratory use of stable mercury isotopes to distinguish dietary sources of methylmercury and their relation to neurodevelopment	NIEHS
Alison Sanders	Icahn School of Medicine at Mount Sinai	Children's exposure to metals, micro RNAs and biomarkers of renal health	NIEHS
Dale Sandler	NIEHS	Environmental and genetic risk factors for breast cancer: the sister study	NIEHS
James Saunders	Dartmouth-Hitchcock Clinic	Central auditory processing abnormalities as an indicator of pediatric heavy metal neurotoxicity	NIDCD
Mary Ellen Turyk	University of Illinois at Chicago	Endocrine disruption by perfluoroalkyl substances and mercury	NIEHS
Edwin van Wijngaarden	University of Rochester	Factors modifying the toxicity of methylmercury in a fish-eating population	NIEHS
Edwin van Wijngaarden	University of Rochester	Leveraging investments in the Seychelles Child Development Study to enable novel investigations of long-term methylmercury exposure, toxicity mechanisms, and health across the life course	NIEHS
Guoying Wang	Johns Hopkins University	*In utero* exposure to metals and vitamin b on placenta and child cardiometabolic outcomes	NIEHS
Xiaobin Wang	Johns Hopkins University	Maternal exposure to low level mercury, metabolome, and child cardiometabolic risk in multi-ethnic prospective birth cohorts	NIEHS
Ganesa Rebecca Wegienka	Henry Ford Health System	Environmental risk factors for uterine fibroids: a prospective ultrasound study	NIEHS
Clarice Weinberg	NIEHS	The Two Sister Study (breast cancer)	NIEHS
Alexandra White	NIEHS	Environment and cancer epidemiology	NIEHS
Tongzhang Zheng	Brown University	A nested case-control study of exposure to toxic metals, essential metals and their interaction on the risk of Type 2 diabetes	NIEHS
Wilco Zijlmans	Academisch Ziekenhuis Paramaribo	Neurotoxicant exposures: impact on maternal and child health in Suriname	FIC
Animal toxicity studies (some with associated mechanistic studies)			
William Atchison	Michigan State University	Environmental metals, excitotoxicity, and ALS (methylmercury)	NIEHS
David Lawrence	Wadsworth Center	Prenatal environmental toxicants induce neuroinflammation causing autistic behaviors (mercuric chloride)	NIEHS

Table 6-1. Ongoing Studies on Mercury Sponsored by the National Institutes of Health (NIH)

Investigator	Affiliation	Research description	Sponsor
Kenneth Michael Pollard	Scripts Research Institute	The effect of age on xenobiotic-induced autoimmunity (mercuric chloride)	NIEHS
Kenneth Michael Pollard	Scripts Research Institute	Do xenobiotics exacerbate idiopathic autoimmunity	NIEHS
Kenneth Michael Pollard	Scripts Research Institute	Modeling xenobiotic-induced autoimmunity using collaborative cross strains (mercuric chloride)	NIEHS
Allen Rosenspire	Wayne State University	Understanding the connection between exposure to mercury, autoimmunity, and tolerance in B cells	NIEHS
Mechanistic studies			
Michael Aschner	Albert Einstein College of Medicine	Mechanisms of methylmercury induced neuronal toxicity	NIEHS
Christy Bridges	Mercer University Macon	Uptake of mercury at the basolateral membrane of isolated proximal tubules	NIEHS
Lawrence Lash	Wayne State University	Mitochondrial and cellular biomarkers of renal injury from environmental and therapeutic agents	NIEHS
Stuart Macdonald	University of Kansas Lawrence	Toxicogenomics of metal response in genetically-variable *Drosophila* populations	NIEHS
Joel Newman Meyer	Duke University	Exposure to mitochondrial toxicants during germ cell development result in lifeline alterations in mitochondrial function mediated by epigenetic changes (methylmercury)	NIEHS
Mathew Pitts	University of Hawaii at Manoa	Mechanisms of neurotoxicity and interactions with selenium	NIEHS
Kenneth Pollard	The Scripps Research Institute	Mechanisms of mercury-induced autoimmunity	NIEHS
Matthew Rand	University of Rochester	Mechanisms of methylmercury toxicity in neuromuscular development	NIEHS
Caren Weinhouse	Oregon Health & Science University	Understanding the causes of DNA methylation response to methylmercury: a novel approach to quantify genetic, environmental, and stochastic factors	NIEHS
Toxicokinetics			
Matthew Rand	University of Rochester	Microbial mechanisms of methylmercury metabolism in humans	NIEHS

Table 6-1. Ongoing Studies on Mercury Sponsored by the National Institutes of Health (NIH)

Investigator	Affiliation	Research description	Sponsor
Biomarkers			
Joe Schwartz	Harvard School of Public Health	Air particulate, metals, and cognitive performance in aging cohort-roles of circulating extracellular vesicles and non-coding RNAs	NIEHS

ALS = Amyotrophic lateral sclerosis; DNA = deoxyribonucleic acid; EARLI = Early Autism Risk Longitudinal Investigation; FIC = Fogarty International Center; MARBLES = Markers of Autism Risk in Babies-Learning Early Signs; NIDDK = National Institute of Diabetes and Digestive and Kidney Diseases; NIDCD = National Institute on Deafness and Other Communication Disorders; NIEHS = National Institute of Environmental Health Sciences; NIMH = National Institute of Mental Health; RNA = ribonucleic acid

Source: RePORTER 2024