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 creosote 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 creosote.

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

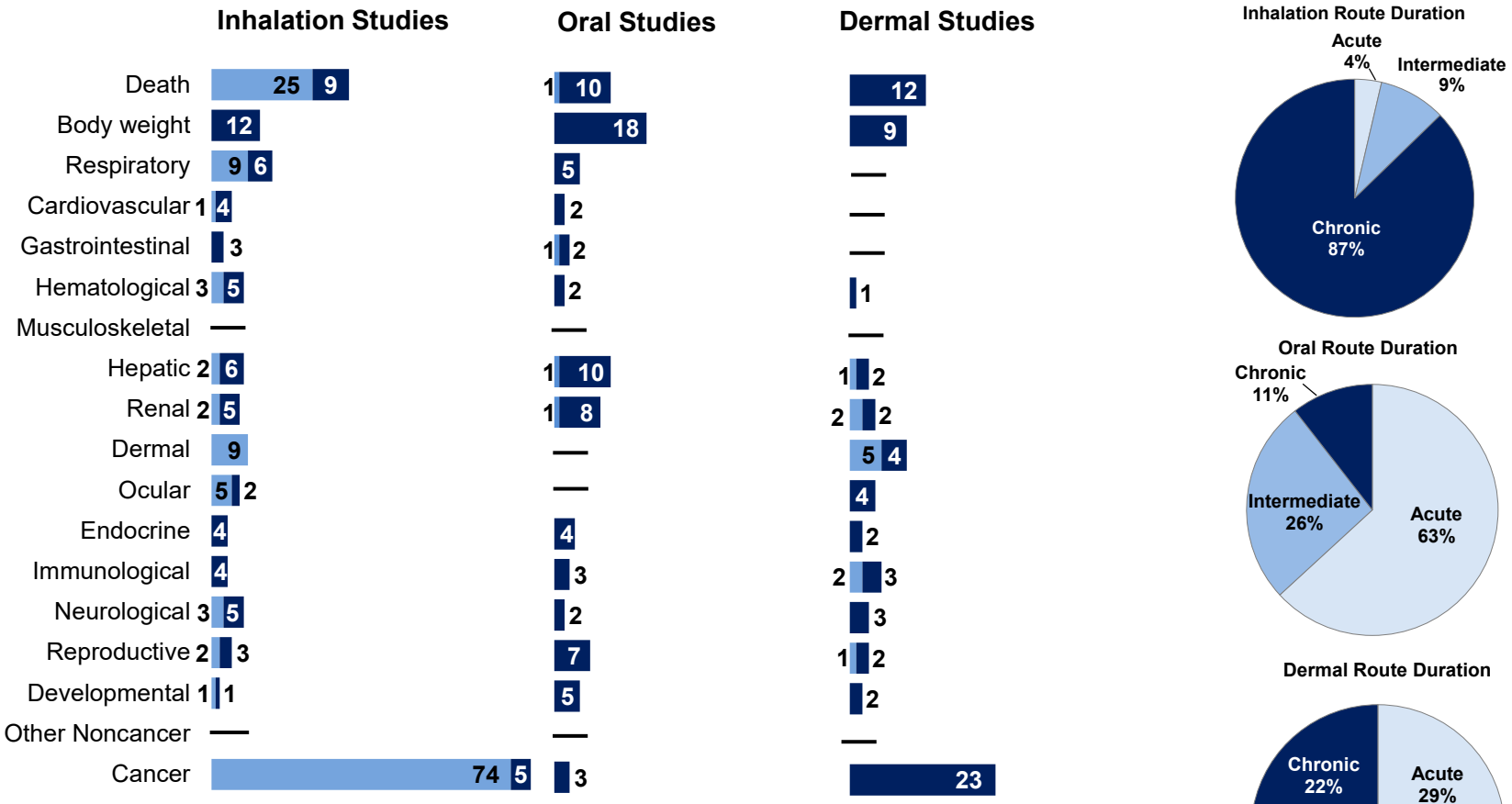
Studies evaluating the health effects of inhalation, oral, and dermal exposure of humans and animals to coal tar products and wood creosotes that are discussed in Chapter 2 are summarized in Figures 6-1 and 6-2, respectively. The purpose of these figures is to illustrate the information concerning the health effects of creosote. 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 and 6-2 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. The toxic effects that have been found for chemicals within the complex creosote mixtures should be used to direct further research for the complex mixtures. With the variability of creosote mixtures, the relevant receptor mechanisms are multiple.

Figure 6-1. Summary of Existing Health Effects Studies on Creosote (Coal Tar Products) by Route and Endpoint*

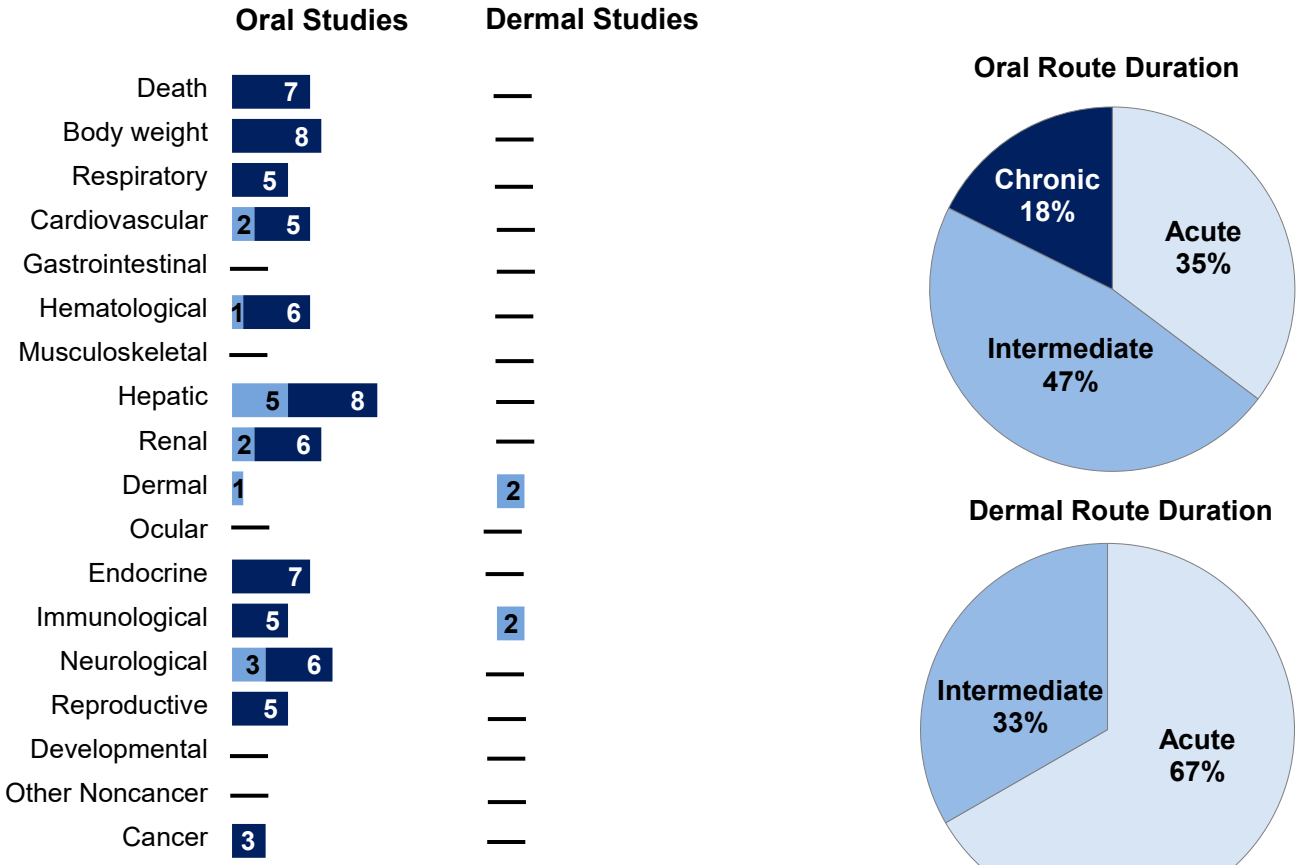
Potential cancer, death, and body weight were the most studied endpoints
The majority of the studies examined oral exposure in **animals** (versus **humans**)



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

Figure 6-2. Summary of Existing Health Effects Studies on Creosote (Wood Creosotes) by Route and Endpoint*

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



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

MRLs. MRLs for coal tar products and wood creosotes have not been derived for any route or duration of exposure. Coal tar creosote, coal tar, coal tar pitch, and coal tar pitch volatiles and wood creosotes are extremely complex mixtures containing numerous compounds; however, the compositions of the mixtures are not consistent. Even within a class of creosote compounds, the chemical mixtures vary such that adverse effect profiles and potency may vary within a class of creosote compounds. This is demonstrated by inconsistent results observed in studies evaluating the same class of compounds. Therefore, derivation of an MRL based on a single study or group of studies may not be protective for other exposures.

Health Effects.

Reproductive. Little information on the reproductive effects of coal tar creosote in humans or animals is available. One epidemiological study in humans indicates no reproductive hazard from exposure through environmental contamination (ATSDR 1994) and another indicated no increased risk of spontaneous abortion from the use of coal tar as a dermal treatment for psoriasis during pregnancy (Franssen et al. 1999). However, animal studies have shown that exposure to coal tar causes decreased ovary weights (with a loss of luteal tissue) and increased testis weights in mice and rats (Hackett et al. 1984; Springer et al. 1982, 1986b, 1987). An increase in relative testis weight was also observed in rats administered beechwood creosote in the diet for 3 months (Miyazato et al. 1981). No accompanying gross or histopathological lesions of the testes in these animals were observed; therefore, the toxicological significance of this change is not known. Given the widespread potential for exposure to coal tar creosote, and industrial exposure to other coal tar products, and the indication from animal studies that creosote may be a reproductive toxicant, multi-generation reproductive toxicity studies should be conducted by the oral and dermal routes of exposure. The pharmacokinetic data on coal tar creosote are insufficient to determine whether similar effects may be expected to occur across different routes of exposure. However, since coal tar has been shown to produce reproductive toxicity in animals by the oral, dermal, and inhalation routes, it appears that reproductive toxicity may not be route dependent.

Developmental. Information on the developmental effects of creosote in humans was not found. Studies in animals have demonstrated serious developmental toxicity for rats and mice exposed to coal tar by all routes, including increases in resorptions and reductions in fetal ossification, crown-rump length, fetal weight, fetal lung weight, and placental weights (Springer et al. 1982), a significant increase in the incidence of cleft palate (Hackett et al. 1984), increased early mortality in pups of treated dams (Springer et al. 1986a), and significant increases in

prenatal mortality in exposed rat and mouse fetuses (Zangar et al. 1989). In many of these studies, it is not possible to exclude the potential role of maternal toxicity in the development of adverse fetal effects. Additional studies on developmental effects, including neurodevelopmental effects, of inhalation, oral, and dermal exposure to coal tar creosote would be important to fully evaluate the developmental toxicity of coal tar creosote. Concerns regarding the contribution of maternal toxicity to developmental effects could be addressed by employing a cross-foster study design. The pharmacokinetic data on coal tar creosote are insufficient to determine whether similar effects may be expected to occur across different routes of exposure. However, since coal tar has been shown to produce developmental toxicity in animals by the oral, dermal, and inhalation routes, it appears that developmental toxicity may not be route dependent.

Immunological. The only available information on the immunological effects of creosote in humans describes the occurrence of acute allergic dermatitis following exposure to creosote bush resin (Leonforte 1986; Smith 1937) and coal tar (Cusano et al. 1992). Animal studies have provided evidence of weight and morphological changes in lymphoreticular tissues following exposure to coal tar (Hackett et al. 1984; Zangar et al. 1989), but no information regarding associated changes in the immune system was identified. The relevance of these findings to human exposure to creosotes is not known. However, these data are suggestive of possible immunotoxic effects. Immunotoxicity studies of coal tar creosote, coal tar, and coal tar pitch by inhalation and dermal routes and studies of wood creosote by inhalation, oral, and dermal routes would fill the data needs for these mixtures.

Neurological. The available information about the possible neurotoxic effects of creosote is very limited, but some signs of neurological involvement in humans and animals following exposure to beechwood creosote and creosote bush (Gordon et al. 1995; Miyazato et al. 1981) and coal tar (Hanlon 1938; NIOSH 1980b) have been described. These effects were generally excitatory in nature (e.g., convulsions). No reliable data are available on the short-term neurotoxic effects of coal tar creosote, coal tar, coal tar pitch, or coal tar pitch volatile exposure by the inhalation, oral, or dermal routes, or on long-term neurotoxic effects of low-level exposure to coal tar creosote, coal tar, coal tar pitch, or coal tar pitch volatiles by the inhalation, oral, or dermal routes in humans or animals. Reports of individuals exposed to creosote suggest that neurotoxicity (e.g., dizziness, altered vision, etc.) may be an early sign of toxic exposure to creosote. Short- and long-term neurotoxicity studies in animals, using sensitive functional and

neuropathological tests, and exposure by the inhalation, oral, and dermal routes would be useful in better characterizing potential neurological effects of coal tar creosote.

Epidemiology and Human Dosimetry Studies. Few controlled epidemiological studies have been conducted in humans on the effects of exposure to coal tar creosote. Epidemiological studies of workers in creosote treatment plants accompanied by accurate occupational exposure data would be useful to assess the risk of inhalation and dermal exposure to coal tar creosote. Most of the available information on the effects of coal tar creosote in humans comes from occupational studies in the wood-preserving and construction industries (Karlehagen et al. 1992; Kerr et al. 2000; Persson et al. 1989; Stern et al. 2000). Limitations inherent in these studies include unknown exposure concentrations and durations, as well as concomitant exposure to other potentially toxic substances. The few available industrial surveys and epidemiological studies are limited in their usefulness because of small sample size, short follow-up periods, and brief exposure periods. Only one epidemiological study of people living near a coal tar creosote-contaminated area was found in the literature (ATSDR 1994). Additional well-controlled epidemiological studies of people with documented exposure to creosote, living near areas where coal tar creosote has been detected in surface water and groundwater, or near hazardous waste sites, and of people occupationally exposed to creosote could add to and clarify the existing database on creosote-induced human health effects. Health effects that should be examined in future studies include cancer, developmental, reproductive, immunotoxic, and neurotoxic effects as well as adverse noncancer dermal effects.

Biomarkers of Exposure and Effect. No method is currently available to measure the parent creosote mixture in human tissues or fluids. However, 1-hydroxypyrene, the metabolite of pyrene, a component of the creosote mixture, can be measured in the urine of exposed individuals following relatively high-level exposures of acute- and chronic-duration (Bos and Jongeneelen 1988; Jongeneelen et al. 1985, 1988). The identification of PAH metabolites in urine could potentially serve as a method of biological monitoring of exposed workers and possibly individuals living in the vicinity of hazardous waste sites where creosote has been detected. However, because of the ubiquitous nature of PAHs in the environment, detection of PAH metabolites in the body tissues or fluids cannot always be attributed to creosote exposure alone. PAHs form DNA adducts that can be measured in body tissues or blood following exposure to creosote containing PAHs. Again, these PAH-DNA adducts are not specific for coal tar creosote, and the adducts measured could have been from exposure to other sources of PAHs. Therefore, a biomarker of exposure specific to creosote would be useful to monitor exposure to this mixture.

The formation of benzo[a]pyrene-DNA adducts has been demonstrated (Pavanello and Levis 1992; Zhang et al. 1990) and may also serve as a biomarker of PAH-induced carcinogenicity. However, these adducts are not specific for coal tar creosote exposure, as exposure to benzo[a]pyrene from sources other than coal tar creosote can occur. Studies to identify and measure effects unique to coal tar creosote-specific injury would be useful. Also, increasing the sensitivity of these tests would be valuable in evaluating the health status of individuals who have been exposed to low levels of creosote.

Absorption, Distribution, Metabolism, and Excretion. Studies monitoring the pharmacokinetics of the coal tar creosote mixture are limited. Much of the information regarding the disposition of creosote is based on indirect evidence or the pharmacokinetic information available on a single class of creosote components, the PAHs. For more information on the toxicokinetics of PAHs, please refer to the ATSDR toxicological profile for polycyclic aromatic hydrocarbons (ATSDR 1995).

Absorption of creosote occurs following all routes of exposure. The presence of creosote components in tissues and the presence of metabolites in urine are evidence of its absorption. However, no studies are available that quantify the extent and rate of creosote absorption. Studies in humans regarding the distribution of creosote are not available and little information is available for animals. Its distribution is based on assumptions derived from studies that monitored the distribution of PAHs, components of creosote.

The metabolism of creosote has not been extensively studied, but preliminary results indicate that hydroxylation of the major PAH components is a principal degradation pathway in both humans and animals following all routes of exposure. 1-Hydroxypyrene is one metabolite that has been identified, but there were no studies available regarding the identification of other metabolites. Elucidation of additional biotransformation pathways and products is also important in examining potential toxic effects of creosote. Also, no studies were located regarding the rate or extent of creosote metabolism.

Studies regarding the excretion of creosote by humans or animals were not available. It is known that PAHs and their metabolites are primarily excreted in the bile and the feces. However, direct excretion studies with creosote would be more useful. Information is available regarding the disposition of creosote's individual components, but no information is available regarding how these components interact to affect the overall disposition.

In summary, no data are available regarding the toxicokinetics of the creosote mixture and all information must currently be inferred from what is known about the PAH components of creosote. Interactions between the components of the creosote mixture could occur that could alter the rate and extent of absorption, distribution, metabolism, and excretion of creosote from what might be predicted based on what is known about the individual PAH components. Therefore, more information on the toxicokinetics of the creosote mixture itself would be useful to predict possible target organs of toxicity as well as allow for extrapolation of toxic effects across routes of exposure.

Comparative Toxicokinetics. The available information indicates that the absorption, distribution, metabolism, and excretion of creosote is qualitatively similar in humans and rodents. This general conclusion was primarily based on evidence derived from studies on the individual PAH components of creosote. Specific kinetic aspects of individual components of coal tar products have been described. Little work has been done to address this topic for wood creosote. Detailed pharmacokinetic studies in humans and animals specific to the creosote mixture would provide a better indication of species differences and indicate whether the ability to extrapolate across species may be possible in the future.

PBPK Models. The pharmacokinetics of creosote have not been defined because of the chemical complexity of these mixtures. Information on individual components is not sufficient to define the properties of the mixture and for this reason no PBPK models have been proposed for creosote. Individual components of creosote are metabolized by several different enzyme systems including phase I and phase II enzymes. Human polymorphisms are known to exist for many of these enzymes and are likely to affect the relative toxicity of creosote for these individuals. The relative activity of metabolic enzymes may also vary with the age of the individual, which will again affect the relative toxicity of particular components of creosote for old or young individuals. However, the interactions taking place when creosote components are metabolized are likely to be extremely complex so that information on age-related activity of any particular enzyme will probably not be very informative as to differential toxicity of the mixture.

Children's Susceptibility. Studies addressing the effects of creosote in children are limited to a single survey of health effects among residents of a housing development that had been built on a creosote waste site (ATSDR 1994). Other human studies are predominantly of occupationally exposed adults. Studies of effects in young animals are also limited but include several developmental studies that demonstrate fetotoxicity and developmental defects in mice and rats due to coal tar exposure (Hackett et al. 1984; Springer et al. 1982, 1986a; Zangar et al. 1989). Data needs relating to both prenatal and childhood

exposures, and developmental effects expressed either prenatally or during childhood, are discussed in detail in the Developmental Toxicity subsection above.

No data are available to determine whether children vary from adults either in the health effects they are likely to experience from creosote exposure, or in their relative susceptibility to these effects. Epidemiological studies of environmentally exposed populations (if such a population could be located), which include children might help to clarify the types of health effects observed in children after creosote exposure. A small retrospective study of women exposed to coal tar (as a treatment for psoriasis) during pregnancy found no increased incidence of abortion or birth defects (Franssen et al. 1999). Expanding this study to include a larger number of individuals and data as to the stage of pregnancy during which the women were exposed, could provide information as to whether the developmental defects observed in animals are also of concern for humans. Animal studies that compare the effects of creosote exposure on animals of different ages would provide information on the comparative susceptibility of young and adult individuals.

Physical and Chemical Properties. Limited physical property data, such as boiling point and density (see Table 4-2), are available for the coal tar creosote mixture. Additional physical and chemical property data, such as water solubility, vapor pressure, K_{oc}, and Henry's law constant values would be useful to predict the partitioning and transformation of coal tar creosote components in air, water, and soil. These values are currently not available because their determination is complicated by the fact that creosote is a mixture of variable composition. However, data on vapor pressure, water solubility, etc., are available for individual components of creosote, and these can be used to estimate the behavior of creosote.

Production, Import/Export, Use, Release, and Disposal. Manufacturing methods are well described in the literature. Production figures are limited because of the confidential nature of this type of business information. Uses of creosote, both coal tar and beechwood, are well described. Since the use of coal tar creosote as a wood preservative has been restricted, the potential of the population to be exposed is greatly diminished. The major releases of creosote resulting from treatment processes at wood-preserving plants are known, but the levels are not well quantified. Current production, release, and disposal information would assist in identifying the levels of creosote present in the environment, and thus, populations potentially exposed as a result of these processes. Creosote sludge from production processes can be treated and disposed on-site with proper groundwater monitoring. Creosote can no

longer be disposed in hazardous waste landfills unless treated to EPA specified standards. Creosote-treated wood used in industrial applications can be burned in an industrial incinerator or boiler.

Environmental Fate. The limited information available regarding transport and partitioning of creosote components among environmental compartments indicates mobility of water-soluble PAHs, phenol, and heterocyclic constituents of the mixture in water; sorption of PAH components in soils; and bioconcentration of creosote-derived PAHs by terrestrial and aquatic organisms. In an examination of the partitioning of coal tar-derived PAHs into groundwater and the usefulness of a computer model to simulate such, Lee et al. (1992) found that theoretically "ideal" behavior was observed for the individual compounds and that the model was useful in estimating concentrations in groundwater. This finding indicates that, although coal tar is a complex mixture of compounds with varying physical and chemical properties, the fate of the individual compounds may be modeled as if they were present as single contaminants. Additional studies on the behavior of the transport of the individual components of creosote when present as a mixture may be necessary. There is a data need to capture airborne levels of individual constituents of these mixtures and report the levels in both the vapor and particulate phases. Biotransformation appears to be the most important degradation process in soils and aquatic environments. Additional data on the transport of volatile creosote components in the atmosphere and the partitioning of creosote released to surface waters and soils would be useful. Quantitative data on the rates of biotransformation in soils, surface water, and groundwater under aerobic and anaerobic conditions would also be useful. Data on the degradation rates or relative persistence of the higher molecular weight PAHs would be particularly useful since these components of creosote are among the more toxic fraction and are less soluble and less readily degraded than the lower molecular weight PAHs. The importance of other transformation processes, such as photolysis, photooxidation, and hydrolysis, in relation to biotransformation and rates of transport between media, should also be defined. These data would be useful to help define potential pathways of human exposure and to estimate ambient concentrations of creosote components in environmental media.

Bioavailability from Environmental Media. Limited information was found in the available literature regarding the uptake of creosote components by living organisms from contaminated water and soil at hazardous waste sites. Studies have been done with persistent constituents (e.g., PAHs), which show that plant uptake from soils is limited (ATSDR 1995; Gile et al. 1982), whereas bioconcentration in aquatic organisms from contaminated surface waters has been demonstrated (Jonsson et al. 2004). Data from human and animal studies indicate that creosote components are absorbed following ingestion or inhalation, or after dermal contact with the mixture. Additional data on the bioavailability of creosote

components following ingestion or inhalation of creosote-contaminated soils would be helpful. Of particular importance are data on the bioavailability of the high molecular weight PAHs that may persist in soil and are resistant to many bioremediation techniques.

Food Chain Bioaccumulation. Very limited information was found in the available literature regarding the biomagnification of creosote-derived compounds among food chain trophic levels. Many aquatic organisms can rapidly metabolize and eliminate PAHs, the major constituents of the commercial mixture (FWS 1987). However, the marsh clam, *Rungia cuneata*, which is a major food item for crustaceans such as the blue crab that are part of commercial fisheries, showed tissue concentrations of benzopyrenes up to 600 ppb after 4 weeks of exposure to creosote after a major spill; total PAH levels in the ambient water were ≤25 ppb (DeLeon et al. 1988). Additional studies are needed to determine whether this bioaccumulation indeed moves up the trophic chain to pose human exposure concerns. Also, vegetables and other produce grown in or around deposits of creosote wastes may uptake or be contaminated by creosote constituents through adsorption to roots or surfaces. Since these materials will be hard to remove through washing or other food preparation processes, consumption of these may provide a route for exposure. Additional data are needed on the ability of agricultural plants to uptake creosote constituents.

EPA (1993) has issued a fish sampling and analysis guidance that provides an overview of the issues involved in considering fish consumption advisories for PAHs. Since PAHs may be derived from creosote or other sources such as the combustion of petroleum products, state-issued advisories for PAHs should also be examined to see if creosote-derived sources are at issue.

Exposure Levels in Environmental Media. Monitoring data typically consist of levels of well-known PAHs in air, water, soil, and sediment near coal tar or coal tar creosote sources. Limited information is available regarding ambient concentrations of creosote-derived PAHs in air (Chen et al. 2002; IPCS 2004). Monitoring data at facilities that use coal tar creosote have shown high levels of PAHs in soil, sediment, groundwater, and surface water (Davis et al. 1993; DeLeon et al. 1988; EPA 1988b, 2017a; IPCS 2004).

Monitoring data for the levels of creosote in contaminated media at hazardous waste sites should be continued.

Exposure Levels in Humans. A population exists that is potentially exposed to creosote through contact with contaminated media at hazardous waste sites and with treated wood products. A second potentially exposed workforce population exists at wood treatment facilities and in other industries in which creosote-derived products are produced or used. Currently, no information exists that demonstrates tissue levels of any components of the mixture in these populations. Although exposure is now estimated in occupationally exposed workers using urinary concentrations of biomarkers, such as 1-hydroxypyrene, actual exposure levels are harder to determine. Estimates of human exposure to creosote constituents, or body burdens of creosote components, are complicated by the lack of information on exposure to creosote constituents and levels of creosote-derived components in the environment. Collecting information on tissue levels of creosote components in humans would be necessary to examine the relationship between levels of creosote-derived compounds in the environment, human tissue levels, and subsequent development of health effects. This information is necessary for assessing the need to conduct health studies on these populations.

Exposures of Children. Data on the exposure levels and body burden measurements of creosote constituents in children are needed to determine the risks associated with exposure. Because small children are likely to engage in hand-to-mouth activity (with unwashed hands) and to be in close contact with dirt, lawns, and indoor (carpet) dust, and because creosote residues bound to soil or dust particles in carpets or on bare floors, may present an exposure route for infants and toddlers through dermal contact and oral ingestion, bioavailability from soil data are necessary. Bioavailability data are also necessary to determine the amount of contaminant that children may be exposed to through dermal contact with treated wood, such as may occur when children play on railroad tracks and/or near railroad ties. Data on the bioavailability of creosote constituents from treated wood are also necessary because through behaviors such as putting their mouths on objects or chewing on objects, children may be exposed to creosote through oral ingestion of the chemical through chewing on treated wood, such as fences, bridges, or pier railings.

Data are also necessary on whether children are different from adults in their weight-adjusted intake of creosote compounds. Creosote compounds may be present in dietary sources such as fish or food grown in or near contaminated soils. While data on the oral bioavailability of some soil-bound components of creosote are available, it is necessary to determine the exposure contribution of such sources to children and to determine the contribution to body burden in children.

6.3 ONGOING STUDIES

No ongoing studies were identified in the National Institute of Health (NIH) RePORTER (2024) database.