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Mercury Study Report to Congress

Volume VI: Characterization of Human Health and Wildlife Risks from Anthropogenic Mercury Emissions in the United States

SAB REVIEW DRAFT

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CHARACTERIZATION OF HUMAN HEALTH AND WILDLIFE RISKS FROM ANTHROPOGENIC MERCURY EMISSIONS IN THE UNITED STATES

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LOAEL	Lowest-Observed-Adverse-Effect Level
NOAEL	No-Observed-Adverse-Effect Level
RfD	Reference Dose

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EXECUTIVE SUMMARY

Section 112(n)(1)(B) of the Clean Air Act (CAA), as amended in 1990, requires the U.S. Environmental Protection Agency (U.S. EPA) to submit a study on atmospheric mercury emissions to Congress. The sources of emissions that must be studied include electric utility steam generating units, municipal waste combustion units and other sources, including area sources. Congress directed that the Mercury Study evaluate many aspects of mercury emissions, including the rate and mass of emissions, health and environmental effects, technologies to control such emissions and the costs of such controls.

Volume VI presents the risk characterization for mercury emitted to the environment from anthropogenic sources. Risk characterization is the last step of the risk assessment process as originally described by the National Academy of Sciences (NAS, 1983) and adopted by U.S. EPA (U.S. EPA, 1984, 1992). This step evaluates assessments of human health and ecological effects, identifies human subpopulations or ecological species exposed to mercury, assesses exposures from multiple environmental media and describes the uncertainty and variability in these assessments. In addition to the NAS (1983) source, guidance from the recent report *Science and Judgment in Risk Assessment* (NAS/NRC 1994) and from the *Policy for Risk Characterization at the U.S. Environmental Protection Agency* (issued in March, 1995, by the Administrator of U.S. EPA) were also followed. This latter document reaffirmed the principles and guidance found in the Agency's 1992 policy *Guidance on Risk Characterization for Risk Managers and Risk Assessors.*

Volume VI of this Report summarizes and integrates the exposure and effects information for mercury presented in Volumes III, IV and V into an overall risk characterization for humans and wildlife. First, technical characterizations of the human and wildlife health effects of mercury are described, with accompanying discussion of uncertainty in the quantitative risk estimates. In Chapter 4 a technical characterization of the exposure of selected human and wildlife populations to mercury is presented, again accompanied by a discussion of uncertainty. Also in Chapter 4 are estimates of the size of the wildlife and human populations that are exposed to methylmercury. Literature reports on mercury tissue levels in piscivorous wildlife species and the size of selected wildlife populations are also presented. An overall characterization of the risk is presented in Chapter 5, taking two approaches. In the first, RfD values and lowest adverse effect levels (LOAELs) for wildlife and humans are used to estimate fish tissue concentrations of mercury that are below the risk level for selected piscivorous wildlife species and hypothetical human populations. Chapter 5 concludes with a comparison of recommendations from various groups with an interest in mercury.

During episodes of methylmercury poisoning, both human subpopulations and wildlife species have been affected by mercury poisoning. Clinical poisoning of humans from methylmercury occurred in epidemics in Iraq (Bakir et al., 1973; Amin-Zaki et al., 1979) and Japan (Harada, 1968, 1977, 1995), and smaller outbreaks have occurred in additional populations. In the middle decades of this century, consumption of grain treated with mercury fungicides produced severe and frequent poisoning among wildlife species (Borg et al., 1979). Consequently, in the risk characterization both human subpopulations and wildlife species were considered.

As a chemical element mercury cannot be created or destroyed. The same amount has existed on the planet since the earth was formed. Mercury, however, can cycle in the environment as a result of both natural and anthropogenic activities. Both measured data and the results from global modeling have led to the understanding that anthropogenic mercury emissions equal or exceed those from

natural sources (such as volcanic activity, volatilization from the oceans, etc.). Human and natural activity has the overall effect of making more mercury biologically available. Emissions of mercury from human activity are thought to contribute from between 50 to 75 of the current total annual input of mercury to the atmosphere. There are data and modeling results that indicate that the amount of mercury mobilized and released into the biosphere has increased since the beginning of the industrial age.

The Inventory of Anthropogenic Mercury Emissions in the United States (Volume II of this Report) comprehensively examined mercury sources to the extent supported by available data. The inventory included many manufacturing processes, a variety of combustion sources (including sewage sludge burning and crematories) and miscellaneous sources (such as laboratory use, electrical lamp breakage and dental amalgam preparation). The exposure assessment in Volume III of this Report focussed on those source categories having significant emissions in the aggregate, sources with the potential for individual facilities to have a localized impact on the environment and sources for which there were sufficient data to support an intelligent use of exposure models. The sources were electric utility boilers, municipal waste incineration, medical waste incineration, chlor-alkali plants, primary lead smelters and copper smelters.

In this Mercury Study Report to Congress, three species of mercury were considered: elemental (Hg^0), inorganic mercury or mercuric mercury (Hg^{2+}) and methylmercury. Data in both humans and experimental animals show that all three forms of mercury evaluated in this Report (elemental, inorganic and methylmercury) can produce adverse health effects. Except for people whose occupation brings them in contact with elemental mercury, humans will be exposed primarily to methylmercury; that exposure will be largely through consumption of fish.

Methylmercury can produce a variety of adverse effects, depending on the dose and time of exposure. To present a comprehensive estimation of methylmercury effects in humans, many different health endpoints were evaluated by U.S. EPA using established Risk Assessment Guidelines. Methylmercury has been shown to cause tumors in mice at doses that produce severe non-cancer toxicity. The data are limited but lead to the conclusion that low dose exposures to methylmercury are not likely to cause cancer in humans. Based on data on effects related to mutation formation (changes in DNA), there is concern that methylmercury could increase frequencies of mutations in human eggs and sperm. These data were not sufficient, however, to permit estimating the amount of methylmercury that would cause a measurable mutagenic effect in a human population. Data in both humans and animals are sufficient to judge methylmercury to be a human developmental toxicant; that is, a material that would produce effects during the period of human development (from conception to sexual maturity). The developmental deficits noted have been associated with nervous system damage, or neurotoxicity. Neurotoxicity is also the effect of concern when adults are exposed to methylmercury, but developmental delays are the critical effect.

Data were sufficient for calculation of quantitative estimates for general systemic toxicity for elemental mercury (reference concentration, or RfC, of 3.0×10^{-4} mg/m^3), inorganic mercury (RfD of 3×10^{-4} mg/kg-day) and methylmercury (RfD of 1×10^{-4} mg/kg-day). These estimates seem to be very close in magnitude. The endpoints for the methylmercury and elemental mercury estimates are similar: neurologic deficits. It should be noted, however, that the endpoint for methylmercury was the observation of developmental delays in children exposed *in utero* and the endpoint for elemental mercury was measurement of sensitive indicators of neurologic damage in adults. There may be route-specific effects on dose response that have not been investigated. The endpoint for inorganic mercury was measurement of changes leading to immune-mediated kidney damage in rats. There is evidence

of kidney damage in mercury-exposed humans. The inorganic mercury RfD has a relatively large uncertainty factor (1000 due to lack of a NOAEL, lack of a life-time study and extrapolation from animal data to humans); thus, the RfD may not be strictly comparable to the methylmercury RfD in terms of magnitude.

A previous RfD for methylmercury of $3x10^{-4}$ mg/kg-day had been calculated by U.S. EPA based on observation of paresthesia in adults who had consumed contaminated seed grain in Iraq in the early 1970s. Both a quantitative uncertainty analysis and a consideration of reporting errors in adult paresthesia have led to the conclusion that this is not the most reliable endpoint for use in a quantitative estimate of risk. Concern had been raised as to whether the RfD based on effects in adults was protective of developmental effects. A new RfD based on application of a benchmark approach to developmental neurotoxicity in children exposed *in utero* is within a numerical factor of three of the older estimate based on observation in adults. A quantitative uncertainty analysis of this RfD indicates that it is likely to be protective for all developmental endpoints.

The exposure assessment made use of computer-based models for long range transport of mercury (RELMAP) and impact of mercury emissions near the point of emissions (COMPDEP and IEM 2). Data on measured mercury levels in various environmental media were not sufficient for a nationwide survey of mercury but were used for comparison with the modeled estimates. For RELMAP results, measured data corroborate modeled estimates and geographic trends. Exposure assessments were conducted for nine different hypothetical human receptors in several settings (near a lake, urban, etc.). The assessment of exposure pathways consequent to emissions of mercury from anthropogenic sources indicates that the major exposure to both humans and wildlife is to methylmercury in fish.

The broad ecosystem effects of mercury are not completely understood. No applicable studies of the effects of mercury on intact ecosystems were found. Consequently, characterization of risk for non-human species did not attempt to quantify effects of mercury on ecosystems, communities, or species diversity. The characterization focused on (1) quantities of mercury that adversely affect the health of sensitive subpopulations of wildlife species; and (2) the co-location of these populations with areas of elevated mercury exposure secondary to ambient, anthropogenic emissions of methylmercury. To this end wildlife criteria (WC) were calculated for three piscivorous (i.e., fish-eating) birds and two mammals. The WC is a mercury level in water that is expected to be without harm for the species. The WC considers the bioaccumulation of mercury in the large and small fish eaten by the mammals or birds. WC calculation used bioaccumulation factors (BAF) to estimate mercury tissue level for trophic level 3 and trophic level 4 fish, given a concentration of mercury in the water column. The BAFs were derived by application of two (BAF_3) or three (BAF_4) methodologies and field data on fish and water mercury concentrations; derivation of the BAFs and the quantitative uncertainty analysis are described in Volume V. The effects data for mammals were from a short-term study of neurotoxicity in mink. The data for piscivorous birds were from a three-generation study in mallard ducks. The WC are these: mink, 415 pg mercury/L water; otter, 278 pg/L; kingfisher, 193 pg/L; osprey, 483 pg/L; bald eagle 538 pg/L.

There is uncertainty and variability associated with each WC. These include lack of long-term studies for mammals, lack of a no adverse effect level (NOAEL) for birds, and extrapolation from one species to another. It is not known if the species selected for WC development are the most sensitive or appropriate species, nor if protecting individual animals or species will guarantee protection of their ecosystem from harmful effects of mercury. There are uncertainties and expected variability in the BAF; it was the subject of a quantitative uncertainty analysis.

Sizes of populations potentially at risk for methylmercury exposure were estimated for both humans and wildlife species. These were compared to measured levels of mercury contamination. Women of child-bearing age are one group of concern, because methylmercury is a developmental toxicant. Even short-term exposures to methylmercury could adversely affect development because of the sensitivity of the developmental process. Moreover methylmercury persists in tissues; dietary intakes just prior to pregnancy may be of concern in addition to methylmercury intakes during pregnancy. Another cause for concern is that using estimates on the number of pregnant women in the age group 15 through 44 years, 9.5% of women are pregnant in any given year; thus the size of the impacted population is not negligible. The number of women of child-bearing age were determined in the 1990 U.S. Census. This census estimated that the total female population ages 15 through 44 years was 58,222,000 in the 48 contiguous states.

Data on fish consumption for a general population of women in the United States were developed from the United States Department of Agriculture's Continuing Surveys of Individual Food Consumption for the period 1989-1991 (CSFII 89/91). Cross-sectional data on food consumption collected over a three year period were used to estimate longer-term dietary patterns. CSFII 89/91 reported that 30.5% of women ages 15 through 44 years consume fish at least once in a 3-day period. This does not mean that the other 69.1% of women avoid fish consistently; rather that fish did not appear as a dietary item during the three days during which the food diaries were kept. There are 17,371,000 women who are fish consumers. If the 95th percentile is determined to be "high end" and as 9.5% of the female population from ages 15 through 44 years are pregnant in a given year, the number of pregnant, "high end" fish consumers in the contiguous United States number about 84,300. Fish consumption, measured mercury in fish and the human RfD and LOAEL are compared graphically in Chapter 4. Comparisons are made for the general U.S. population, women of child-bearing age and children 15 years and younger.

Additional data on fish consumption from a longitudinal food survey were also analyzed. The National Purchase Diary, Inc. surveyed families in 1973 and 1974 and found that 94% of persons reported consuming fish at least once during a month long period. The top one percent of consumers ingested fish and shellfish at levels over 100 grams per day. Using these data on fish consumption the number of maternal-fetal pairs at risk in any given year was estimated to be in excess of 50,000 women and developing infants.

A quantitative assessment of risk methylmercury exposure from contaminated fish has been performed for three hypothetical humans receptors and five wildlife species. Estimated LOAELs and RfDs were combined with modeled fish mercury levels and amounts of fish consumed; the result was a level of mercury in fish that if consumed on a daily basis would result in exposure to the RfD or LOAEL. These numbers are presented for interspecies comparison; if health endpoints are considered equivalent, then the kingfisher is the most impacted by mercury contamination in fish. There are a number of uncertainties in this analysis, including the lack of comparability in terms of sensitivity (or, conversely, adversity) of the endpoints used in the effects assessments.

Conclusions

The following conclusions are presented in approximate order of degree of certainty in the conclusion, based on the quality of the underlying database. The conclusions progress from those with greater certainty to those with lesser certainty.

- There is a plausible link between methylmercury concentrations in freshwater fish and anthropogenic mercury emissions. The degree to which this linkage occurs cannot be estimated quantitatively at this time.

- Among humans and wildlife that consume fish, methylmercury is the predominant chemical species contributing to mercury exposure.

- Methylmercury is known to cause neurotoxic effects in humans via the food chain.

- The human RfD for methylmercury is calculated to be $1x10^{-4}$ mg/kg body weight/day. While there is uncertainty in this value, there are data and quantitative analyses of health endpoints that corroborate and support a reference dose within a range of an order of magnitude. A quantitative uncertainty analysis indicates that the human RfD based on observation of developmental neurotoxicity in children exposed to methylmercury *in utero* is likely to be protective of human health.

- The RfD is a confident estimate (within a ~~factor~~ factor of 10) of a level of exposure without adverse effects on those human health endpoints measured in the Iraqi population exposed to methylmercury from grain. These included a variety of developmental neurotoxic signs and symptoms. The human RfD is for ingested methylmercury; no distinction was made regarding the food or other media serving as the ingestion vehicle.

- U.S. EPA calculates that members of the U.S. population ingest methylmercury through the consumption of fish at quantities of about 10 times the human reference dose. This amount of methylmercury is equivalent to the benchmark dose used in the calculation of the reference dose; the benchmark dose was taken to be an amount equivalent to the NOAEL. The NOAEL was an ingested amount of 1.1 µg per kg body weight per day. Consumption of mercury equivalent to the NOAEL is predicted to be without harm for the majority of a population. Individual risks cannot be determined from the available data.

- Prediction of risk cannot be made for ingestion of methylmercury above the benchmark dose given the currently available data in humans.

- Concentrations of mercury in the tissues of wildlife species have been reported at levels associated with adverse health effects in laboratory studies in the same species.

- Dietary survey data based on short-term, cross-sectional sampling periods indicate that approximately 30 percent of the general U.S. population consumes fish at least once during a three-day period. Among this group of fish consumers, roughly 50 percent are predicted to consume methylmercury at the RfD. Consuming methylmercury at levels equal to the RfD is equated to be without harm.

- Based on longer-term data that recorded fish consumption for one-month periods, approximately 94% of the population consumed fish at least once during that period.

- Using both the longitudinal and cross-sectional survey data, it is estimated that 1 to 2 percent of women of child-bearing age consistently consume fish and shellfish at intakes of 100 grams per day or greater. Whether or not methylmercury intakes are elevated above the estimated NOAEL depends on the concentration of methylmercury in the fish and shellfish consumed.

- U.S. EPA estimates that approximately one-third of fish and shellfish consumed are from freshwater/estuarine habitats that may be affected by local sources of mercury.

- Case reports in the literature document that sick and/or dying animals and birds with seriously elevated tissue mercury concentrations have been found in the wild. These wildlife have mercury concentrations elevated to a level documented in laboratory studies to produce adverse effects in these species. For a specific case report concurrent exposure to other sources of ill health cannot be excluded.

- Modeled estimates of mercury concentration in fish around hypothetical mercury emissions sources predict exposures at the wildlife WC. The wildlife WC, like the human RfD, is predicted to be a safe dose over a lifetime. It should be noted, however, that the wildlife effects used as the basis for the WC are gross clinical manifestations or death. Expression of subtle adverse effects at these doses cannot be excluded.

- Data are not sufficient for calculation of separate reference doses for children, *in utero* exposure and the aged.

- Comparisons of dose-response and exposure estimates through the consumption of fish indicate that certain species of piscivorous wildlife are more exposed on a per kilogram body weight basis than are humans. The implications for wildlife health are uncertain.

<u>There are many uncertainties associated with this analysis. The sources of uncertainty include the following</u>:

- There is considerable uncertainty and apparent variability in the movement of mercury from the abiotic elements of the aquatic system through the aquatic food chain.

- U.S. EPA has developed a BAF in an attempt to quantify the relationship between dissolved mercury concentrations in the water column and methylmercury concentrations in fish. This BAF was developed using a four-tier food chain model and extant field data. A quantitative uncertainty analysis of the BAF and the variability of the BAF was examined.

- There is considerable uncertainty in atmospheric processes that affect emitted mercury. U.S. EPA has attempted to predict the fate and transport of mercury through the use of atmospheric models. The results of these models are uncertain. For the regional

1. INTRODUCTION

Section 112(n)(1)(B) of the Clean Air Act (CAA), as amended in 1990, requires the U.S. Environmental Protection Agency (U.S. EPA) to submit a study on atmospheric mercury emissions to Congress. The sources of emissions that must be studied include electric utility steam generating units, municipal waste combustion units and other sources, including area sources. Congress directed that the Mercury Study evaluate many aspects of mercury emissions, including the rate and mass of emissions, health and environmental effects, technologies to control such emissions and the costs of such controls.

In response to this mandate, U.S. EPA has prepared a seven-volume *Mercury Study: Report to Congress*. The seven volumes are as follows:

I. Findings and Recommended Actions
II. An Inventory of Anthropogenic Mercury Emissions in the United States
III. An Assessment of Exposure from Anthropogenic Mercury Emissions in the United States
IV. Health Effects of Mercury and Mercury Compounds
V. An Ecological Assessment for Anthropogenic Mercury Emissions in the United States
VI. Characterization of Human Health and Wildlife Risks from Anthropogenic Mercury Emissions in the United States
VII. An Evaluation of Mercury Control Technologies and Costs

Risk characterization is the last step of the risk assessment process as originally described by the National Academy of Sciences (NAS, 1983) and adopted by U.S. EPA (U.S. EPA, 1984, 1992). This step evaluates assessments of human health and ecological effects, identifies human subpopulations or wildlife species at elevated risk from mercury, assesses exposures from multiple environmental media, and describes the uncertainty and variability in these assessments.

In March, 1995, the Administrator of U.S. EPA issued the *Policy for Risk Characterization at the U.S. Environmental Protection Agency* reaffirming the principles and guidance found in the Agency's 1992 policy *Guidance on Risk Characterization for Risk Managers and Risk Assessors*. The purpose of this policy statement was to ensure that critical information from each stage of a risk assessment be presented in a manner that provides for greater clarity, transparency, reasonableness, and consistency in risk assessments. Most of the 1995 *Policy for Risk Characterization at the U.S. EPA* was directed toward assessment of human health consequences of exposures to an agent. This guidance refers to an ongoing parallel effort by the Risk Assessment Forum to develop U.S. EPA ecological risk assessment guidelines that will include guidance specific to ecological risk characterization. The 1995 *Policy for Risk Characterization at the U.S. EPA* makes reference to the use of data from wildlife species in assessing the consequences of exposure to an agent through environmental media.

Key aspects of risk characterization identified in the 1995 *Policy for Risk Characterization at the U.S. EPA* include these: bridging risk assessment and risk management, discussing confidence and uncertainties and presenting several types of risk information. Risk characterization is the summarizing step of the risk assessment process. In this volume of the Report, information from the three preceding components of risk assessment are summarized, and an overall conclusion about risk is synthesized that is complete, informative, and useful for decision-makers. One aim of the process is to highlight clearly both the confidence and the uncertainty associated with the risk assessment. The risk

characterization conveys the assessor's judgment regarding the nature and existence (or lack of) human health or ecological risks that accompany exposures to an agent.

Integration of multiple elements of risk assessment for both human health or ecological impacts is a complex process that is intrinsically nonsequential. Assessment of the likelihood of hazard depends on the magnitude of exposure to human or wildlife species, which requires an understanding of dose-response relationships. For an element such as mercury, which can exist in multiple valence states and numerous chemical compounds, risk characterization requires a broad-based, holistic approach to the risk assessment process. This holistic approach encompassing human health and ecological hazard assessments, as well as analysis of exposures, has been described in greater detail (Harvey et al., 1995).

In this Report, three species of mercury are considered: elemental (Hg^0), inorganic or mercuric mercury (Hg^{2+}), and methylmercury. The assessment of exposure pathways consequent to emissions of mercury from anthropogenic sources indicates that the major exposure to both humans and wildlife is to organic mercury (largely methylmercury) in fish. A quantitative assessment of risk of mercury exposure to both humans and wildlife has been determined for three subpopulations of humans and for representative piscivorous avian and mammalian wildlife species. Assessments were made of all three forms of mercury for potential human health effects; because exposure to humans is likely to be as ingested methylmercury, that form is emphasized in this volume. Estimated Lowest Observed Adverse Effects Levels (LOAELs) and No Observed Adverse Effect Levels (NOAELs) and water criteria for wildlife were limited to methylmercury. These assessments were drawn from exposure modeling and doses of mercury associated with adverse health effects.

2. HUMAN HEALTH EFFECTS: HAZARD IDENTIFICATION AND DOSE-RESPONSE

2.1 Health Hazards Associated with Mercury Exposure

The three forms of mercury considered in this Report (mercury vapor, divalent inorganic mercury, and methylmercury) are characterized by somewhat different health endpoints for human health risk assessment. All three chemical species of mercury have been associated with adverse human health effects, and human and animal data on all three forms of mercury indicate that systemic toxic effects (rather than cancer or germ cell mutagenicity) are most likely to occur in humans as a consequence of environmental exposures. Available information on health endpoints relevant to human health risk assessment is described in Volume IV. A brief characterization of endpoints other than systemic toxicity is given in Chapter 2 of Volume IV.

Data are insufficient to support comparisons of innate toxicity among the three forms of mercury. Human data adequate for quantitative dose-response assessment have not been reported for inorganic, divalent mercury. The RfD for inorganic mercury is within a factor of 3 of the RfD for methylmercury; the RfD for inorganic mercury, however, includes a large uncertainty factor (1,000). Furthermore, the extent to which the endpoints for inorganic and methylmercury are comparable (based on either the severity or sensitivity) is unknown. The RfD for methylmercury and the RfC for inhaled elemental mercury were both based on observation of neurotoxicity (from exposure in adults for elemental mercury and from exposure *in utero* for methylmercury). The two quantitative risk estimates are an RfD of $1x10^{-4}$ mg/kg-day for methylmercury and an RfC of $3x10^{-4}$ mg/m^3 for elemental mercury. In order to compare the toxic potency implied by these values, some conversion to internal dose appropriate to the route of exposure would be necessary. This has not been done for this Report.

Assessment of health end-points, dose-response and exposure suggests that methylmercury is the chemical species of major concern. Methylmercury is the chemical species of greatest concern because of the fate and transport of mercury to water bodies and sediments with subsequent bioaccumulation of methylmercury in the aquatic food-web. In short, the exposure assessment in this Report (as well as other exposure assessments) indicates that most human exposure is likely to be due to methylmercury in food, primarily fish. Fish-eating wildlife will also be exposed in the main to methylmercury.

Adverse effects on the nervous system and reproduction are the predominant effects of methylmercury exposure on humans and several wildlife species. In multiple species, the neurological effects of methylmercury exposure are mainly on the motor and sensory systems, especially in the areas of sensory-motor integration. The type of information available differs markedly across species resulting in gross disparity in the severity of the hazard. For example, marked incoordination in gait (ataxia) is the most sensitive endpoint identified in previous research on methylmercury toxicity in mink. By contrast, human subjects can identify altered sensory perception (such as paresthesia), a much more subtle indicator of neurological effect. Nonetheless, the consistent pattern observed across human and wildlife species is adverse effects of methylmercury on sensory-motor function.

Human epidemics of methylmercury poisoning have occurred in this century. During the 1950s and 1960s in Japan, major epidemics of fatal and nonfatal neurological disease were caused by methylmercury exposure from consumption of seafood in Minamata and fresh-water fish in Niigata (Tsubaki and Irukajama, 1977). Additional epidemics of methylmercury poisoning from consumption of methylmercury on grain occurred in Iraq in the 1960s and 1970s (Jalili and Abbasi, 1961;

Kantarjina, 1961; Bakir et al., 1973). These epidemics have provided the strongest possible evidence linking exposure to methylmercury with human fatalities and neurological disease. The fundamental question for risk characterization is not whether methylmercury from fish can produce neurological disease, but rather what quantities of methylmercury in fish and what duration of this exposure produce neurological disease in humans.

Exposure to high doses of methylmercury *in utero* has produced neurological sequelae. Developmental effects in humans consequent to methylmercury exposure have been reported for offspring of women who consumed contaminated seed-grain in Iraq (Amin-Zaki et al., 1976; Marsh et al., 1981, 1987) and infants born to mothers who ate contaminated fish from Minamata Bay in Japan (Harada, 1978). An inverse correlation was observed between IQ in children in New Zealand and maternal hair mercury level (Kjellstrom et al., 1989). Maternal hair mercury level has been correlated with abnormal muscle tone in Cree Indian male children (McKeown-Eyssen et al., 1983). These multiple episodes of disease among numerous groups of people widely separated geographically provide the basis for high confidence in the association of methylmercury exposure and adverse developmental deficits of the nervous system. Developmental effects have been reported in three strains of rat and two strains of mice and in guinea pigs, hamsters, and monkeys. While some studies are limited in their usefulness to assessment of developmental risk, the database taken as a whole supports a judgment of Sufficient Human and Animal Data for developmental toxicity of methylmercury, in the language of the Risk Assessment Guidelines. The RfD of $1x10^{-4}$ mg/kg-day was derived using an estimate of threshold (bench mark) for the Iraqi neurodevelopmental observations.

The neurological scores used in developing the benchmark dose for effects in children were based on clinical evaluation for cranial nerve signs, speech, involuntary movement, limb tone-strength, posture, and the ability to sit, stand and run. A limitation on these data is that the Iraqi mothers did not know with accuracy the ages of their infants; cultural mores did not dictate use of Western calendars for recording of family events. Consequently, reliability of data on which these endpoints are based is compromised. A resulting uncertainty in the Iraqi data (because of the comparatively short-term exposures) is classification bias secondary to whether or not methylmercury exposure occurred during a particular gestational period.

Development of a quantitative estimate of human non-cancer risk for methylmercury has proved to be a complex undertaking. Difficulty arises from attempts to quantify daily doses of human exposure. The conventional approach for methylmercury is to use hair concentrations and back-calculate to blood concentrations and then to a daily intake level. (Methods and assumptions for this calculation are found in Volume IV, Section 5.3.1.1.) There is variation in the hair-to-blood ratios and other physiological parameters, such as biologic half-lives.

At the present time, there is limited agreement in the scientific community concerning the optimal neurological endpoints to use for assessment of mercury toxicity. It is generally agreed that methylmercury exposure adversely affects cellular processes in broad areas of the nervous system. Sensory and motor functions appear to be particular adversely affected. A wide range of endpoints have been used to assess nervous system function in studies of mercury toxicity. Individual scores on developmental tests were used for the New Zealand study (Kjellstrom, 1989); however, these data are limited because of cultural differences between the subjects and the populations on which the tests were standardized. Because of the different cultural practices, the neurological deficits of delayed onset of walking and talking among children exposed prenatally in the Iraqi population may not be appropriate measures for risk estimates for Western cultures. Extensive data from laboratory studies

with research animals are available. These data clearly support neurological changes as the critical adverse effect for methylmercury.

A number of additional studies evaluating the association between neurological endpoints and exposure to methylmercury from fish are underway in the mid-1990s. These ongoing studies evaluate far more subtle endpoints of neurotoxicity than were assessed in the epidemics in Minamata and Niigata. These studies also use far more sophisticated neurobehavioral and neuromotor assessments than were feasible under conditions of the Iraqi studies. Neurobehavioral and neuromotor development assessments are being carried out on more than 1,600 maternal-infant pairs from fish-consuming populations in the Seychelles Islands and the Faroe Islands. These studies differ from the epidemics that occurred in Iraq, in that exposures to methylmercury have extended for many years. Steady-state conditions were clearly established before testing for the adverse effects was performed. In addition, the Agency for Toxic Substances and Disease Registry of the United States Public Health Service is sponsoring a group of studies conducted in the United States that assess neurological end-points among infants of mothers consuming substantial quantities of fish. An example of these studies is the neuromotor/neurobehavioral evaluations of infants of high-fish-consuming mothers located in the vicinity of Oswego, New York and monitored by the Department of Psychology of the State University of New York. As results from these investigations become available, some of the issues of variability and uncertainty in understanding the threshold for adverse neuro-developmental effects of methylmercury may be clarified. In particular, this evaluation should contribute greatly to an assessment of the relationship between dose and response in which fish is the vehicle of exposure to methylmercury.

2.2 Dose-Response to Methylmercury

2.2.1 Calculation of Methylmercury RfD

U.S. EPA has on two occasions published RfDs for methylmercury which have represented the Agency consensus for that time. These are described in the sections below. At the time of the generation of the Mercury Study Report to Congress, it became apparent that considerable new data on the health effect of methylmercury in humans were emerging. Among these are large studies of fish or fish and marine mammal consuming populations in the Seychelles and Faroes Islands. Smaller scale studies are in progress which describe effects in populations around the U.S. Great Lakes. In addition, there are new evaluations of published work described in section 3.3.1.1 of Volume IV, including novel statistical approaches and application of physiologically based pharmacokinetic models.

As the majority of these new data are either not yet published or have not yet been subject to rigorous review, it was decided that it was premature for U.S. EPA to make a change in the methylmercury RfD at this time. An inter agency process, with external involvement, will be undertaken for the purpose of review of these new data evaluations and evaluations of existing data. An outcome of this process will be assessment by U.S.EPA of its RfD for methylmercury to determine if change is warranted.

Human and animal data on elemental, inorganic and methylmercury indicate that systemic toxic effects (rather than carcinogenicity or germ cell mutagenicity) are most likely to be observed in humans as a consequence of environmental exposures. The exposure assessment for environmental mercury from anthropogenic sources appears in Volume III and is summarized in Chapter 3 of Volume VI. This assessment points to the necessity of considering ingestion of inorganic mercury in water and

in food as a component of any site-specific or scenario-specific risk assessment. The modeled exposure assessment indicates, however, that for the majority of people in the United States, methylmercury exposure via contaminated fish is the major pathway. It is clear that in the segments of the population that consume fish or seafood, the majority of mercury exposure will be to methylmercury. Because methylmercury is the form to which humans are most exposed, the remainder of the risk characterization will deal with only that form of mercury.

2.2.1.1 Neurotoxicity of Methylmercury

Neurotoxicity of methylmercury has been determined as the critical effect for the RfD; that is, the adverse effect that is expected to occur at the lowest level of exposure. The RfD was based on statistical analysis of data from human subjects in Iraq in the 1970s. For a period of approximately three months this population consumed bread made from seed-grain treated with methylmercury fungicide. In 1985 an RfD was determined to be $3x10^{-4}$ mg/kg-day, based on observation of paresthesia in adults (Amin-Zaki et al., 1981). The LOAEL was determined to be $3x10^{-3}$ mg/kg-day (corresponding to 200 µg/L blood concentration), and an uncertainty factor of 10 was applied for use of a LOAEL in the absence of a NOAEL. A further uncertainty factor of 10 for sensitive individuals for chronic exposure was not deemed necessary at the time, because the adverse effects were seen in what was regarded as a sensitive group of individuals.

Since 1985, there have been questions raised as to the validity of this RfD and, specifically, whether or not this RfD is applicable to developmental effects. This resulted in the re-opening of discussion of the methylmercury RfD by the U.S. EPA RfD/RfC Work Group in 1992 and 1994. Consensus on a new RfD was reached in January of 1995. A detailed description of the derivation of the RfD can be found in Section 6.3.1.1 of Volume IV, and summary information appears on IRIS.

A study of Iraqi populations by Marsh et al. (1987) was chosen as the most appropriate study for determination of an RfD protective of a putative sensitive subpopulation, namely infants born to mothers exposed to methylmercury during gestation. This report described neurologic abnormalities observed in progeny of women who consumed bread prepared from methylmercury-treated seed grain while pregnant. Among the signs noted in the infants exposed during fetal development were cerebral palsy, altered muscle tone and deep tendon reflexes, as well as delayed developmental milestones (i.e., walking by 18 months and talking by 24 months). The data collected by Marsh et al. (1987) summarize clinical neurologic signs of 81 mother and child pairs. From x-ray fluorescent spectrometric analysis of selected regions of maternal scalp hair, concentrations ranging from 1 to 674 parts per million (ppm) mercury were determined, then correlated with clinical signs observed in the affected members of the mother-child pairs. Among the exposed population there were affected and unaffected individuals throughout the exposure range.

2.2.1.2 Estimation of Mercury Ingestion

In order to quantify an average daily ingestion rate for the mothers, hair concentrations were determined for periods during gestation when actual methylmercury exposure had occurred. A ratio of 250:1 (µg mercury/mg in hair:µg mercury/L of blood) was used to derive the RfD critical dose. A complete discussion for the choice of this ratio is provided in Volume IV, Section 6.3.1.1. Conversion of the hair mercury level to a blood mercury level was done according the following equation:

$$11 \text{ mg/kg hair} / 250 = 44 \text{ µg/L blood}$$

To obtain a daily dietary intake value of methylmercury corresponding to a specific blood concentration, factors of absorption rate, elimination rate constant, total blood volume and percentage of total mercury that is present in circulating blood must be taken into account. Calculation was by use of the following equation based on the assumptions that steady state conditions exist and that first-order kinetics for mercury are being followed.

$$d = \frac{C \times b \times V}{A \times f}$$

where:

d = daily dietary intake (μg of methylmercury/day)
C = concentration in blood (44 μg/L)
b = elimination constant (0.014 $days^{-1}$)
V = volume of blood in the body (5 liters)
A = absorption factor (expressed as a unitless decimal fraction of 0.95)
f = fraction of daily intake taken up by blood (unitless, 0.05)

The rationales for use of specific values for equation parameters are in Volume IV, Section 6.3.1.1.

Solving for d provides the daily dietary intake of mercury that results in a blood mercury concentration of 44 μg/L. To estimate a daily dose (μg/kg-day) the assumed body weight (bw) of 60 kg is included in the equation denominator. While the critical endpoint for the RfD is developmental effects in offspring, the critical dose is calculated using parameters specific to the mothers who ingested the mercury-contaminated grain. Data on body weights of the subjects were not available. A default value of 60 kg (rounded from 58) for an adult female was used.

$$d = \frac{C \times b \times V}{A \times f \times bw}$$

$$d = \frac{44\ \mu g/L \times 0.014\ days^{-1} \times 5L}{0.95 \times 0.05 \times 60\ kg}$$

$$d = 1.1\ \mu g/kg\text{-}day$$

Thus 1.1 μg/kg-day is the total daily quantity of methylmercury that is ingested by a 60 kg individual to maintain a blood concentration of 44 μg/L or a hair mercury concentration of 11 ppm, the benchmark dose derived below.

2.2.1.3 Grouping of the Response Data

Data on neurotoxic effects in children exposed to methylmercury *in utero* were used to determine a benchmark dose used in the calculation of the RfD. Data used in the benchmark dose calculation were excerpted from the publication *Seafood Safety* (NRC/NAS, 1991). Because the tables of incidence of various clinical effects in children that were provided in this document readily lent

themselves to the benchmark dose modeling approach. The continuous data for the Iraqi population that were reported by Marsh et al. (1987) were placed in five dose groups, and incidence rates were provided for delayed onset of walking, delayed onset of talking, mental symptoms, seizures, neurological scores above 3, and neurological scores above 4 for affected children. Neurologic scores were determined by clinical evaluation for cranial nerve signs, speech, involuntary movement, limb tone strength, deep tendon reflexes, plantar responses, coordination, dexterity, primitive reflexes, sensation, posture, and ability to sit, stand and run. The effects of late walking, late talking, and neurologic scores greater than 3 were also combined for calculation of a benchmark on all effects in children. Alternative dose groupings are described in section 2.2.2.6.

2.2.1.4 Derivation of a Benchmark Dose

Benchmark dose estimates were made by calculating the 95 percent lower confidence limits on doses corresponding to the 1 percent, 5 percent and 10 percent extra risk levels using a quantal Weibull model (K.S. Crump Division of Clement International). The Weibull model was chosen for the benchmark dose calculations for the methylmercury data as recent research suggests it may be the best model for developmental toxicity data (Faustman et al., 1994). The form of the quantal Weibull that was used is:

$$P(d) = A0 + (1-A0)(1-\exp[-A1 * d^{A2}])$$

where d is dose, A0 is the background rate, A1 is the slope, and A2 is a shape parameter. For each endpoint and for the combined endpoints, the incidence of response was regressed on the dose. A Chi-squared test of goodness-of-fit was used to test the null hypothesis (H_o) that the predicted incidence was equal to the observed incidence, so that H_o would be rejected for p-values less than 0.05.

2.2.1.5 Adjustments for Background Incidence

As an adjustment for background rates of effects, the benchmark dose estimates for methylmercury were calculated to estimate the dose associated with "extra risk." Another choice would have been to calculate based on "additional risk." Additional risk (AR) is defined as the added incidence of observing an effect above the background rate relative to the entire population of interest: AR = [P(d)-P(0)]/1. In the additional risk calculation, the background rate is subtracted, but still applied to the entire population, including those exhibiting the background effect. Thus, background effects are in a sense "double counted". Extra risk (ER) is always mathematically greater than or equal to additional risk, and is thus a more conservative measure of risk whenever the background rate is not equal to zero. Conceptually, extra risk is the added incidence of observing an effect above the background rate relative to the proportion of the population of interest that is not expected to exhibit such an effect. Extra risk is more easily interpreted than additional risk, because it applies the additional risk only to the proportion of the population that is not represented by the background rate. Extra risk has been traditionally used in U.S. EPA's cancer risk assessments (Anderson et al., 1983) and is discussed in detail in a report on the benchmark dose by U.S. EPA's Risk Assessment Forum (U.S. EPA, 1995).

The RfD/RfC Work Group chose the benchmark (95% lower bound on the dose for 10 percent effect level) based on modeling of all effects in children. Recent research (Allen et al., 1994a, b) suggests that the 10 percent level for the benchmark dose roughly correlates with a NOAEL for developmental toxicity data. Note that this conclusion was based on controlled animal studies and on calculation of additional risk. Both the polynomial and Weibull models place a lower 95 percent confidence limit on the dose corresponding to a 10 percent risk level at 11 ppm hair concentration for methylmercury. The benchmark dose rounded to 11 ppm was used in the calculation of the RfD.

2.2.1.6 Calculation of the Methylmercury RfD

A composite uncertainty factor of 10 was used. This uncertainty factor was applied for variability in the human population, in particular the wide variation in biological half-life of methylmercury and the variation that occurs in the hair to blood ratio for mercury. In addition, the factor accounts for lack of a two-generation reproductive study and lack of data for possible chronic manifestations of the adult paresthesia that was observed during gestation. The default value of one was used for the modifying factor.

The RfD for methylmercury was calculated using the following equation:

$$RfD = \frac{Benchmark\ Dose}{UF \times MF}$$

$$= \frac{1.1\ ug/kg\text{-}day}{10}$$

$$= 1 \times 10^{-4}\ mg/kg\text{-}day$$

where

UF is the uncertainty factor and MF is the default of 1.

Confidence in the supporting database and confidence in the RfD were considered medium by the U.S. EPA RfD/RfC Work Group.

2.2.2 Human Dose-Response Issues

The RfD is characterized by variability and uncertainty; an assessment of which is presented in Appendix D to Volume IV, and in Section 2.3 of Volume VI. Fetal effects of methylmercury exposure were based on hair mercury analyses of 83 women in Iraq. The dose-response data derived from this data set are a best estimate from a relatively small number of human subjects. The size of the data set becomes a limitation for identifying adverse effects that may occur in a small fraction of subjects due to factors such as individual variability. The duration of the exposure to methylmercury (approximately three months in the Iraqi outbreak) was long enough to identify the effects of methylmercury exposure on the fetus.

2.2.2.1 Sensitivity of Human Subpopulations

Neurotoxicity of methylmercury to the developing nervous system is well documented among several populations of human subjects. Dose-response data have been most extensively analyzed for the Iraqi population identified in the 1970s epidemic. Additional analyses of methylmercury poisoning data have been published in 1995. Kingjo et al (1995) estimated threshold doses for adults following consumption of methylmercury from fish in Niigata, Japan, and Harada (1995) published an extensive review of the epidemiology of Minamata disease.

An important issue is the extent to which results from the Iraqi and Japanese populations can be generalized to other human populations. The task of identifying the nature and extent of exposures that represent thresholds of dose-response to methylmercury is more complex. Do the Japanese and Iraqi populations represent particularly sensitive subpopulations among the general population of human subjects who can respond to methylmercury exposure with developmental neurotoxicity? Or are there unique characteristics of these populations and patterns of methylmercury exposure that resulted in them being unusually susceptible to the adverse effects of methylmercury exposure?

It is useful to clarify that there can be at least three broad areas that can render a population particularly sensitive to methylmercury: responsiveness of the organism to the adverse effect, differences in dose-response curves, and differences in exposure to the agent.

The first basis for sensitivity is that the subpopulation of concern is physiologically susceptible to the effect. The neurological effect in adults that occurs at the lowest dose is sensory disturbance or paresthesia. These changes have been reported in both male and female adults regardless of age (Tsubaki and Irukayama, 1977; Harada, 1995). By contrast methylmercury toxicity that occurs following fetal exposure to methylmercury is secondary to maternal consumption of fish or grain products contaminated with methylmercury. For this effect the sensitive subpopulation is the maternal-fetal pair. Because an estimated 9.5 percent of women of reproductive age in the United States is pregnant in a given year, and because the half-life of methylmercury is estimated to range from 35 to more than 189 days, all women of reproductive capacity can be considered as a sensitive subpopulation for the developmental effects of methylmercury. A major uncertainty in identification of dose-response in susceptible populations is the lack of data to generate separate RfDs for *in utero*, childhood and adult exposures.

The second basis for sensitivity is differences in dose-response to methylmercury. For example, individual differences exist in the biological half-life of mercury in the body. Persons with longer body retention of mercury can be anticipated to be more sensitive to the adverse effects of methylmercury if all other factors are equivalent. It has been reported by Kershaw et al. (1980) and Sherlock et al. (1984) that the half-lives for methylmercury in blood were 52 (39 to 67) and 50 (42 to 70) days, respectively. Generally, the average biological half-life for methylmercury in humans is considered to be approximately 70 days (Harada, 1995). However, reported individual values of biological half-lives range from 33 to 270 days (Birke et al., 1972). The data from the study of Iraqi methylmercury poisonings indicated a bimodal distribution of biological half-lives; one group accounting for 89 of the samples had a mean value of 65 days, and the remaining group had a mean value of 119 days (Al-Shahristani and Shinab, 1974). Lactating women have shorter biological half-lives for methylmercury (average value 42 days), compared with nonlactating women (average value 79 days) (Greenwood et al., 1978). This is presumably a reflection of excretion of mercury into milk. These differences can form the basis for individual and subpopulation sensitivity to methylmercury.

The third basis for sensitivity to methylmercury is the magnitude of exposure. Because methylmercury exposure for humans is almost entirely through fish and shellfish, sensitivity of a subpopulation will be determined by the extent that they consume fish and shellfish. Analyses of data for the general United States population indicate that based on dietary surveys conducted during 1989/ 1991 only 30.9 percent of the general population reported eating fish at least once during a three-day period. Subpopulations comprised chiefly of anglers, subsistence fishers, and some Native American populations report fish consumption rates far in excess of the general population. High fish consumption is another basis for sensitivity of a subpopulation to methylmercury.

2.2.2.2 Modification of Dose

Critical elements of the dose-response relationship reflect the uncertainty and variability that are an intrinsic part of this assessment. Separation of these identifiable bases for differences may help establish group variability by contrast to individual variability.

As with other toxic chemicals response to methylmercury exposure is influenced by physiological characteristics of the human subpopulation, as well as by individual characteristics of members of that subpopulation. Typical factors considered to modify dose-response include these: presence of concurrent disease; concurrent exposure to other toxic agents; altered nutritional status; genetic differences in the way the agent is metabolized; and differences in biokinetics, or metabolic response that depend on physiological statues such as pregnancy or lactation.

Gestation may be the time period in which the adverse effects occur at lowest doses of methylmercury. In the Japanese epidemic in Minamata it became clear that a considerably higher number of children than usual were born with cerebral palsy (Harada, 1995). Many of the mothers of these infants were themselves either initially asymptomatic or had only mild symptoms of methylmercury neurotoxicity. Records of the number of inhabitants in the region and onset of disease are detailed for the Japanese epidemics; however, the exposures were chronic, extending over decades. The initial cases were of severe methylmercury poisoning and resulted in fatalities (Tsubaki and Irukayama, 1977). Milder cases, atypical cases and incomplete cases were essentially overlooked in earlier years (Harada, 1995). Many of the cases showed increasingly severe signs and symptoms over the years, producing a group labelled as "chronic" Minamata disease patients (Harada, 1995). The basis for progressive cases is not entirely established; however, manifestation of symptoms by accumulation of methylmercury caused by a relatively low-level exposure over long periods is one of the possible mechanisms (Harada, 1995). Generally the thresholds for chronic Minamata disease are for a lower level of methylmercury than is associated with acute onset of Minimata disease.

The data from Iraq obtained during the epidemic of methylmercury poisoning that occurred in the early 1970s form another basis for dose-response analyses. Because the epidemic occurred in a region where maintenance of medical surveillance systems was comparatively undeveloped, and many of the affected people were from very rural villages or were members of nomadic tribes, there is not a reliable estimate of the size of the potentially exposed population; that is, in terms of incidence there are no denominator data. It is uncertain why some subjects who consumed methylmercury-treated seed-grain responded with adverse effects, whereas other persons with presumably comparable exposures did not experience toxicity.

Among the Iraqi population reporting methylmercury toxicity, there are reports of the presence of concurrent disease in the form of parasitism and renal and/or urinary tract disease. Whether or not these conditions modify the dose-response relationship between methylmercury concentrations in hair

and/or blood and prevalence of neuromotor deficits associated with methylmercury remains an uncertainty.

2.2.2.3 Media Factors that Affect Dose-Response

An additional source of uncertainty and variability in the dose-response assessment is the biotoxicity of methylmercury in the food vehicle that was the source of methylmercury. Or, stated another way, is methylmercury from various biological sources bioavailable? Methylmercury toxicity has been observed following ingestion of fish, pork, and grain contaminated with methylmercury. The methylmercury exposure in Iraq occurred from seed-grain treated with methylmercury fungicide, whereas the methylmercury exposures in Minamata, Niigata, New Zealand, and Canada (Kjellstrom, 1989; McKeown, 1983) occurred from methylmercury incorporated into the protein of fish tissue.

Both of the Japanese epidemics wherein methylmercury exposure was from contaminated fish and the Iraqi epidemic in which grain contaminated with methylmercury was the vehicle for methylmercury exposure have been extensively reported in the biomedical literature. Although the dose at which these effects occur more frequently than background incidence is uncertain and variable, it is clear that clinically significant neurological deficits occur following methylmercury ingestion from several foods.

2.2.2.4 Time-Course of Dose-Response Assessment: Comparison of Short-Term and Long-Term Exposures in Human Epidemics

The duration of exposure is also a source of uncertainty. It is unclear whether or not it is physiologically appropriate to generalize conditions associated with paresthesias developed after a three-month exposure to methylmercury to a lifetime exposure, as the RfD implies. Analyses of the Iraqi data and additional analyses of the Niigata data published in 1995 (Kinjo et al., 1995; Harada, 1995) provide useful insights on duration of methylmercury exposure. These epidemics differ in two major ways. The Japanese dose-response data were obtained from chronic exposures to methylmercury-contaminated fish and shellfish that occurred over several decades. The methylmercury was bioaccumulated through the aquatic food chain producing an exposure pathway that is highly similar to that currently under consideration in this Report to Congress. The Iraqi data were obtained from a population that experienced short-term exposure (approximately three months) to high levels of methylmercury ingested as organomercurial- fungicide-contaminated seed grain. The extent to which differences in exposure vehicle (fish contrasted with grain) and duration of exposure (years contrasted with months) influence time-course and dose-response to methylmercury among human subjects is not fully known.

Groups of endpoints from the Iraqi data have served as the bases for RfDs — paresthesia among adults and neurological deficits among infants of women ingesting methylmercury during or just preceding gestation. In the Japanese epidemics, signs and symptoms of methylmercury poisoning included sensory disturbances, constriction of visual field, ataxia, impairment of speech and impairment of hearing. Sensory disturbances and constriction of visual field were present in 100 percent of Minamata disease cases described in 1968 by Tokuomi, ataxia in 93.5 percent of cases, impairment of speech in 88.2 percent of cases and impairment of hearing in 85.3 percent of cases [Tsubaki et al. (1977) in Tsubaki and Ireheuta, 1977]. Among chronic Minamata disease patients described by Harada (1995) sensory disturbances (glove and stocking type and generalized type) were present in 72 percent (1724/2383) of patients. In both the Minamata disease cases described in 1968 and in the chronic Minamata disease cases, sensory disturbance was the neurological change that

occurred first. The sensory disturbances initially were described as "glove and stocking" paresthesia with about 10 percent of cases having perioral sensory disturbances (Harada, 1995). When exposures continued and the disease progressed, the clinical course of the disease progressed from sensory disturbances of the extremities, followed by perioral hypesthesia, ataxia and constriction of the visual field, with a time lag of several months to several years (Tsubaki and Irukayama, 1977).

In Iraq an outbreak of methylmercury poisoning occurred in 1960 and affected an estimated 1,000 patients resulting in 370 hospital admissions (Jalili and Abbasi, 1961; Kantarjina, 1961). These early outbreaks alerted clinicians and public health officials to the etiology of the most catastrophic epidemic of methylmercury poisoning ever recorded. A total of over 6,500 poisoning cases were admitted to hospitals in provinces, and 459 hospital deaths were attributed to methylmercury poisoning (Bakir et al., 1973). Unlike the chronic methylmercury poisoning from contaminated fish that occurred in Minamata and Niigata, Japan, the Iraqi epidemic was acute in onset. Distribution of grain treated with methylmercurial fungicide began in September, 1971. The rate of admissions of cases to hospitals throughout the country increased in early January, 1972 to several hundred cases per day. No new hospital admissions were recorded after March, 1972. Thus this epidemic occurred following acute, high-dose exposure to methylmercury.

Data used in the quantitative analysis of uncertainty and variability in the U.S. EPA RfD are based on the Iraqi data reported by Bakir et al. (1973) as further analyzed by Marsh et al., (1987). As noted above there are no records of the size of the population who consumed grain treated with methylmercury fungicide. Likewise, there are no reliable estimates of the numbers of people who consumed methylmercury-treated grain and developed signs and symptoms of mercury toxicity, but did not obtain medical attention or become identified as part of the epidemic. Similar signs and symptoms of methylmercury poisoning were noted for the short-term exposure in Iraq and the chronic exposure in Japan. The symptoms progressed in severity as in Japan with increased exposure. The frequency of effects is not directly comparable between the two populations as the size of the exposed Iraqi population is not known because communication and record-keeping were less than optimal, and at least part of the population of concern consisted of nomads. Whether or not those who obtained medical care represented a more sensitive subpopulation is not known. What is known, however, is estimates of body burden of mercury based on analysis of hair and/or blood mercury concentrations and the occurrence of a constellation of signs/symptoms of methylmercury toxicity.

2.2.2.5 Delivered Dose Estimation

Data obtained during the Japanese epidemic included analyses of hair mercury concentrations. In the Iraq epidemic analyses of mercury concentration in hair and blood were carried out. Both sets of data have been used to estimate dose of methylmercury to affected subjects. An analysis of the threshold dose for adults exposed to methylmercury in Niigata was published by Kinjo et al. (1995). To be included as subjects the individuals had been classified as having Minimata Disease. This definition is presented in multiple publications including that of Tamashiro et al. (1985). The sign common to the syndrome of Minamata disease is the bilateral sensory disturbance which is more severe in the distal parts of the extremities and which also occurs sometimes in the perioral area (Takashiro et al., 1985). The raw data on hair mercury concentrations did not take hair length or hair growth rate into account. Consequently the actual mercury measurements can be considered to represent average values over the period of exposure to pollution derived from hair length and hair growth rate. Kinjo et al. (1995) include thresholds based on raw data; however, these investigators considered the maximum hair mercury concentration to be the more appropriate measure for dose-response analysis. Maximum hair mercury concentrations were estimated using actual mercury

concentrations and estimates of hair growth rate and biological half-lives for methylmercury. The biological half-life primarily used in their model was 70 days with a hair length of 10 cm for males and 20 cm for females and a hair growth rate of 1.5 cm/month. Additional biological half-lives (35 and 120 days) and different hair lengths (5 cm for males, 15 cm and 25 cm for females) were evaluated by changing these variables in the equations used to predict thresholds. The threshold dose of hair mercury concentration was estimated to be between 40 and 70 ppm by hockey-stick regression analysis. A wider range of threshold doses was observed when raw hair mercury data were used. Based on raw data from female subjects a threshold of 21 ppm mercury in hair was identified. Using a 70-day biological half-life and a hair length of 5 cm, a threshold of 67 ppm was observed.

Data from the Iraqi epidemic were used in development of U.S. EPA's RfD which was developed in 1994. These data were input parameters to a physiologically based dose conversion model for mercury. This model served as the mathematical basis for estimating exposure to mercury per kilogram body weight per day. Although this model has been extensively used (among other applications, the National Research Council/National Academy of Sciences' committee report entitled *Seafood Safety*, the World Health Organization's *Criteria Document on Methylmercury)* any differences between model parameters and actual values will determine the predictions made. This model relies on fundamentals such as the hair-to-blood ratio and the half-life of methylmercury in the blood.

Variability in biological half-life of mercury has been cited above. Generally a value of 70 days has been used. However, individual values as long as 250 days have been reported by Birke et al. (1972). Al-Shahristani and Shihab (1974) reported biological half-lives of methylmercury to vary between 35 and 189 days with an average of 72 days based on data from 48 patients. It is known that at least one subpopulation has a different value for the half-life of mercury that differs from the general adult population; lactating women had a shorter half-life for mercury than did nonlactating adults (Greenwood, 1978).

Extrapolation of dose-response conversions across a wider range than the range of the actual data results in uncertainty; this occurs when modeled data are used to predict beyond the range of observed data. Significant departures from non-linearity or differences between the shape of the modeled dose-response curve and the observed data may occur at extreme in the distribution. This is an intrinsic issue when modeled data are utilized. Whether or not intermittent exposures resulting from occasional consumption of highly contaminated media results in similar biokinetics of methylmercury remains an uncertainty.

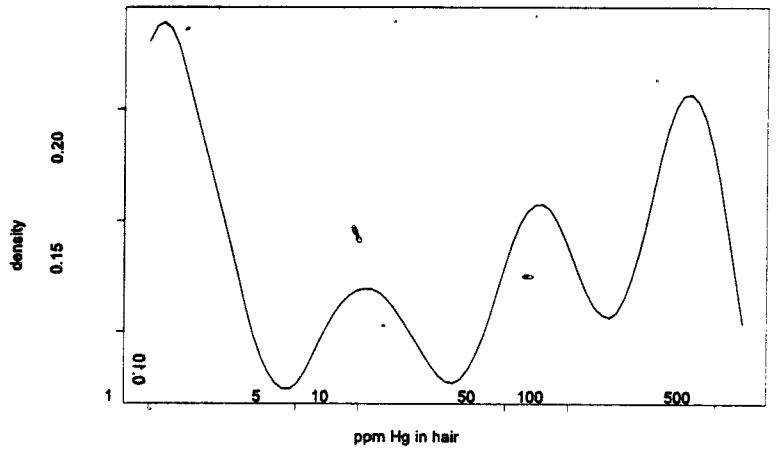
2.2.2.6 Grouping of Data

Dose groupings other than those used in *Seafood Safety* were also done and benchmark doses run as above for comparison. Both density-based grouping and uniform concentration intervals were used.

The local density of observations relative to the mercury level in hair was analyzed using a density estimation algorithm (ksmooth function in S-PLUS for Windows, Ver. 3.1; S-PLUS Guide to Statistical and Mathematical Analysis). The function estimates a probability density for the distribution of a variable by calculating a locally-weighted density of the observations. That is, the function estimates the probability that an observation will be near a specific value based on how the actual values are clustered. In this case, the function was used to estimate the probability density for an observation in the neighborhood of any given maternal hair mercury concentration. The density

plot is shown in Figure 2-1. The peaks represent relatively greater numbers of data points than the troughs in the vicinity of the associated hair mercury concentrations.

Figure 2-1
Density of Data Points Relative to Hg Concentration in Hair for Iraqi Cohort Data



The density distribution is characterized by four distinct peaks. Exposure dose groups were defined as trough-to-trough intervals with the peak values taken as the nominal value for each interval. The nominal dose-group value, concentration ranges and incidence of combined developmental effects are given in Table 2-1. A benchmark dose was calculated from the incidence of all effects as grouped in Table 2-1. The lower 95% confidence interval on the benchmark dose for 10% response is 13 ppm compared to the 11 ppm value used as the basis for the RfD.

Table 2-1
Density-Based Dose Groupings

Nominal Dose (ppm)	Dose Range (ppm)	Incidence
1.18	1 - 4	5/27
10.6	5 - 28	3/16
78.8	29 - 156	10/17
381	157 - 674	18/21

The other alternative dose grouping approach was to divide the entire exposure range into four equal log-dose intervals. The geometric midpoint of each interval was taken as the nominal value for the interval. The nominal dose-group value, concentration ranges and incidence of combined developmental effects are given in Table 2-2. The benchmark calculated as the lower bound on the 10% incidence for all effects is 10.3 ppm, compared to the 11 ppm used for the RfD.

Table 2-2
Uniform Dose Groupings

Nominal Dose (ppm)	Dose Range (ppm)	Incidence
2.25	1 - 5	5/28
11.5	6 - 25	3/14
58.6	26 - 132	9/17
299	133 - 674	19/22

2.2.2.7 Paresthesias as a Reliable Endpoint

The former RfD of $3x10^{-4}$ mg/kg-day was based on paresthesia in adults. A re-evaluation of the data set and exposure calculation was done with subsequent determination of a benchmark dose for paresthesia in adults of 3.6 µg/kg body weight/day (RfD Work Group Notes of 13 October 1994). Among the uncertainty and variability issues in use of transient paresthesias as an adverse health effect is the subjectivity of the condition. Transient paresthesias refers to tingling and numbness of extremities or the mouth area for a temporary period and is a clinically defined endpoint. These temporary paresthesias are fully reversible and occur in a number of benign (e.g., position of a limb during sleep) or serious conditions (e.g., osteoarthritis or diabetes). The duration of a temporary paresthesia is an important consideration and can range from a few minutes to hours or days.

In the epidemics of methylmercury poisoning in Minamata and Niigata, the development of paresthesias was extensively described (among others see Tsubaki et al., *Neurological Aspects of Methylmercury Poisoning* in Tsubaki and Irukayama, 1977). Sensory abnormalities were identified and considered an early indication of methylmercury poisoning in the Iraqi epidemic (Bakir et al., 1973). It is unclear from the published materials what duration of effect was needed to be classified as paresthesia. Reporting of paresthesia may reflect subject or examiner recall bias in either a negative or positive direction. Consequently this endpoint is quite subject to classification bias; however, personal communication from one of the investigators (Dr. Thomas Clarkson, University of Rochester, July, 1995) indicated that the clinicians who conducted the initial Iraqi investigation were familiar with the paresthesias produced by methylmercury exposure because they had evaluated Iraqi patients in the earlier epidemic in 1960. Although a standardized definition of paresthesia was very likely not developed, the investigators were familiar with the clinical picture of methylmercury-induced sensory disturbance.

A second issue for analyses of data on paresthesias is the background prevalence of temporary paresthesias in the subpopulation of interest. If temporary paresthesias were narrowly defined as caused only by methylmercury exposure, one interpretation of an appropriate background rate would be zero. Temporary paresthesias occur, however, in a number of benign and disease conditions. In the uncertainty analysis (Appendix D to Volume IV) carried out in support of this risk characterization, determination of a background rate was based on Bakir et al. (1972). The response data for exposed individuals do not show any background response, and so there does not appear to be an appreciable background rate of paresthesia in the general population. An estimate of 7.2 percent was developed from the data of Bakir et al. (1972, 1973) representing 40 hospitalized subjects. The

benchmark dose modeling for paresthesias used the prevalence of paresthesias among 35 female subjects whose hair mercury concentrations were under 10 parts per million.

The calculated dose for subjects with paresthesia used a 70-day half-life as the measure of central tendency. Duration of exposure is also a major concern in calculation of dose of methylmercury exposure that produces paresthesias. Methylmercury is retained in tissues. In the methylmercury poisoning epidemic in Iraq, the duration of exposure to methylmercury was estimated to be three months duration, although exposures as long as six months could have occurred (using September, 1971 the date when methylmercurial seed-grains were introduced and March, 1972 as the date of last hospitalization of cases). If exposure is prolonged, the dose estimated to produce paresthesias may differ based on laboratory data identifying the mechanisms of action by which methylmercury produces nerve damage. A detailed discussion of exposure duration, short vs. long exposure to methylmercury in production of paresthesias is shown in Appendix D of Volume IV.

2.2.2.8 Neuro-Developmental Effects

As with other health-based endpoints, the general issues of representativeness of the population who sought medical attention and became subjects in the study is a concern. In the Japanese epidemics extensive medical surveys were done during the 1960s in Minamata and Niigata (1965 and 1967) (Tsubaki and Irukayama, 1977; also reviewed by Harada, 1995). Identification of severe developmental disturbances were among the earlier changes identified among patients born from 1955 and later in the Minamata area of Kyushu, Japan (Harada, 1977, 1995). Under the conditions present in Minamata area during 1955-1957, Harada identified an overall morbidity of 6.9 percent, which was much higher than the rate of usual congenital cerebral palsy present in Japan (Harada, 1977). Harada noted (Harada, 1995) that for congenital Minamata disease, as with other cases of infantile cerebral palsy, the diagnosis occurs only after an extended time has elapsed since birth. In small fishing villages of Yudo, Tsukinowa, and Modo, Japan between 1955 and 1958 there were 188 births with a 9.0 percent incidence of cerebral palsy (Harada, 1995). During this period the overall national incidence of cerebral palsy was approximately 0.2 percent (Harada, 1995).

In the Iraqi epidemic, the first reports of infant-mother pairs exposed to methylmercury did not indicate an unusual sensitivity of the fetus compared to the exposed adult (Amin-Zaki et al., 1976). Follow-up at five years, however, indicated developmental delays in motor skills and impaired intelligence in one-sixth of the young children (Amin-Zaki et al., 1981). Delayed motor development was defined as inability of the infant to sit without support by the age of 12 months, to pull himself/herself to standing position by 18 months, or to walk two steps without support by 2 years of age. Language development was considered to be delayed when, at the age of 2 years, a child with good hearing failed to respond to simple verbal communication. There are no standardized intelligence quotient ranges for Iraqi children. The child's mental development was judged based on a combination of the mother's impressions of the child's development and the judgment of two physicians.

The background prevalence of late talking/late walking among the Iraqi population not exposed to methylmercury is an uncertainty. The major part of the variance in the developmental effects threshold distribution arises from uncertainty in the estimate of the threshold based on ppm mercury in hair, which accounts for 84 percent of the variance. These data show a very broad range of susceptibilities in this exposed population, up to a 10,000-fold span between the 5th and 95th percentiles when projected to the general population (data of Marsh et al., 1987, as analyzed by Hattis and Silver, 1994). A primary factor is that hair methylmercury concentrations imprecisely predict

toxicity, either because some important data are missing or because significant nonlinear processes are involved. For example, in the Marsh et al. (1987) data, it is noted than an individual with the highest estimated methylmercury exposure is a non-responder when the endpoint is developmental effects on the nervous system. This could reflect individual susceptibility to methylmercury toxicity. Alternatively, this observation may be a consequence of misclassification — the individual may have been exposed during a period of time which was not a critical developmental window. There is potential for misclassification as calculation of exposure time was dependent on subject recall of the gestational period and birth date.

Recall of birth data for the infant is of major importance in assessing the prevalence of developmental delays such as late walking or late talking. This uncertainty is particularly an issue with the Iraqi data set because of cultural differences. Published information and personal communication with the study authors suggest that within the Iraqi nomadic culture no particular significance is attached to the age at which walking and talking first occur. The database used to assess the distribution of ages in which late walking and late talking are assessed is a European database. It is known that ethnicity and race are factors that influence age at which motor skills are acquired.

2.3 Uncertainty in the Human Health RfD for Methylmercury

2.3.1 Qualitative Discussion of Uncertainties in the RfD for Methylmercury Alternate Analyses

Two additional human epidemiologic studies of separate populations (Kjellstrom et al., 1986a,b, 1989; McKeown-Eyssen et al., 1983) generally support the dose range of the benchmark dose level for perinatal effects. Both of these studies are described in section 3.3.1.1 of Volume IV. A recent analysis of the Kjellstrom data was published by Gearhart et al. (1995). In this analysis the authors used a PBPK model which incorporated a fetal compartment. They calculated a benchmark dose on all 28 tests included in the initial study design by Kjellstrom; this was done assuming values of 1 and 5% for background deficiency in test scores. The range of benchmark doses calculated was 10 to 31 ppm maternal hair mercury. The authors' preferred benchmark was 17 ppm, for an estimated background incidence of 5% and the lower bound on the 10% risk level.

Chronic rodent (Bornhausen et al., 1980) and nonhuman primate studies (Burbacher et al., 1984; Gunderson et al., 1986; Rice et al., 1989a,b) provide data to support LOAELs for other developmental end points.

The principal study (Marsh et al., 1987) is a detailed report of human exposures with quantitation of methylmercury by analysis of specimens from affected mother-child pairs. A strength of this study is that the quantitative data are reported on the affected population, and quantitation is based upon biological specimens obtained from affected individuals. A threshold or presumed no effect level was not easily defined; application of modeling techniques were needed to define the lower end of the dose-response curve. This may indicate high variability of response to methylmercury in the human mother-child pairs or misclassification of assigning pairs to the cohort. Concerns have been raised as to the applicability of a risk assessment based upon data from grain-consuming population when the application of this risk assessment is for segments of the U.S. population consuming fish. It is thought that a diet rich in animal protein (such as fish) also delivers selenium. Selenium appears to interact with mercury in some experimental systems and has been suggested to increase the latency period for onset of symptoms of neurotoxicity which has been observed in exposed humans. It is not

thought that the exposed Iraqi population was selenium-deficient or significantly malnourished; however, the effect of additional dietary selenium on the dose-response curve is uncertain.

The most appropriate basis for calculation of an RfD for methylmercury has been the subject of much scientific discussion; several plausible alternatives to the U.S. EPA assessment have been proposed. ATSDR used the analysis reported by Cox et al. (1989, see discussion below) of the Iraqi developmental data in the derivation of an intermediate MRL (minimal risk level). Using delayed onset of walking as the critical effect, a LOAEL of 14 ppm mercury in hair was determined. A dose conversion from ppm hair to daily intake to maintain blood mercury levels in pregnant women was done in a very similar manner to that employed by U.S. EPA. Values for parameters in the equation were consistent between the two agencies with one exception; namely the use of a blood volume of 4.1 L by ATSDR compared to 5 L by U.S. EPA. The methylmercury intake level calculated by ATSDR to maintain a hair level of 14 ppm is 1.2 μg/kg-day compared to 1.1 μg/kg-day to maintain a hair level of 11 ppm (used by U.S. EPA), this is not a significant difference.

The state of New Jersey currently uses an RfD of 0.7×10^{-4} mg/kg-day (described in Stern, 1993) compared to U.S. EPA's RfD of 1×10^{-4} mg/kg-day. The critical effect chosen was developmental endpoints in the Iraqi children exposed *in utero* including delayed onset of walking. The LOAEL chosen was the mercury hair level equivalent to a mercury blood level of 44 μg/L. To determine the intake level, the equation in Section 2.2.1.2 of this volume was used, but with different values for two parameters, namely, b and f.

Crump et al. (1995) reanalyzed data from the Iraqi methylmercury poisoning episode presented by Marsh et al. (1981). Using a hockey stick parametric dose-response analysis of these data, Cox et al. (1989) concluded that the "best statistical estimate" of the threshold for health effects was 10 ppm mercury in hair with a 95 percent range of uncertainty between 0 and 13.6. In their analysis, Crump et al. (1994) reported that the statistical upper limit of the threshold could be as high as 255 ppm. Furthermore, their maximum likelihood estimate of the threshold using a different parametric model was said by the authors to be virtually zero. These and other analyses demonstrated that threshold estimates based on parametric models exhibit high statistical variability and model dependency, and are sensitive to the precise definition of an abnormal response.

Using a statistical analysis for trend that does not require grouping of the data, Crump et al. (1994) demonstrated that the association between health effects and methylmercury concentrations in hair is statistically significant at mercury concentrations in excess of about 80 ppm. In addition, Crump et al. (1994) calculated benchmark doses by applying dose-response models to each of the three endpoints: late walking, late talking and neurological score. Their calculation of the 95 percent lower bounds on the hair concentration corresponding to an additional risk of 10 percent ranged from 54 ppm to 274 ppm mercury in hair. Crump et al. (1994) concluded that the trend analyses and benchmark analyses provided a sounder basis for determining RfDs than the type of hockey stick analysis presented by Cox et al. (1989). They felt that the acute nature of the exposures, as well as other difficulties with the Iraqi data, present limitations in the use of these data for a chronic RfD for methylmercury.

Cox et al. (1995) have published a recent analysis of the data on late walking in Iraqi children exposed *in utero* to methylmercury. The authors indicate that dose-response analyses based on the "late walking" endpoint are unreliable because of four influential observations in the data set from Marsh et al. (1978). The data points in question are the only responders below 150 ppm (Hg in hair). In particular Cox et al. (1995) state that the four observations are isolated from the remainder of the

responders and would be expected to have considerable influence on threshold estimate. This conclusion is based on a visual interpretation of a plot of the data (Figure 2 in Cox et al., 1995). Based on visual inspection of the same figure, an argument could be made that the separation is not that marked considering the first eight responders. No quantitative sensitivity analysis was performed to investigate the effect of removing one or more of these data points. Cox et al. (1995) point out that if the four points are assumed to represent background, then the threshold for late walking would be greater than 100 ppm. It would seem unlikely, however, that these observations represent background given that no responses were observed in the 37 individuals with lower levels of exposure. It should be noted that the U.S. EPA benchmark dose was done on incidence of all effects, rather than on late walking only.

The Cox et al. (1995) and Crump et al. (1995) analyses deal primarily with one endpoint; namely, late walking. This appears to be the most sensitive of the endpoints described in March et al. (1978). Both Cox et al. and Crump et al., as well as the U.S. EPA analysis in Appendix D of Volume IV, show considerable uncertainty in thresholds estimated from the data on late walking.

Late walking, as assessed in the exposed Iraqi population (March et al., 1978) is almost certainly a valid indicator of methylmercury toxicity but may well be unreliable as the sole basis for detailed dose-response analysis. The primary reason for this may be the uncertainty in maternal recall for both birth date and date of first walking. The uncertainty, in this particular case could be quite large, given the lack of recorded information. The primary impact of this kind of uncertainty would be on the response classification of individuals at the upper bound of normal (18 months for first walking) and at the lower bound of abnormal. The lowest abnormal first walking times presented in March et al. (1978) 20 months. The impact of assuming uncertainty in the classification of the observations in these two groups is large given the large number of observations in the two groups (19 data points at 18 months and 8 data points at 20 months). The analysis in Appendix D to Volume IV of the Report to Congress shows that thresholds estimated for late walking are unstable when classification uncertainty is considered. The same kind of subjective uncertainty is applicable to the late walking endpoint, as well. The thresholds for late walking, however, are much more stable, statistically, as there are fewer observations that are near the normal/abnormal threshold value of 24 months.

Marsh et al. (1995) have published results of a study conducted between 1981 and 1984 in residents of coastal communities of Peru. The prospective study was of 131 child-mother pairs; testing for potential effects of fetal methylmercury exposure was patterned after the study of children exposed *in utero* in Iraq. Peak maternal hair methylmercury ranged between 1.2 to 30 ppm with a geometric mean of 8.3 ppm. These authors showed no effects of methylmercury on measures similar to those performed on the Iraqi children (including time of first walking and talking). A NOAEL (in the absence of a LOAEL) from this study would be 30 ppm maternal hair mercury. This is consistent with the U.S. EPA benchmark dose of 11 ppm.

Fetal effects of methylmercury exposure were based on hair mercury analyses from 83 women in Iraq. Recommendations based on this data set are a best estimate based on a relatively small number of human subjects. The size of the data set becomes a limitation for identifying adverse effects that may occur in a small fraction of subjects due to factors such as individual variability. A limitation of these data is the relatively small number of maternal-infant pairs (81) whose exposures fell within the range of interest for this assessment. Efforts to interpret these data have considered the issue of threshold modeling (among other references see the NIEHS Report to Congress on Methylmercury, 1993). The duration of the exposure to methylmercury (approximately three months

in the Iraqi outbreak) was long enough to identify the effects of methylmercury exposure on the outcome of pregnancy.

Concern has been raised by various scientists as to the impact that as yet unpublished studies will have on the risk assessment for methylmercury. Reports have delivered at scientific meetings results of studies of populations in the Faroes and Seychelles Islands known to consume large amounts of seafood. Data on parts of the Seychelles Study have recently been published. The interpretation by some risk assessors is that the effects noted in the Iraqi population exposed to contaminated grain are not being seen at similar doses of methylmercury delivered *in utero* via contaminated seafood.

As the majority of these new data are either not yet published or have not yet been subject to rigorous review, it was decided that it was premature for U.S. EPA to make a change in the methylmercury RfD at this time. An interagency process, with external involvement, will be undertaken for the purpose of review of these new data, evaluations of these data and evaluations of existing data. An outcome of this process will be assessment by U.S. EPA of its RfD for methylmercury to determine if change is warranted.

It has been suggested that a developmental toxicity RfD is needed for methylmercury. This may not be necessary, however, if the critical effect is developmental toxicity and the uncertainty factors used to estimate the lifetime RfD do not involve an adjustment for less than lifetime exposure nor lack of complete database.

2.3.2 Quantitative Analysis of Uncertainty in the Methylmercury RfD

2.3.2.1 Introduction

This section summarizes the methylmercury RfD uncertainty analysis presented in Appendix D to Volume IV of this Report. Details of the methods applied and the results obtained can be found in Appendix D. The purpose of this analysis is two-fold: first, to determine plausible bounds on uncertainty associated with the data and dose conversions used to derive the methylmercury RfD; second, to compare the RfD to estimated distributions of human population thresholds for adverse effects. This analysis is a modeled estimate of the human threshold for specific health effects attributable to methylmercury exposure. The basis for the analysis and the RfD is the data from the 1971 Iraqi methylmercury poisoning incident, specifically the data from the Marsh et al. (1987) population referred to as the Iraqi cohort. An adult paresthesia benchmark dose was also based on data presented in Bakir et al., (1973). The analysis also includes studies pertinent to the conversion of mercury concentrations in hair to estimated ingestion levels.

For purposes of this analysis, the human population threshold was defined as the threshold for the most sensitive individual of an identified sensitive subpopulation. The definition of sensitive subpopulations excludes hypersensitive individuals whose susceptibilities fall far outside the normal range. A threshold is defined as the level of exposure to an agent or substance below which a specific effect is not expected to occur. The definition of threshold does not include concurrent exposure to other agents eliciting the same effect by the same mechanism of action. In other words, there is an assumption that the induced response is entirely a result of exposure to a single agent. The 81 pregnant female/offspring pairs comprising the Iraqi cohort were taken as a surrogate for the most sensitive subpopulation expected in the general U.S. population consuming fish. The sensitive subpopulation was identified for the uncertainty analysis as humans exposed to methylmercury *in utero*.

The uncertainty analysis examined the major sources of uncertainty explicitly and implicitly inherent to the methylmercury RfD and attempted to bound them quantitatively. The principal uncertainties arise from the following sources: the variability of susceptibilities within the Iraqi cohort; population variability in the pharmacokinetic processes reflected in the dose conversion; and response classification error.

The response classification is the assignment of an individual observation to one of two categories — responder or nonresponder. The response classification for each of the developmental endpoints reported by Marsh et al. (1987) was based on a fixed value (response decision point) that, when exceeded, constitutes a response. It is possible that some responses were misclassified, particularly those for responses in the immediate vicinity of the response decision point; a responder may have been classified as a nonresponder or vice versa. The response classifications for late walking and late talking are particularly susceptible to this type of error. The response estimates were based on subject recall in members of a population that does not traditionally record these events.

Other areas of uncertainty are those directly related to the RfD methodology. Specifically, it was concluded by an Agency Work Group that there were no adequate chronic or reproductive studies. An uncertainty factor of 10 is generally applied when chronic studies are not available. This uncertainty factor is based on an assumption inherent to the RfD methodology that increased exposure duration will lower the dose required for observation of the effect. Support for this assumption has been published (Weil and McCollister, 1963; Dourson and Stara, 1989) and is discussed in Section D.2.2.2 of Appendix D to Volume IV. An uncertainty factor of 3 is generally applied if reproductive studies are not available. NOAELs for reproductive studies are generally two-fold to three-fold higher than NOAELs for chronic studies and are not expected to be the basis for the RfD more than 5 percent of the time (Dourson et al., 1992).

2.3.2.2 Methods

Thresholds were estimated in a two-stage process. The first stage was the estimation of threshold distributions based on hair mercury concentrations, which was accomplished by applying a regression model to successive bootstrap samples of the observations in Marsh et al. (1987). This process is detailed in Section D.2.1 of Appendix D to Volume IV. The second stage was the conversion of the thresholds expressed as ppm mercury in hair to mg methylmercury per kg body weight per day (mg/kg-day); this involved a Monte Carlo analysis of the variability of the underlying biological processes. For details of methods, see Appendix D to Volume IV.

Because the Iraqi cohort is considered to be a sensitive subgroup, as defined in the RfD methodology, the output distributions of the uncertainty analysis are meant to reflect the uncertainty around an estimate of the thresholds for effects in humans including sensitive individuals. The results for each endpoint should be interpreted as the distribution of the uncertainty around the human population threshold. The results should not be interpreted as the distributions of individual thresholds within the population. Estimates of risk above the threshold cannot be obtained from this analysis.

The uncertainty analysis was limited to only those data and equations directly related to the derivation of the methylmercury RfD. Other data sets or models were not considered. A few sources of uncertainty in the data used to derive the methylmercury RfD have not been included in this analysis. Exposure classification error arising from uncertainty as to the correspondence of actual exposure and critical exposure period cannot be estimated from the data as published by Marsh et al. (1987). This source of uncertainty could be a major contributor to the apparent extreme variability of

susceptibilities in the Iraqi cohort. Variability in the interpretation of the definition of a response was not estimated in this analysis. That is, there would be expected differences in individual interpretation of first walking or first talking (probably for the latter). The classification errors assumed for this analysis only accounted for uncertainty in the timing of the event given an unequivocal positive response. Also, the response decision points defining an adverse effect were accepted uncritically. For example, changing the definition of late walking to either greater than 16 months or greater than 20 months would have a significant effect on the analysis. Measurement error for hair mercury concentrations has not been estimated for this analysis; the necessary data are unavailable in the published reports (Marsh *et al.*, 1987; Cox *et al.*, 1989).

The results of this analysis are conditional on a specific representation of population variability in the parameters of the dose conversion variables. That is, the choice of the form and parameters for the distributions assigned to each of the variables is largely a matter of judgment; the particular set of parameters chosen for each distribution is only one option of a number of possible choices; and uncertainty as to the value of the parameters is not included in the analysis. For example, the choice of the (log-triangular) distribution for half life of methylmercury was made on the basis of best fit with respect to the 5^{th}, 50^{th} and 95^{th} percentiles of the combined data from several studies. This particular distribution does not allow for values less than 28 days or greater than 125 days, but could be easily modified to do so. Such a modification would, however, have only a small effect on the Monte Carlo-generated distribution for the dose conversion factor.

The threshold analysis shows that adult paresthesia was the most sensitive individual effect observed for the Iraqi cohort, particularly when adjusted for the effects of continuing exposure. That is, in this analysis, paresthesia in adults was estimated to be observable at a lower exposure than the developmental endpoints. The adult paresthesia bootstrap thresholds were also the most unstable as measured by the frequency of nonsignificant slopes. The RfD fell between the 39^{th} and 91^{st} percentiles of the duration-adjusted adult paresthesia threshold distribution, a considerably larger range than that for any of the developmental effects. On the average, the RfD fell below the 1^{st} percentile for all developmental effects, with only a 5 percent chance that it was as high as the 16^{th} percentile. A discussion of factors affecting reliability of paresthesia as an endpoint is provided in Section 5.1.3.1 of this volume.

The results of the response-classification uncertainty analysis suggest that the late walking endpoint and adult paresthesia were unreliable as measures of methylmercury toxicity for the Iraqi cohort. The exclusion of late walking from the combined developmental effects would not have a very large impact on the threshold distribution, increasing the thresholds by about 50 percent. Although the response-classification uncertainty analysis was based on hypothetical classification error rates, a two-month uncertainty in recall of these events was not unlikely in this particular situation. These results suggest that strong conclusions should not be based on the late walking and adult paresthesia endpoints.

2.3.2.3 Conclusions of Analysis of Uncertainty Around Human Health Effects of Methylmercury

A major source of the variability was in the estimation of bootstrap thresholds from the Iraqi cohort data as evidenced by the 12- to 20-fold difference in the 5^{th} and 95^{th} percentiles of the bootstrap threshold distributions. The uncertainty arising from limited exposure duration contributed almost as much, with a 12.5-fold difference in the 5^{th} and 95^{th} percentiles. The corresponding spreads in the dose conversion distributions were 2.4-4.2 fold. Correlations between variables were important

with respect to the variance of the Monte Carlo simulations but were not well-defined by empirical data. Additional areas of uncertainty remain to be modeled.

Of the developmental endpoints, the neurological effects, which are determined by a battery of tests and do not depend on subject recall, would seem to be the most objective measure of methylmercury toxicity. Late walking was not a reliable endpoint because of sensitivity to classification error.

The RfD of $1x10^{-4}$ mg/kg-day is very likely below the threshold for developmental effects but may be above the threshold for exposure duration-adjusted adult paresthesia. Strong conclusions based on the latter result are not warranted because of the sensitivity of the adult paresthesia threshold to classification error and the general lack of data addressing the effects of exposure duration.

3. WILDLIFE HEALTH EFFECTS: HAZARD IDENTIFICATION AND DOSE-RESPONSE

3.1 The Framework for Ecological Risk

U.S. EPA defines ecological risk assessment as "a process that evaluates the likelihood that adverse ecological effects may occur or are occurring as a result of exposure to one or more stressors" (U.S. EPA, 1992a). Although ecological risk assessment follows the same basic risk paradigm as human health risk assessment, there are three key differences.

- Ecological risk assessment can consider effects on populations, communities and ecosystems in addition to effects on individuals of a single species.
- No single set of ecological values to be protected is applicable in all cases; instead, they must be selected for each assessment based on both scientific and societal merit.
- Nonchemical stressors (e.g., physical disturbances) often need to be evaluated as well as chemical stressors.

The problem formulation phase of an environmental risk assessment consists of three main components: (1) characterizing the stressors, potential exposure pathways, ecosystems potentially at risk, and ecological effects; (2) selecting endpoints (the ecological values to be protected); and (3) developing a conceptual model of the problem (U.S. EPA, 1992a).

In this Report only terrestrial and freshwater aquatic ecosystems were considered for evaluation. It is recognized that mercury deposited in coastal areas can be translocated to estuarine environments, and biota that inhabit these and nearby marine systems have the potential to be adversely impacted. Presently, however, uncertainties regarding mercury deposition, cycling and effects in marine environments are so great as to preclude even a qualitative risk assessment.

Of the pathways by which ecosystems and components of ecosystems might be exposed to atmospheric mercury, exposure of high trophic level wildlife to mercury in food is particularly important. The trophic level and feeding habits of an animal influence the degree to which that species is exposed to mercury. Mercury biomagnifies in aquatic food chains with the result that tissue concentrations of mercury increase as trophic levels increase. Predatory animals primarily associated with aquatic food chains accumulate more mercury than those associated with terrestrial food chains. Thus, piscivores and carnivores that prey on piscivores generally have the highest exposure to mercury. In a study of fur-bearing mammals in Wisconsin, the species with the highest tissue levels of mercury were otter and mink, which are top mammalian predators on aquatic food chains (Sheffy and St. Amant, 1982). Top avian predators of aquatic-based food chains include raptors such as the osprey and bald eagle. Smaller birds feeding at lower levels in aquatic food chains also may be exposed to substantial amounts of mercury because of their high food consumption rate (consumption/body weight/day) relative to larger birds. In the methylmercury poisoning epidemics in Minamata, Japan, extensive poisoning of marine life, birds that fed on the marine life, and domestic animals were reported in years preceding the severe human poisonings that occurred (Irukayama et al., 1977). The general picture was one of severe neurological damage to multiple species in the aquatic food chain, including death of fish; severe incoordination and death in birds; ataxia and convulsions in domestic cats; and finally gross neurological defects and death in humans (Tsubaki and Irukayama, 1977).

Although clear causal links have not been established, mercury originating from airborne deposition may be a contributing factor to population effects on bald eagles, river otters and mink. Evidence is available to support the possibility of toxic effects on the common loon and the Florida panther. Effects of mercury originating from point sources on restricted wildlife populations have been conclusively demonstrated and provide a tissue residue basis for evaluation of risk to other populations.

Effects data were insufficient for evaluation of any intact ecosystem, community of species or population of animal or plants. This limitation of data necessitated the choice of individual wildlife effects for selected species as the ecological value to be protected.

3.2 Health Hazards of Methylmercury Exposure to Wildlife

Methylmercury present in terrestrial and aquatic food chains creates risks to the health and reproductive success of wildlife. The epidemics of human disease from grain treated with mercurial fungicides and from fish contaminated with methylmercury were preceded by major epizootic outbreaks of death, neurological disease, and reproductive failure among wildlife and domestic animals. During the period 1940 through the 1970s, treatment with seed grains with organomercurial fungicides resulted in poisonings of massive numbers of seed-eating birds and their predators (Borg et al., 1970). In Minamata death and serious neurological disturbances among birds and cats were reported in the years preceding the first cases of human Minamata disease in 1956 (Tsubaki and Irukayama, 1977). As is the situation for humans, the risk characterization issues for wildlife and domestic animal effects of methylmercury from fish center on the quantities of methylmercury that produce disease and on the likelihood of exposure to these quantities of methylmercury.

A principal weakness identified in the current risk characterization for methylmercury is the limitations of the toxicity database for the wildlife species. Problems identified during risk characterization included these: limited information in case reports of small numbers of animals, and either no, or limited, exposure data; uncertainty about the agent that caused the toxic response in wildlife potentially exposed to pesticides, PCB, etc.; no monitoring for subtle indicators of effect (e.g., paresthesias) even in experimental situations; questions on whether or not sensory deficits were of concern for wildlife; shorter than chronic studies; dose-groups in experimental studies that did not span the range of the NOAEL to development of frank effects; limited data on tissue mercury concentrations; and limited histopathological data.

3.2.1 Mammalian Species

Methylmercury toxicity in non-human mammals appears to follow the pattern observed in humans: neurotoxicity is the endpoint of concern. Methylmercury adversely affects the central nervous system of multiple species of wildlife producing sensory, visual, auditory and motor impairment. In chronic studies by O'Connor and Nielse (1981) using river otters (*Lutra canadensis*) fed methylmercury, 2 ppm (0.09 mg/kg bw/day) caused anorexia and ataxia during the six-month test period. In mink, 27 ppm of dietary phenylmercuric chloride caused lethality in 40 percent of the males and 31 percent of the females within six weeks of exposure (Borst and Lieshout, 1977). Wobeser et al. (1976a,b) reported neurotoxicity in adult mink and kits fed methylmercury in fish or chow. Methylmercury has been implicated in Florida panther deaths and population decline, and has been reported to produce neurotoxic effects in domestic cat.

3.2.2 Avian Species

The most complete dose-response information for avian wildlife species describe the adverse effect of methylmercury on reproduction. These data exist for multiple avian wildlife species. For example, Fimreite (1971) identified a LOAEL for reproductive effects (reduced survival, reduced egg production, defective shells) of 0.18 mg/kg-day in ring-necked pheasants (*Phasianus colchicus*) fed seed treated with methylmercury dicyandiamide. Scott (1977) identified a LOAEL for reproductive effects (reduced fertility, reduced egg number, reduced survival, defective shells) of 4.9 mg/kg/day in domestic chickens. Heinz observed reproductive and behavioral effects in a three observation study in mallards; the LOAEL of 0.064 mg/kg-day from this study served as the basis for the avian wildlife criterion.

3.3 Dose-Response to Methylmercury for Wildlife Species

Despite major gaps in information on methylmercury toxicity to wildlife, adverse effects of mercury exposure have been evaluated for selected species. The species identified for risk characterization were wildlife chosen because they are predicted to be the most highly exposed to methylmercury, not because of any known inherent sensitivity to methylmercury toxicity. Lacking additional toxicity information, little guidance is available concerning which wildlife species are likely to be the most sensitive to methylmercury.

The adverse health outcomes considered in risk characterization for wildlife species are neurotoxicity and reproductive and/or developmental effects. The databases for wildlife species are extremely limited. A major uncertainty in this risk characterization is cross-species extrapolation. Compared with endpoints for humans, the wildlife effects are far more severe. Wildlife effects are either lethality or gross clinical poisoning.

3.3.1 Mammalian Species

Dose-response to methylmercury has been estimated in greater detail for mink than for other mammalian wildlife species. The data of Wobesser (1973) and Wobeser et al. (1976a,b, 1979) on mink (*Mustela vison*) have been used to estimate risk for mammalian wildlife species. The LOAEL for mink based on nervous system lesions identified through histopathology was 1.1 ppm methylmercury in diet (0.24 mg/kg bw/day in males and 0.16 mg/kg bw/day in females).

The most complete evaluation of quantities of methylmercury in fish fed to wildlife species are those of Wobeser et al. (1976a). Wobeser et al. (1976a) studied the effects of dietary consumption of mercury in the form of contaminated fish, caught locally and mixed with the normal mink chow to produce an average dose of 0.33 ppm methylmercury in the diet. Materials and methods are described in the original publications and in Volume V. Wobeser et al. (1976b) fed minks diets containing 1.1, 1.8, 4.8, 8.3 and 15 ppm total mercury from contaminated fish in the mink chow. A LOAEL was identified for mink as 1.1 ppm (0.24 mg/kg body weight/day in males and 0.16 mg/kg bw/day in females) based on a finding of nervous system histopathology without clinical signs. Higher doses of methylmercury caused anorexia, ataxia, and death within 60 to 80 days at 1.8 ppm; death occurred within 26 to 36 days at 4.8 ppm, and death resulted within 19 to 26 days at 8.3 ppm (Wobeser, 1976b). From these studies (Wobeser, 1976a and 1976b) a NOAEL of 0.05 mg/kg bw/day and a LOAEL for nervous tissue lesions of 0.16 mg/kg bw/day based on male mink is identified.

Under the study conditions (Wobeser, 1973; Wobeser et al., 1976a,b), exposure to 1.1 ppm methylmercury in the diet for 93 days produced histopathological changes in the central nervous system (specifically neuronal necrosis) but no clinical signs and symptoms of methylmercury poisoning. When the dietary level of methylmercury was increased by 0.7 μg/g (from 1.1 to 1.8 μg/g diet) the mink became anorexic, developed ataxia (severe incoordination) and died with clinical signs and symptoms of methylmercury poisoning (Wobesser, 1973). These changes occurred after 50 to 60 days of exposure (for anorexia) and 60 to 78 days of exposure (for ataxia) to the 1.8 ppm diet. The increase of 0.7 μg/g dietary methylmercury resulted in appearance of signs and symptoms of methylmercury poisoning and death. Ingestion of diet with higher concentrations of methylmercury (4.8 and 8.3 μg/g diet) decreased the survival time of mink to 26-36 and 19-26 days, respectively (Wobeser, 1973). All mink dying after receiving higher concentrations of dietary methylmercury (Wobeser, 1973) had gross clinical symptoms of methylmercury poisoning including anorexia and ataxia. Overall, the dose-response curve for methylmercury was very steep as reflected by the onset of mercury-related signs and symptoms of severe poisoning if methylmercury were increased from 1.1 to 1.8 μg/g diet. Higher concentrations of dietary methylmercury decreased the time that mink survived on these diets.

In the studies of Wobeser et al., methylmercury had been incorporated into the diet on a weight/weight basis yielding study groups for which methylmercury concentrations were expressed on a parts per million (ppm or μg/g) basis. Assumptions needed to interpret these data were body weight of the mink and food consumption by mink; these were obtained from the Exposure Factors Handbook (U.S. EPA, 1994).

An additional uncertainty is whether or not the dose-response pattern for mink will apply to river otters. Application of mink dose-response data to otters is supported by the observations of O'Connor and Nielson (1981). These investigators identified dietary levels of 2.0 μg/g methylmercury as acutely toxic to otter.

3.3.2 Avian Species

The most comprehensive studies of adverse reproductive effects of methylmercury exposure to avian species are based on the research of Heinz (1974, 1975, 1976a,b, 1979). Initially, Heinz (1974) identified a NOAEL of 0.5 ppm based on reproductive effects in a 21-week duration study. In a later study, reproduction in the first and second generation ducks was evaluated (Heinz 1976a,b) and the NOAEL for the first generation was again determined to be 0.5 ppm. The second generation, however, suffered adverse reproductive effects that included the following: eggs laid outside nest box at the 0.5 ppm dose. Consequently, the LOAEL for reproductive effects for the second generation was 0.5 ppm with no NOAEL identified. A third generation of mallards also demonstrated adverse reproductive effects at 0.5 ppm mercury in the diet. Effects observed included reduced numbers of sound eggs laid per day and thinner egg shells.

Heinz (1975, 1976a,b, 1979) also examined behavioral effects of mercury exposure in the approach response of chicks to maternal calls and avoidance of frightening stimuli. In third-generation ducklings there was a reduction in the response rate and speed of response to maternal calls. When data were pooled from all studies and subjected to analysis of variance with multiple comparisons, alterations of behavior were observed in the lowest dose groups in all generations. These alterations included the following: reduction in the number of ducklings that approached maternal calls, and an increase in the distance traveled to avoid a threatening stimulus. In summary, no NOAEL could be

demonstrated for behavioral effects, and the NOAEL for reproductive effects could only be demonstrated for the first generation.

For the determination of the appropriate selection of the LOAEL, consideration was given to using 3 ppm in the first generation with 0.5 ppm NOAEL. It was concluded, however, that effects observed in subsequent generations at 0.5 ppm should not be discounted. It seems likely that the effects observed in the second and third generations were a result of the earlier onset of dosing (adult onset vs. onset as ducklings). For this reason, 0.5 ppm was selected as a LOAEL for mallard ducks. Assuming a feeding rate of 128 g/kg/day for adult mallards, the LOAEL for reproduction and behavior is 0.064 mg/kg/bw day. Dose-response data for the mallard has not been estimated beyond the LOAEL. An additional uncertainty in this assessment is the extent that the dose-response data for mallards apply to osprey, kingfishers, bald eagles and other piscivorous birds.

3.4 Wildlife Criteria

3.4.1 Wildlife Criteria Methodology

Calculation of wildlife criteria (WC) for mercury was based upon the use of a wildlife reference dose approach, combined with knowledge of the extent to which mercury becomes concentrated in aquatic food chains. The methods used to calculate these values were based on those described in the *Proposed Great Lakes Water Quality Guidance* for the Great Lakes Water Quality Initiative (henceforth referred to as the "Proposed Guidance," U.S. EPA, 1995b). This approach yields a measurement endpoint, which is the total mercury concentration in water that is believed to be protective of piscivorous wildlife. A similar equation was first used by the State of Wisconsin to set Wild and Domestic Animal Criteria (State of Wisconsin, 1989). The entire approach, including both the equation and data requirements for its parameterization, was later modified by U.S. EPA for incorporation into the Proposed Guidance (U.S. EPA, 1993c) and Final Guidance (U.S. EPA, 1995b). Description of the calculation of the wildlife criteria, description of terms of the equation and support for the values used are found in Chapter 4 of Volume V.

The WC for mercury is defined as the concentration of total mercury in surface water that, if not exceeded, protects both avian and mammalian wildlife that use the water as a drinking or foraging source. Thus, the WC is the highest aqueous concentration of mercury that causes no significant reduction in growth, reproduction, viability or usefulness (in a commercial or recreational sense) of a population of animals exposed over multiple generations. For the purpose of this analysis, the term "aqueous concentration" refers to the total concentration of all mercury species in filtered water, including both freely dissolved forms and mercury that is associated with dissolved organic material. It is recognized that methylmercury is the form of mercury that bioaccumulates in fish.

The method, in its current form, was reviewed in 1992 at a workshop entitled the National Wildlife Criteria Methodologies Meeting, sponsored by U.S. EPA (1994). Subsequently, it was used to develop interim Tier I WC for four compounds (PCBs, DDT, dieldrin and mercury) in the Great Lakes Basin (U.S. EPA, 1993b). These criteria have received public comment. The method has been reviewed by the Science Advisory Board (SAB) on two occasions, most recently in June of 1994. Detailed descriptions of the method, including comparisons with other proposed methods for setting wildlife criterion values, are presented in U.S. EPA (1994, 1995b).

The equation used in Volume V to calculate wildlife criteria for mercury is that described in the Proposed Guidance to the GLWQI (U.S. EPA, 1995b):

$$WC = \frac{(TD \times [1/UF]) \times Wt_A}{W_A + [(FD_3)(F_A \times BAF_3) + (FD_4)(F_A \times BAF_4)]}$$

where:

WC	=	wildlife criterion value (pg/L; after converting from µg/L)
TD	=	tested dose (µg/g bw/day)
UF	=	uncertainty factor
Wt_A	=	average species weight (g)
W_A	=	average daily volume of water consumed (L/d)
FD_3	=	fraction of the diet derived from trophic level 3
F_A	=	average daily amount of food consumed (g/d)
FD_4	=	fraction of the diet derived from trophic level 4
BAF_3	=	aquatic life bioaccumulation factor for trophic level 3 (L/g; methylmercury concentration in fish/total mercury in water)
BAF_4	=	aquatic life bioaccumulation factor for trophic level 4 (L/g; methylmercury concentration in fish/total mercury in water)

In the equation used in this Report the term F (defined in the GLWQI as the food ingestion rate of prey for a tropic level) was broken into the terms F_A and F_D above. The UF considers uncertainty in three areas described below.

This equation encompasses both a hazard and an exposure component. The GLWQI equation includes a term TD for "tested dose". In this Report, data were reviewed to ascertain an appropriate NOAEL, which was used for the TD. In the absence of a NOAEL, a LOAEL was used with the addition of an appropriate uncertainty factor (UF_L) to indicate uncertainty around the toxic threshold. An uncertainty factor (UF_A) may be used to provide a margin of safety when applying data from a species other than the species of concern. A third uncertainty factor (UF_S) may be used to extrapolate from subchronic to chronic exposures. Collectively, the application of the UF to the TD results in the estimation of a "reference dose" for subsequent calculation of WC.

3.4.2 Bioaccumulation Factors

Bioaccumulation factors (BAFs) for trophic levels 3 and 4 (forage fish and larger, piscivorous fish, respectively) were estimated in Appendix A to Volume V. The BAF for any given trophic level is defined as the ratio of the total mercury concentration in fish flesh divided by the concentration of total dissolved mercury in the water column. The BAF represents the accumulation of mercury in fish of a specific trophic level from both water intake and predation on contaminated organisms.

In Volume V BAFs were estimated for trophic level 3 (foraging fish) and trophic level 4 (piscivorous fish) designated as BAF_3 and BAF_4, respectively. BAF_3 was estimated by two different methods: the method of the GLWQI which combined use of bioconcentration factors for lower trophic levels with predator-prey factors; and calculation of a BAF from field measurement data.

BAF_4 was calculated by three methods: the GLWQI method: calculations based on field measurement data; and multiplication of the field-data-based BAF_3 by a predator-prey factor for trophic level 4. Results of Monte Carlo simulations for each of the methods are given in Table 3-1. The equations used in the Monte Carlo analyses are given in Section 5.4.1.2 of Volume V.

Table 3-1
Summary of Bioaccumulation Factors for Trophic Levels 3 and 4
(mean, 5 Percent, and 95 Percent values)

Recommended	BAF_3		BAF_4		
	66,200		335,000		
Method	Field-Derived	GLWQI	BAF_3 x PPF_4[b]	Field-Derived	GLWQI
Geometric Mean	66,200	25,200	335,000	400,000	136,000
5th pctl	6,400	2,310	22,700	23,600	8,760
95th pctl	684,000	308,000	4,700,000	6,780,000	2,070,000
GSD[a]	4.14	4.41	5.05	5.59	5.25

[a] Geometric Standard Deviation
[b] Predator Prey Factor

The selection of the $BAF_3 \times (PPF_4)$ as the recommended approach was based on several considerations. Although the mean values of all three BAF_4 simulations agree within a factor of three, the GLWQI results stand somewhat apart. The mean value of 136,000 for the GLWQI method falls at the 30th and 35th percentile of the BAF_4 distributions for the field-derived and BAF × PPF methods, respectively. The GLWQI method is also more complex with more variables and assumptions than the other two approaches. The BAF × PPF and field-derived methods represent a consolidation of earlier stages of the GLWQI method and should give more accurate results than the GLWQI method provided that the data defining the distributions are at least as good as the data defining the GLWQI variables. Five studies are available for defining BAF_3; however, three of the critical variables in the GLWQI method are based on only one or two studies. In addition the field measurements for BAF_3 and PPF_4 apply directly to variables, while the bioconcentration factor (BCFs) in the GLWQI approach do not. That is, the measurements are taken directly from fish at the appropriate trophic levels for BAF_3 and PPF_4; BCF_{mHg} (the BCF for methylmercury) and BCF_{iHg} (the BCF for inorganic mercury) apply to phytoplankton (trophic level 1) but are estimated from measurements in trophic level 3 fish. The $BAF_3 \times PPF_4$ approach is also less variable than either of the other two methods, as indicated by the geometric standard deviation. Uncertainty and variability in the BAF are described in Sections 3.4.6.3, 3.4.6.8 and 3.4.6.12.

3.4.3 Other Exposure Parameters

Exposure parameters for the present analysis are shown in Table 3-2. The scientific basis for these parameters is reviewed elsewhere (U.S. EPA, 1993a, 1995a,b). For this analysis, it was assumed that prey not attributed to trophic levels 3 and 4 were derived from non-aquatic origins and do not

contain mercury. Were these prey to contain mercury, WC values calculated for the relevant species would decrease.

Table 3-2
Exposure Parameters for Mink, Otter, Kingfisher, Osprey, and Eagle

Species	Body Wt. (Wt_A) kg	Ingestion Rate (F_A) kg/day	Drinking Rate (W_A) L/day	Trophic Level of Wildlife Food Source	Percent Diet at Each Trophic Level
Mink	0.80	0.178	0.081	3	90
Otter	7.40	1.220	0.600	3,4	80,20
Kingfisher	0.15	0.075	0.017	3	100
Osprey	1.50	0.300	0.077	3	100
Eagle	4.60	0.500	0.160	3,4	74,18

3.4.4 Health Endpoint (TD)

Based on the information in Sections 3.3.1 and 3.3.2, the TDs used for calculation of a WC for mercury were these:

For avian wildlife - A LOAEL of 64 µg/kg bw/day
For mammalian wildlife - A NOAEL of 55 µg/kg bw/day

3.4.5 Calculation of Wildlife Criterion Values

WC values were calculated for each of the wildlife species of concern using exposure parameters values recommended in previous sections. UF_As were employed as recommended in the GLWQI to extrapolate from test species to the species of interest. Because the mammalian TD (NOAEL) was derived from studies with mink, the UF_A for species extrapolation of the mink WC was set equal to 1.0. Otter were considered sufficiently similar to mink so that a UF_A of 1 was also considered appropriate. A UF_S of 10 (for a subchronic study) was applied. UF_A of 3 was used for extrapolation of mallard data to the kingfisher, eagle and osprey. A UF_L of 3 was employed for use of a LOAEL in the absence of a NOAEL. Calculations of WC values for each of the selected species follow.

For the mink:

$$WC_S = \frac{(TD \times [1/(UF_A \times UF_S \times UF_L)]) \times Wt_A}{W_A + [(0.9)(F_A \times BAF_3)]}$$

$$WC_S = \frac{(0.055\ mg/kg/d \times [1/(1 \times 10 \times 1)] \times 0.8\ kg}{0.081\ L/d + [(0.9)\ (0.178\ kg/d \times 66{,}200)]}$$

$$WC_S = 415\ pg/L$$

For the otter:

$$WC_S = \frac{(TD \times [1/(UF_A \times UF_S \times UF_L)] \times Wt_A}{W_A + [\ (0.8)\ (F_A \times BAF_3) + (0.2)\ (F_A \times BAF_4)\ ]}$$

$$WC_S = \frac{(0.055\ mg/kg/d \times [1/(1 \times 10 \times 1)] \times 7.4\ kg}{0.60\ L/d + [\ (0.8)\ (1.22\ kg/d \times 66{,}200) + (0.2)\ (1.22\ kg/d \times 335{,}000)]}$$

$$WC_S = 278\ pg/L$$

For the kingfisher:

$$WC_S = \frac{(TD \times [1/(UF_A \times UF_S \times UF_L)] \times Wt_A}{W_A + [\ (1.0)\ (F_A \times BAF_3)\ ]}$$

$$WC_S = \frac{(0.064\ mg/kg/d \times [1/(3 \times 1 \times 3)] \times 0.15\ kg}{0.017 + [\ (1.0)\ (0.075 \times 66{,}200)\ ]}$$

$$WC_S = 193\ pg/L$$

For the osprey:

$$WC_S = \frac{(TD \times [1/(UF_A \times UF_S \times UF_L)] \times Wt_A}{W_A + [(1.0)\ (F_A \times BAF_3)]}$$

$$WC_S = \frac{(0.064\ mg/kg/d \times [1/(3 \times 1 \times 3)] \times 1.5\ kg}{0.077\ L/d + [(1.0)\ (0.3\ kg/d \times 66{,}200)]}$$

$$WC_S = 483\ pg/L$$

For the bald eagle:

$$WC_S = \frac{(TD \times [1/(UF_A \times UF_S \times UF_L)] \times Wt_A}{W_A + [(0.74)\ (F_A \times BAF_3) + (0.18)\ (F_A \times BAF_4]}$$

$$WC_S = \frac{(0.064\ mg/kg/d \times [1/(3 \times 1 \times 3)] \times 4.6\ kg}{0.16\ L/d + [(0.74)\ (0.5\ kg/d \times 66{,}200) + (0.18)\ (0.5\ kg/d \times 335{,}000)]}$$

$$WC_S = 538\ pg/L$$

The geometric mean of the two WC_s values calculated for mammals is 346 pg/L. The geometric mean of the three avian values is 405 pg/L. The lowest of these is the WC calculated for avian species; therefore, the WC for mercury is 346 pg/L.

The evaluation of data and calculation of WC in this Report ~~was~~ were done in accordance with the methods and assessments published in the Final Water Quality Guidance for the Great Lakes System: Final Rule (U.S. EPA, 1995). Availability of additional data led to differences in calculated values of the WC in this Report and those published in the final rule. Differences were the result of three factors. The Report uses more recent data to derive BAF. Second, the final rule appropriately used some region-specific assumptions that were not used in the nationwide assessment in the Report; for example, consumption of herring gulls by eagles. Finally different endpoints were used for the evaluation of mammals because the purposes of the assessments in the Report and final rule were different. In the final rule, a risk-management decision was made to base the wildlife criterion on endpoints likely to influence whole populations (mortality, growth). In this Report a more sensitive endpoint was selected with the goal of assessing the full range of effects of mercury. The difference in the results reflects the amount of discretion allowed under Agency Risk Assessment Guidelines.

3.5 Uncertainty Around the Dose-Response Assessments for Methylmercury

3.5.1 Uncertainty in the Wildlife Criteria

The species selected for the present analysis were chosen because they are the most exposed to methylmercury, not because of any known inherent sensitivity to methylmercury. Lacking toxicity information, little guidance is available concerning which wildlife species are likely to be the most sensitive to mercury.

A formal analysis of uncertainty around the wildlife criteria estimate was not attempted. Such an analysis would require specification of numeric distributions for each of the parameters in the equation. While theoretically possible, this approach is of questionable value because the overall analysis is intended to be protective of that subset of each species that feeds extensively at the top of aquatic food chains. Thus, incorporation of data reflecting the range of dietary items upon which the bald eagle feeds would tend to generate an extremely broad range of wildlife criteria values for this species. In addition, data for several of the parameters in the equation, in particular the NOAEL and UF estimates, are presently sufficient only to generate point estimates.

A restricted uncertainty analysis involving only incorporation of numeric distributions for each of the BAF estimates could be accomplished using existing data, but would probably not be useful. BAF distributions generated by Monte Carlo analysis of field data are thought to reflect real, naturally-derived variation in mercury bioaccumulation and biomagnification. Despite the relative abundance of such data, BAFs expressed on a total mercury basis remain difficult to interpret. Because methylmercury is the form of mercury accumulating in fish, wildlife criteria distributions based on the distribution of methylmercury BAFs are more likely to yield information of value to risk assessors.

3.5.2 Sensitivity Analysis

In a sensitivity analysis, an attempt is made to characterize the extent to which a calculated value changes with the parameters upon which it depends. Examination of the equation for calculation of wildlife criteria values suggests that a proportional relationship exists between the wildlife criterion and the NOAEL, UF or average species weight (Wt_A). The relationships between the wildlife criteria and parameters that appear in the denominator are not as apparent and must be explored by varying these parameters one-by-one in systematic fashion. The analysis is also complicated by the variable relationship that exists between fraction of diet from trophic level 3 (FD_3) and fraction of diet from trophic level 4 (FD_4). In the otter and eagle, FD_3 and FD_4 tend to be reciprocal (although in the eagle these values do not add up to 1.0). In the mink, however, FD_3 is assigned a value of less than 1.0 and the remainder of the diet is assumed to consist of prey that are not aquatic in origin and are not contaminated with mercury.

General conclusions can be reached regarding the sensitivity of wildlife criteria estimates to changes in these parameters. These can be described as follows:

(1) A decrease in any parameter that appears in the denominator will have a larger effect on the wildlife criterion than an equivalent percentage-wise increase.

(2) When BAF_3 appears alone in the denominator, a percentage-wise increase in BAF_3 or FD_3 will cause a less than proportional decrease in the wildlife criterion; conversely a

decrease in BAF_3 or FD_3 will cause a greater than proportional increase in the wildlife criterion.

(3) When both BAF_3 and BAF_4 appear in the denominator, an equivalent percentage-wise change in BAF_4 (and by extension PPF_4) has a greater impact on the wildlife criterion than a change in BAF_3, but in either case the effect is less than proportional.

(4) If BAF_3 and BAF_4 are both allowed to change (holding PPF_4 constant), a percentage-wise increase in BAF_3 (and by extension BAF_4) will have a less than proportional effect on wildlife criterion, while a decrease in BAF_3 will have a greater than proportional impact.

(5) Under all circumstances, a percentage-wise increase in F_A will cause a less than proportional decrease in wildlife criterion, while a decrease in F_A will cause a greater than proportional increase in wildlife criterion.

(6) Owing to its small contribution to the analysis as a whole, large changes in W_A have a very small impact on the wildlife criterion.

With the exception of F_A, it is not possible to conclude that for all species the wildlife criterion is most sensitive to one or the other of the parameters in the denominator of the equation. For species that feed at one trophic level, all parameters other than F_A have the potential to change wildlife criterion in a proportional or greater than proportional manner. For species that feed at two trophic levels, the BAF at the lower trophic level becomes relatively less important, but it may still have a large impact on wildlife criterion if the percentage of the diet represented by this lower trophic level is large (e.g., in the mink).

3.5.3 Uncertainties Associated with the GLWQI Methodology

Efforts to develop wildlife criteria for the protection of piscivorous wildlife are relatively recent in origin, and the methods employed for this purpose continue to undergo modification and refinement. Owing to the complexity of natural systems, uncertainties associated with the development of wildlife criteria are to be expected. Additional uncertainties derive from the relative scarcity of wildlife toxicity information and the necessity of extrapolating individual-based effects to higher levels of biological organization (e.g., populations).

Uncertainties associated with the GLWQI methodology have been reviewed elsewhere (U.S. EPA, 1994). Those areas that are especially pertinent to the development of a wildlife criterion for mercury are described below.

3.5.3.1 Limitations of the Toxicity Database

Substantial uncertainties underlie most of the toxicity data for mercury in wildlife. Comparison of NOAELs and LOAELs between species requires adoption of unproved assumptions about the uptake, distribution, elimination and toxic effects of mercury. Additional uncertainties derive from the necessity of extrapolating from LOAELs to NOAELs, and extrapolating from subchronic endpoints to chronic endpoints. In some instances there may also be a need to account for the possibility that test results do not adequately protect the most sensitive individuals. This may be

particularly germane to the case of the Florida panther, wherein there is concern for individual animals.

Existing data on wildlife populations are complicated by the possibility that "naturally incorporated" mercury is accompanied by other contaminants that are exerting some or all of the observed effect. Ideally, it is desirable to compare the effects of mercury that has been incorporated naturally with effects due to mercury that has been added to a prepared diet. By adding mercury into the diet, the researcher can better control the dose to the animal. The bioavailability of mercury in such a formulation may be very different from that which exists naturally. Charbonneau et al. (1976), however, have demonstrated that the bioavailability and toxicity of methylmercury to cats is equivalent whether given in contaminated fish or added in the diet.

Despite a lack of toxicity information and problems concerning its interpretation, NOAELs estimated for piscivorous birds and mammals are very similar (55 μg/kg for mammals versus 21 μg/kg for birds). Moreover, the existence of toxicity information for the mink eliminates the need to incorporate additional uncertainty factors into the analysis. Unfortunately, similar data for piscivorous birds do not exist.

All wildlife species of interest cannot be tested. The use of uncertainty factors for species extrapolation is likely, therefore, to continue. Existing information can be used, however, to suggest which species should be singled out for testing. Properly applied, species sensitivity factors probably represent a relatively small source of error in the calculation of wildlife criteria values.

Finally, comparisons between wildlife and human NOAELs are complicated by differences in the ability of a given study to reveal an adverse effect when it occurs. For wildlife, most of the endpoints selected can be considered severely adverse or frank effects. Very few studies to date have been designed to study subtle adverse effects or precursors to adverse effects in wildlife. Developmental neurotoxicity endpoints are of particular interest because of their demonstrated sensitivity in humans. The question arises, therefore: what would the LOAEL or NOAEL for a given wildlife species have been had the researcher been looking for (or was able to detect) these more subtle effects? One possible approach to this question is to examine the results of studies in which both frank and more subtle effects were observed and determine the corresponding difference between dosage levels.

The available data suggest that uncertainty factors presently employed to derive chronic reference doses for birds and mammals are unlikely to be greatly underprotective or overprotective, and are, therefore, reasonable.

3.5.3.2 LOAEL-to-NOAEL Uncertainty Factor UF_L

In determining the wildlife criteria for mercury exposure in wildlife, a NOAEL is preferred as the value to be used as the term TD. The wildlife criterion can be considered a wildlife WC with an adjustment for exposure assumptions. As is the case for human health RfDs, the wildlife WC is an attempt to estimate a threshold dose for adverse effects and then to determine a level below that threshold dose. It is assumed that daily consumption of an amount of material below the threshold for adverse effects should be without ill effect.

In cases in which studies do not identify a NOAEL, the data are examined to identify a LOAEL to be used in estimating the WC. A UF_L of 3 or 10 (based on U.S. EPA Reference Dose methodology) is typically applied when a LOAEL is used in the absence of a NOAEL.

In determining the RfD for human exposure to methylmercury, a large number of laboratory animal studies on methylmercury toxicity were summarized as supporting data. Results from many of those studies permitted estimation of both a LOAEL and a NOAEL. Those studies were examined in an effort to determine the most appropriate UF_L for wildlife exposure to mercury. Details of this analysis can be found in Section 4.5.2 of Volume V.

The ratios of LOAEL to NOAELs for laboratory animal studies were plotted versus frequency. These ratios can be thought of as the reduction in the LOAEL necessary to estimate the corresponding NOAEL. The majority of ratios lie between one and two (n=6) and between four and five (n=9). Only one ratio of the 19 was greater than 10. A ratio of five indicates that the NOAEL observed following exposure to methylmercury is five-fold less than the corresponding LOAEL. These data imply that most ratios between LOAELs and their corresponding NOAELs will be less than 10.

A similar analysis of animal toxicity data (Weil and McCollister, 1963) was provided by Dourson and Stara (1983). None of the LOAEL-to-NOAEL ratios from studies of 52 chemical substances exceeded 10. Only two of the 52 ratios exceeded five. The Dourson and Stara (1983) analysis has been cited in support of the use of a variable UF_L of as much as 10 in deriving reference doses for humans. Dourson and Stara (1983) recommended the application of a relatively large UF_L when estimating a NOAEL from a LOAEL for a severe or frank toxicological effect. Conversely, a low UF could be applied when the toxicological effect was considered to be relatively mild.

The UF_L of three was selected by the authors of this Report for use with the avian LOAEL from the same data (Heinz, 1975, 1976, 1979) as a reasonable compromise between UF ratios of two and five.

3.5.3.3 Validity of BCF/BAF Paradigm

The wildlife criteria for mercury calculated in the GLWQI relied on bioconcentration factors (BCF) values determined from laboratory data. This methodology is based on a bioaccumulation paradigm (steady-state BCF x FCM) that was developed for neutral hydrophobic organic compounds and that may be inappropriate for application to mercury.

Field studies indicate that many fish, if not most, accumulate mercury throughout their lives, often in a nearly linear fashion with age. Moreover, most of the mercury accumulated by fish at trophic levels 3 and 4 is thought to be taken up from dietary sources. Thus, particularly for long-lived piscivorous fish, a relatively short (one year or less) waterborne exposure cannot duplicate the extent of accumulation that takes place in nature. In addition, the relationship between a concentration of an applied mercury species in the laboratory and the concentrations of multiple species present in the environment (some of which may not be bioavailable) is completely unknown.

The apparent progress to "steady-state" observed in several chronic laboratory studies (see McKim et al., 1976) should not be misinterpreted as an actual steady-state condition, but instead probably reflects growth dilution with rapidly growing fish. Such growth dilution will tend to depress BCF values during the period of rapid growth, but as the growth rate slows continued accumulation of mercury would result in an increase in whole-body concentration with age.

BAF values for trophic levels 3 and 4 were estimated using field residue data. Uncertainties remain, however, with respect to the naturally-derived variability that exists around these estimates. A growing body of information suggests that much of this variability can be attributed to site-specific factors that control the net rate of mercury methylation, but numerous additional factors may influence the extent to which mercury accumulates and biomagnifies in aquatic food webs.

3.5.3.4 Selection of Species of Concern

The species identified for the present analysis were selected because they were considered likely to be exposed not because of their inherent sensitivity to mercury. Lacking toxicity information, little guidance is available concerning which wildlife species are most sensitive to mercury. In addition, there are problems associated with any comparison of laboratory and field data. Such comparisons, however, are complicated by the presence/absence of additional stressors such as confinement, handling, and weather, differences between natural and prepared diets, and the interplay between "inherited" (egg) residues and that which the chick consumes. Toxicity can be difficult to observe in a field study, even when it is occurring, due to any number of factors.

Exposure and sensitivity are related. If a species was 10 times more sensitive than the eagle on a delivered dose basis, but because of its dietary habits received less than 10 percent of the dose, it would not be expected to show adverse effects at water concentrations protective of the eagle. Pharmacokinetic considerations may also be important. Thus, it has been suggested that birds eliminate a substantial amount of mercury through incorporation into plumage. The frequency and extent to which birds molt may, therefore, impact their apparent sensitivity in an environmental setting. It has also been suggested that some birds and mammals demethylate, or otherwise eliminate mercury by some route other than in hair or plumage (Wren et al., 1976). Enhanced elimination would be particularly important if it represented an adaptive strategy for piscivorous species. The need for toxicity information has already been noted. As such information becomes available it may be necessary to revise the wildlife criteria for mercury.

There is a need also to consider animals other than birds and mammals. In particular, there is a need to characterize the exposure of carnivorous reptiles such as the alligator, which is known to consume considerable quantities of fish and which also feeds on piscivorous animals (e.g., raccoon) that are known to accumulate mercury (Roelke et al., 1991).

3.5.3.5 Trophic Levels at Which Wildlife Feed

It can be expected that representatives of the same species will be exposed to different levels of mercury due to different feeding habits and/or differences in the availability of specific prey items. For example, bald eagles living on the shores of the Great Lakes may consume significant numbers of herring gulls (Kozie and Anderson, 1991). Since the gulls themselves are piscivores, feeding primarily at trophic level 3, it has been argued that when an eagle consumes a gull it is feeding at trophic level 4 or higher. Eagles living in other parts of the country, or migrating into an area during a particular time of year, may consume relatively few fish, feeding instead on carrion, including rabbits, squirrels, and dead domestic livestock such as pigs and chickens (Harper et al., 1988). Other populations, however, are critically dependent upon the seasonal availability of fish, particularly spawning salmonids.

For some species, such as the kingfisher and river otter, it can be reasonably assumed that fish always comprise a high percentage of the diet. For others, such as the eagle and mink,

considerable variations in diet are likely to exist. Still others, such as the Florida panther, consume prey (e.g., the raccoon) that, as a species, consume variable amounts of aquatic biota, but are thought to represent a close link to the aquatic food chain in South Florida.

3.5.3.6 Variability in BAFs at Each Trophic Level

A concern related to the issue of feeding preference is the possibility that trophic levels presently assigned to the wildlife species in this analysis overestimate the actual extent to which they are exposed to mercury. This is because BAFs are developed to represent the average value for a trophic level, when in fact piscivorous birds and mammals are more likely to target prey at the lower end of the size (age) distribution. Thus, eagles are more likely to consume a 1 kg northern pike than a 10 kg individual, yet both are represented in the BAF for trophic level 4. Similarly, kingfishers are probably limited to smaller representatives of trophic level 3 than would be true of an osprey. The reason that these differences are important is that mercury tends to accumulate throughout the life of an individual fish with the result that concentrations in an older individual at a given trophic level may far exceed those in a younger individual.

3.5.3.7 Natural History Considerations

Natural exposures are likely to vary in both spatial and temporal domains. This is particularly true of species that migrate, including the bald eagle, osprey and belted kingfisher. The necessity of incorporating this type of information and the means by which this can be accomplished are open questions.

3.5.3.8 Individuals Versus Populations

The methods used to develop wildlife criteria for mercury are based on effects data from individual organisms. The stated assessment endpoint for this analysis, however, is the health of wildlife populations. The relationship between individuals and populations is likely to vary with the species and a large number of environmental factors (e.g., availability of food in a given breeding season). For a given population, the loss of a significant number of individuals may have little effect, particularly if environmental factors (like carrying capacity) limit population size. For other populations, in particular those with low fecundity, loss of a relatively few individuals could have a large impact. Clearly, there is a need to be able to extrapolate toxic effects on individuals to effects on populations. Unfortunately, this type of analysis is complicated by numerous factors (such as relationship of one population to other populations) and is essentially impossible to apply on a national scale.

Finally, a focus on populations may not always be appropriate, particularly when endangered species are involved. The same may also be true when various factors contribute to the possibility of regional effects. For example, 95 percent of eagles nationwide might be protected by a wildlife criterion for avian species, but in a given region mortality could approach 100 percent if low pH of surface waters contribute to higher than average accumulation of mercury in the aquatic food chain.

3.5.3.9 Species Versus Taxa

The wildlife criterion developed for mercury in birds was calculated as the geometric mean of values for three species. Similarly, the geometric mean of values for two species was used to represent all mammals. This approach is reasonable if the wildlife criteria calculated for each species

within a taxa are similar, but would fail to protect species for which the wildlife criterion value is much lower than the others with which it was averaged. In the latter case, averaging would effectively lead to protection to <100 percent of all species.

In the present analysis, wildlife criteria values calculated for eagles, osprey and kingfisher were within a factor of three of one another. Wildlife criteria values for mink and otter agreed within a factor of about two. As additional data are gathered, there is a need to identify species that, by virtue of sensitivity and/or exposure, are particularly vulnerable to mercury. Decisions could then be made concerning the advisability of special measures to ensure their protection.

3.5.3.10 Discussion of Uncertainties Associated with the GLWQI Methodology

The existing limited data suggest that BAF values represent the most important source of uncertainty in present efforts to calculate water-based wildlife criteria values, although a lack of toxicity information and incomplete knowledge of what wildlife eat also contribute substantially to uncertainty. Considerable progress has been made in understanding and predicting how lake water characteristics (e.g., pH, temperature, dissolved organic carbon) affect methylation rates, and in time it may be possible to adjust BAF predictions as needed to represent surface waters of concern. The prospect for continuing uncertainty surrounding these estimates argues, however, for adoption of a residue-based approach, that is, the use of measured mercury residues in fish and wildlife to identify populations at risk.

It is important to recognize that BAF values are calculated as the ratio of a tissue concentration and a water concentration. Emphasis has been placed on problems associated with obtaining the numerator in this equation. Considerable uncertainty, however, also exists with respect to the denominator. In several instances it has been shown that with improved analytical methods, mercury levels in a given water body tend to come "down", resulting in an increase in the apparent BAF. This "decline" is usually not thought to be real but instead reflects improvements in sampling technique and analytical methods.

It is also unclear which of the mercury species are bioaccumulative and should, therefore, appear in the denominator. Presently, the denominator in most studies consists of total amount of mercury in filtered water. It is more likely that there may be multiple "pools" of mercury, each of which is bioavailable to varying degrees. In this regard it is important to realize that even in highly polluted systems >99 percent of all methylmercury is complexed, either in biomass, or with dissolved organic material, particulate material and sediments.

An effort was made to treat the uncertainty in BAF estimates by using a Monte Carlo simulation approach. The advantage of this approach is that it explicitly treats known variation in these parameters thereby providing for the statistical possibility of a high or low end result. In addition, the distributions themselves follow from the processes at work. As more information about mercury is obtained, the distributions can be improved. One example of this relationship has already been discussed, namely, the fact that a skewed BAF distribution for trophic level 4 would tend to follow from random sampling of a fish population due to the relative scarcity of the oldest individuals.

4. CHARACTERIZATION OF MERCURY EXPOSURE OF SELECTED HUMAN AND WILDLIFE POPULATIONS

Exposure of human or wildlife populations to methylmercury may be estimated from the results of modeling or from interpretation of survey and monitoring data. In this Report both approaches have been utilized. Modeling permitted estimation of environmental mercury concentrations and exposures that resulted from anthropogenic sources. Use of dietary survey data combined with measured mercury concentrations in fish were used to estimate exposures to methylmercury to the general United States population and selected subpopulations. For piscivorous wildlife, data on mercury concentrations in fish tissues have been used to estimate the magnitude of mercury exposures to these species.

4.1 The Modeling Analysis

The exposure assessment conducted for this Report examined mercury exposure through two different approaches. The first approach addressed, through the use of models, the atmospheric fate and transport and the exposures that result from atmospheric mercury emissions of selected stationary anthropogenic combustion and manufacturing sources: municipal waste combustors (MWC), medical waste incinerators (MWI), coal- and oil-fired utility boilers, chlor-alkali plants (CAP), primary lead smelters and primary copper smelters. The second approach estimated the current exposures to the general U.S. population that may result from methylmercury concentrations in freshwater and marine fish. This was done through the use of fish consumption surveys and central tendency estimates of chemically-measured methylmercury concentrations in fish.

4.1.1 Study Design of the Modeling Analysis

The fate, transport and exposure modeling of mercury was presented in Chapters 4, 5 and 6 of Volume III, an Assessment of Exposure from Anthropogenic Mercury emissions in the United States. The primary differences in these modeling exercises are the sources of the mercury concentrations in the atmosphere and soil and the mercury deposition rate. In each instance the fate and transport of deposited mercury was modeled for the same two hypothetical sites; that is a Western and an Eastern site. Three different settings were overlayed on each site; rural (agricultural), lacustrine (or water body) and an urban setting. These were selected because of the variety they provide (and to mimic exposure situations likely to be found in the U.S.). Three different hypothetical humans were assumed to reside in each setting (total number was nine). Five hypothetical piscivorous wildlife species (described in the preceding chapter) were also assumed to inhabit the lacustrine setting.

Chapter 4 of Volume III utilized measured atmospheric and soil concentrations and a measured deposition rate as inputs to the aquatic and terrestrial fate, transport, and exposure models (IEM2) at the hypothetical Western and Eastern U.S. sites. See Figure 4-1 for an overview of this modeling effort.

In Chapter 5 of Volume III, modeled estimates were used as inputs. These were the 50th and 90th percentiles of the atmospheric mercury concentrations and the deposition rates that were predicted by the RELMAP model for the Eastern and Western halves of the U.S. These estimates served as inputs to the aquatic and terrestrial fate, transport, and exposure models (IEM2) at the hypothetical Western and Eastern U.S. sites. Additionally, the environmental fate of mercury at a hypothetical site in the Eastern U.S. that is distant from anthropogenic emissions sources was also modeled. See Figure 4-2 for an overview of this modeling effort.

Figure 4-1
Fate and Transport Models Used and Exposure Routes Considered to Examine Exposure Predictions Using Measured Environmental Concentrations

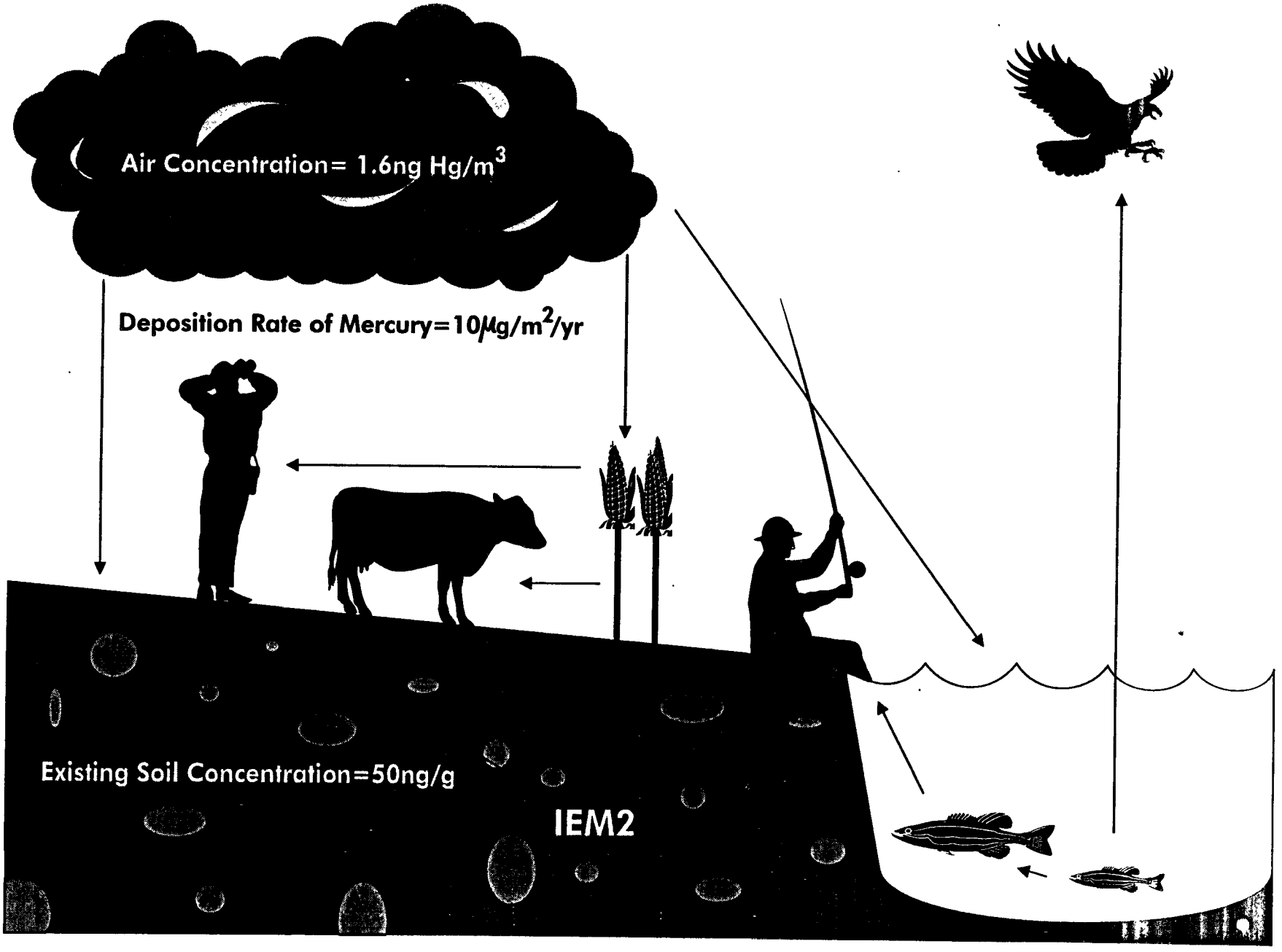
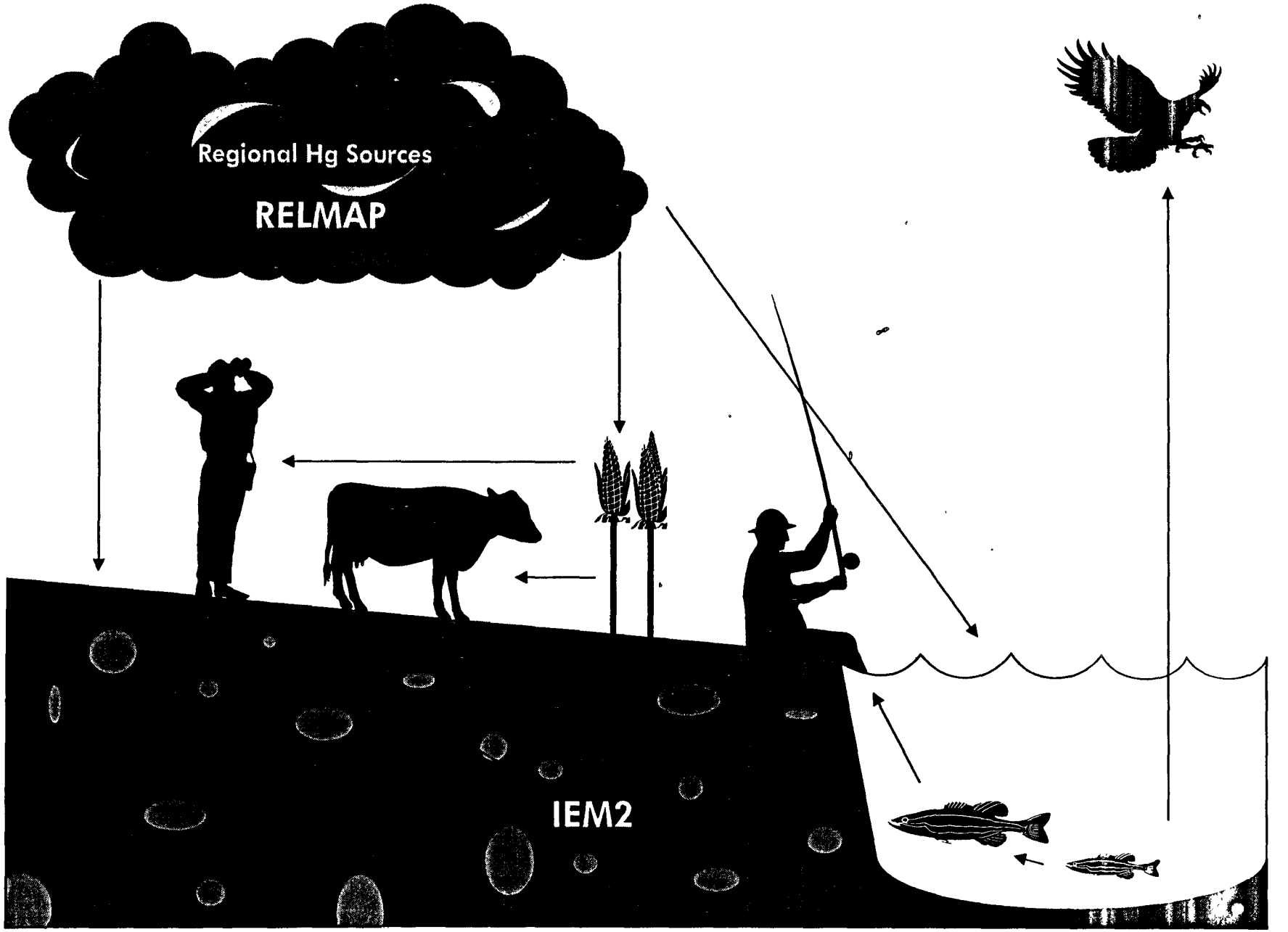


Figure 4-2
Fate, Transport and Exposure Modeling Conducted in the Long Range Transport Analysis



Two separate modeling analyses were conducted for Chapter 6 of Volume III. In the first analysis (Figure 4-3), hypothetical emission sources, or model plants, were developed to represent major anthropogenic combustion and manufacturing sources: municipal waste combustors (MWC), medical waste incinerators (MWI), coal- and oil-fired utility boilers, chlor-alkali plants (CAP), primary lead smelters and primary copper smelters. The atmospheric fate and transport of the mercury emissions from these representative model plants were modeled to determine local mercury deposition using the COMPDEP model. The predicted mercury air concentrations and deposition rates that resulted from individual model plants at 2.5, 10, and 25 kilometers from the source were used as inputs to the aquatic and terrestrial fate, transport, and exposure models (IEM2) at the hypothetical Western and Eastern U.S. sites.

The second modeling analysis in Chapter 6 of Volume III (Figure 4-4) added the predictions of the COMPDEP model for the area around the individual model plants to the hypothetical Western and Eastern locations to either the 50th or 90th percentile predictions of the RELMAP model for the Western or Eastern sites, respectively. These combined model predictions were used as inputs to the aquatic and terrestrial fate, transport, and exposure models (IEM2) at the hypothetical Western and Eastern U.S. sites.

Because of the hypothetical nature of both the individual humans and the sites that were considered, estimates of exposures to mercury resulting from the consumption of nonlocal fish, from occupation or from background sources were not added to the exposure estimates developed in Chapter 6 of Volume III. These sources of mercury exposure may be significant, and for a site-specific assessment it may be appropriate to consider these for members of an exposed subpopulation.

For each modeling analysis listed above, the same two hypothetical sites were used. One site was located in the Eastern U.S. and the other in the Western U.S. The primary differences between the two hypothetical locations were the assumed erosion characteristics for the watershed and the amount of dilution flow from the water body. The eastern site was defined to have steeper terrain in the watershed than the western site. Both sites were assumed to have flat terrain for purposes of the air modeling.

For each modeling analysis at both hypothetical sites, the fate of deposited mercury was examined in three different settings: rural (agricultural), lacustrine (or around a water body), and urban. The primary differences between the urban and rural settings were the three hypothetical humans assumed to inhabit each. In addition to three different hypothetical human inhabitants, the lacustrine setting included the modeling of a circular drainage lake with a diameter of 1.68 Km, average depth of 5 m, and a 2 cm benthic sediment depth. The ratio for the watershed area to surface water area was 15 to 1; the watershed area was 33 Km^2. Piscivorous wildlife species were also assumed to inhabit the lacustrine setting. The wildlife species considered were: mink, otter, bald eagle, osprey and kingfisher; all were assumed to consume fish from the hypothetical lake in this setting.

As noted previously, hypothetical humans were developed to represent several specific subpopulations expected to have both typical and higher exposure levels. These individuals were assumed to inhabit each setting. The high-end rural scenario consisted of a subsistence farmer and child who consumed elevated levels of locally grown food products. The subsistence farmer was assumed to raise livestock and to consume home-grown animal tissue and animal products, including chickens and eggs as well as beef and dairy cattle. It was also assumed that the subsistence farmer collected rainwater in cisterns for drinking. The hypothetical individual used in the average rural scenario was assumed to derive some of his food from a small garden.

Figure 4-3
Fate, Transport and Exposure Modeling Conducted in the Local Impact Analysis

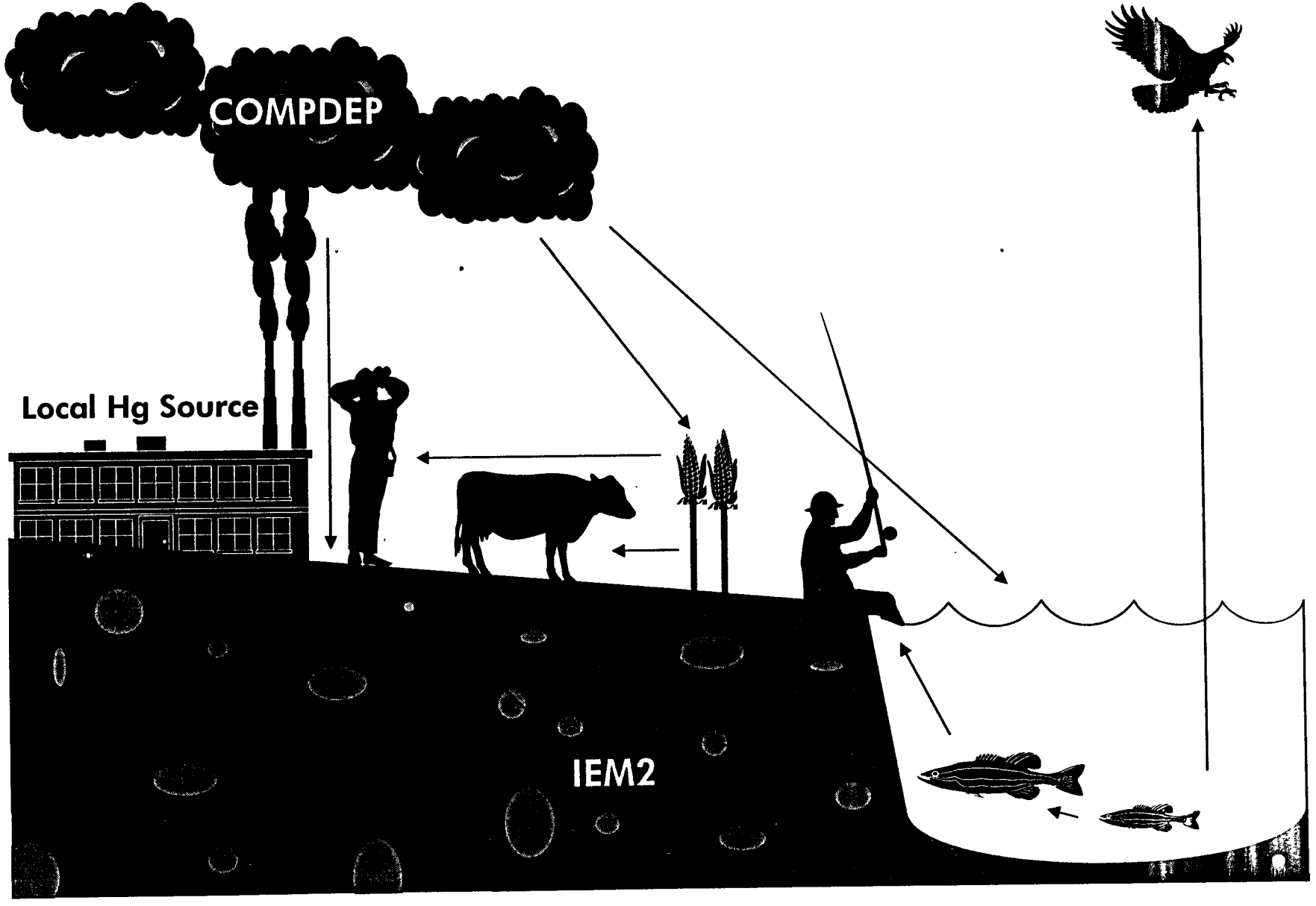
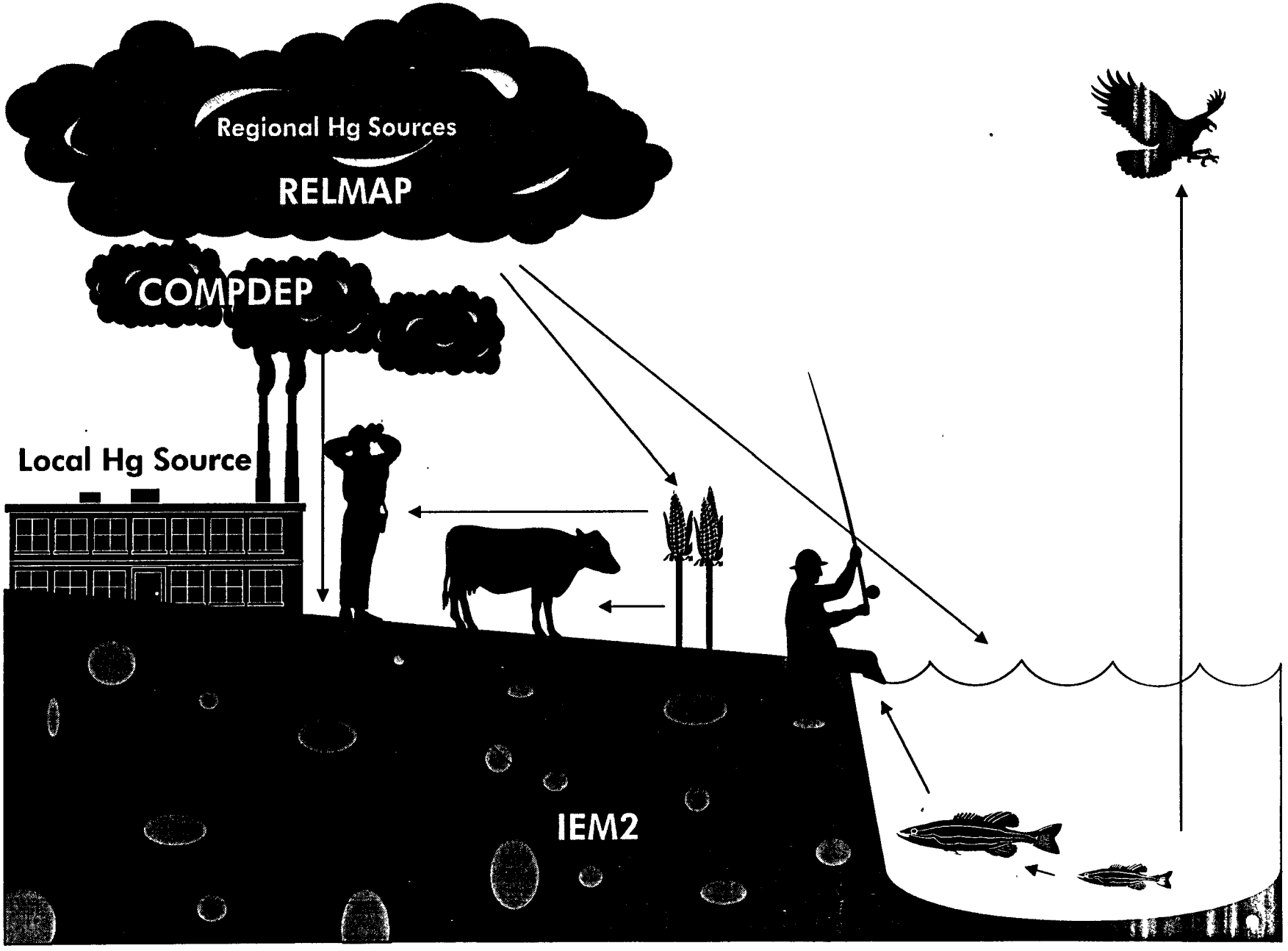


Figure 4-4
Fate, Transport and Exposure Modeling Conducted in the Combined COMPDEP and RELMAP Local Impact Analysis



In the urban high-end scenario, an adult was assumed to derive some food from a small garden similar in size to that of the average rural scenario. To address the fact that home-grown fruits and vegetables generally make up a smaller portion of the diet in urban areas, the contact fractions were based on weight ratios of home-grown to total fruits and vegetables consumed for city households. The high-end urban scenario included a pica child. The average urban scenario consisted of an adult who worked outside of the local area. The exposure duration for inhalation of the average adult, therefore, was only 16 hours a day compared to the 24 hours a day for the rural scenario and high-end urban scenario. The only other pathway (i.e., noninhalation) considered for this scenario was ingestion of average levels of soil.

Three fish-consumption scenarios for humans were considered for the lacustrine setting. For the adult high-end fish consumer scenario (or subsistence fisher), an individual was assumed to ingest large amounts of locally-caught fish, to eat home-grown garden produce (plant ingestion parameters identical to the rural home gardener scenario), to consume drinking water from the affected water body and to inhale the air on a 24-hour basis. A child of a high-end local fish consumer was assumed to ingest local fish, local garden produce, and soil as well as to inhale the affected air. The exposure pathways considered for recreational angler scenario, evaluated only fish ingestion, inhalation, and soil ingestion. These consumption scenarios were thought to represent identified fish-consuming subpopulations in the United States.

Piscivorous birds and mammals were also assumed to inhabit areas adjacent to the hypothetical lakes considered. The piscivorous animals were exposed to be mercury only through the consumption of fish from the lake. The five wildlife species were not selected because they were more sensitive to methylmercury exposure than other wildlife, but rather on the basis of exposure. Fish-consuming species were, thus, the only groups considered in this assessment. All five wildlife species were assumed to consume fish from trophic levels 3 and/or 4 and to inhabit the aquatic environment modeled for a lifetime. Mercury concentrations in food sources other than fish and migratory behaviors were not considered.

4.1.2 Uncertainties and Defaults Used in Exposure Modeling

The exposure analysis relied heavily on the modeling of the fate and transport of emitted mercury because no monitoring data have been identified that conclusively demonstrate or refute a relationship between any of the individual anthropogenic sources in the emissions inventory and increased mercury concentrations in environmental media or biota. To determine if there is a connection between the above sources and increased environmental mercury concentrations, three models were utilized to address many major scientific uncertainties.

(1) The RELMAP model was used to predict average annual atmospheric mercury concentrations as well as wet and dry deposition flux for 40 Km^2 grids across the continental U.S. The model predictions were based on anthropogenic emissions from the sources described in Volume II, Inventory of Anthropogenic Mercury Emissions in the United States.

(2) The COMPDEP model was used to predict average annual atmospheric mercury concentrations as well as the wet and dry deposition resulting from emissions within 50 Km of a single source.

(3) The Indirect Exposure Models (IEM2) was used to predict environmental concentrations and the exposures that result from atmospheric mercury concentrations and deposition.

Volume III and the appendices describe at length the justification for choices of values for model parameters; for example the size of combustors, the stack heights, amount of precipitation, adult body weight and the amount and types of foods consumed. In this section of the Risk Characterization, several of the major areas of uncertainty are highlighted without reiteration of the entire list of parameter justifications generated in Volume III. Obviously, when models are utilized there is an associated uncertainty.

4.1.2.1 Emissions Uncertainties

The degree of uncertainty in the emission rates varies for each hypothetical emission source (model plant). This uncertainty is reflected in the qualitative characterization of the potential human health and ecological risks.

Physical characteristics of anthropogenic emission sources vary. There is general understanding of how these variations of physical characteristics affect dispersion of emitted mercury. The following characteristics affect mercury emission rates, mercury speciation and mercury transport/deposition rates: stack height, stack diameter, exit gas velocity, stack gas temperature, plant capacity factor (relative average operating hours per year), stack mercury concentration, and mercury speciation. In the exposure analysis the physical characteristics that were predicted to have the greatest impact on the modeling of atmospheric transport of mercury were chemical species of mercury emitted, exit gas velocity and stack height.

There is substantial variation in the mercury content of the feed mixes that enter combustors. Emissions of mercury (including the divalent mercury species, and elemental mercury in various speciation percentages) are influenced by the type of fuel used (e.g., coal, oil, municipal waste), flue gas cleaning and operating temperatures. To the extent that these factors vary in a facility, chemical characteristics of mercury emissions will vary. Consequently, the exit stream can vary from nearly all elemental mercury to nearly all divalent mercury, contributing to the variability in fate and transport of mercury.

The chemical species released from anthropogenic sources is expected to determine the atmospheric fate and transport characteristics of the emissions. Modeling of the exact chemical species (e.g., $HgCl_2$, $Hg(OH)_2$) was not attempted. It is possible to break the divalent mercury species down further as, for example, reactive, non-reactive, or particle-bound. This was infrequently measured for the sources considered, which contributes to both variability and uncertainty in the results of the atmospheric modeling. Determining the concentration and speciation of mercury in stack emissions is also complicated by sampling difficulties related to identification of the chemical species in the emitted gas. Sampling procedures may alter the physical characteristics of the emitted mercury. To the extent that the chemical species are uncertain and variable, the predictions of atmospheric fate and transport are uncertain and variable.

4.1.2.2 Atmospheric Reactions of Emitted Mercury

Atmospheric chemistry data for mercury are incomplete. Some atmospheric reactions of mercury, such as the oxidation of elemental mercury to divalent mercury in cloud water droplets have been reported and have been incorporated into the modeling. Other chemical reactions in the

atmosphere such as those which may reduce divalent species to elemental mercury or processes by which mercury attaches to atmospheric particulates have not been adequately reported or modeled.

There is inadequate information on the atmospheric processes which affect wet and dry deposition of mercury. Atmospheric particulate forms and divalent species of mercury are thought to wet and dry deposit more rapidly than elemental mercury; however, the relative rates of deposition are uncertain.

4.1.2.3 Deposition of Atmospheric Mercury

Based on experimental data, divalent mercury and particulate-bound mercury will deposit on land. The deposition velocity of mercury may differ with chemical species and conditions of land use patterns. The deposition velocity for atmospheric mercury over soil and over water is very poorly defined. The following gaps in information result in uncertainties in this risk characterization.

- There is a lack of adequate emission data for various sources, including natural sources. This includes emissions data on the amounts of various forms of mercury that may be emitted from stacks.

- Emissions of particulates from various combustion sources depend on these factors:

  -- Type of furnace and design of combustion chamber,
  -- Composition of feed/fuel;
  -- Particular matter removal efficiency and design of air pollution control Equipment; and
  -- Amount of air in excess of stoichiometric amount that is used to sustain temperature of combustion.

These conditions are highly variable in actual operation of specific incinerators. Consequently, emission of mercury and particulates is highly variable.

- There is a lack of information on the effect of atmospheric transformation processes on wet and dry deposition; for example, how deposition is affected by the transformation of elemental mercury to divalent mercury, or vice versa.

- There is no validated air pollution model that estimates local wet and dry deposition of an emitted gas (such as elemental mercury).

- There is a lack of data on methylation processes in water bodies; thus, assumptions related to this transformation of mercury must be made in modeling.

- There is a lack of data on the transfer of mercury between environmental and biological compartments (e.g., uptake of mercury into aquatic organisms).

The parameters exerting the most influence on the exposure assessment are these:

- Total mercury emission rate (grams/second);
- Assumption regarding speciation of the total mercury;
- Vapor/particle phase partition estimate;
- Stack height for the plant; and

- Exit gas velocity.

4.1.2.4 Mercury Concentrations in Water and Aquatic Biota

Available measured mercury concentrations in water, soil and fish near anthropogenic mercury emissions sources do not consistently indicate local deposition of mercury around a point source. These observations raise questions with respect to uncertainty in the models used to estimate indirect exposures to mercury.

A bioaccumulation factor (BAF) was used in the estimation of mercury concentrations in fish as a consequence of mercury in the water body. Discussion of the BAF derivation is in Section 2.7.2.3 of Volume V. Determination of an appropriate BAF relies on analyses of mercury in water and mercury in fish. There is a major limitation on the analytical quality (detection limits, contamination control, chemical speciation) for mercury in both water and in fish. This makes estimation of the bioaccumulation factor uncertain.

Transport to water bodies from watersheds varies with local soil conditions including extent of erosion, run-off and the soil-water partition of mercury. Likewise transport of various species of mercury within water bodies is highly variable. These chemical species of mercury may be bound to suspended soil/humus or attached to dissolved organic carbon. These local conditions are highly variable and poorly documented. Removal of divalent mercury and methylmercury from the groundwater into upper soil layers is poorly characterized. There are likely to be concentration-dependent differences in the distribution of mercury between the donating and receiving water bodies and between water and soil. Within the water bodies, the species of mercury is expected to be concentration-dependent.

Data indicate that 25-60 percent of divalent mercury and methylmercury organic complexes in the water column are particle-bound. This variation in the fraction of mercury that is bound to particles influences the fate and transport of environmental mercury.

The bioaccumulation of methylmercury from the environment differs for plants and animals in the terrestrial food chain and fish/fish-eating mammals in the aquatic food chain. For example, the total mercury concentrations in fish are often 100 to 1,000 times greater than in terrestrial mammalian tissue (meat). Most of the mercury in meat is not likely to be methylmercury, in contrast to fish in which nearly 100 percent of the mercury is methylmercury. Depending on the type of diet chosen (e.g., fraction of total caloric intake from fish or fish-eating mammals), the methylmercury content of the diet will vary greatly.

4.1.2.5 Mercury Accumulation in Fish

Mercury accumulation in fish was modeled using bioaccumulation factors (BAF) and predator-prey factors (PPF) at the higher trophic levels. The BAF paradigm was modified from methodology developed in the Great Lakes Water Quality Initiative. BAFs were calculated for trophic levels 3 and 4; that is, for small fish and for larger predatory fish.

Field studies indicate that many, if not most fish, accumulate mercury throughout their lives, often in a nearly linear fashion with age (see for example: Scott and Armstrong, 1972; MacCrimmon et al., 1983; Wren et al., 1983; Mathers and Johnansen, 1985: Skurdal et al., 1984; Wren and MacCrimmon, 1986; Sorenson et al., 1990; Jackson, 1991; Gutenmann et al., 1992; Glass et al., 1993; Suchanek, 1993; Lange et al., 1993). The bioaccumulation factor depends on the age of the fish.

Differences in the age (and consequently the size) of fish consumed by either wildlife or humans are a major source of variability in the bioaccumulation factor.

Methylmercury as a percentage of total mercury present in the bodies of aquatic organisms appears to decrease with decreasing trophic level. Organisms at trophic levels 1 and 2 are, in general, short-lived and do not have the opportunity to accumulate mercury for periods lasting many years. As mercury is transferred up the food chain there appears to be a progressive enrichment of the most bioaccumulative form, methylmercury.

Most of the mercury accumulated by fish at trophic level 4 is thought to be taken up from dietary sources. Thus, particularly for long-lived piscivorous fish, a relatively short (one year or less) waterborne exposure will not duplicate the extent of accumulation that takes place over a longer period of time.

A probabilistic Monte Carlo simulation approach was used for the estimation of BAFs; this is described in Appendix A to Volume V. This approach was taken to allow explicit quantitative expression of the overall variability surrounding the various estimates of the BAFs. This analysis was also done to determine the relative sensitivity of the estimates to specific individual variables. The distributions were based on data from field studies which measured mercury concentrations in fish at trophic levels 3 and 4.

Because of the large variance in the BAF distributions, it is most appropriate to apply BAFs derived from valid data collected at the site of concern. The geometric mean values of the BAF distributions were used for this exposure assessment rather than the upper or lower percentiles. The values based on the probabilistic simulations were 66,200 and 335,000 for the BAF for trophic level three (BAF_3) and the BAF for trophic level four (BAF_4), respectively.

There is uncertainty as to whether a single BAF value is appropriate for derivation of water concentrations when the fish size range of the fish-consuming populations is known. For example, kingfishers feed on smaller fish while human recreational anglers primarily consume large fish. This is handled in the exposure assessment by assigning a portion of the total fish consumed to either trophic level 3 or 4. For example, only BAF_3 is used in estimating king fisher mercury exposure.

4.2 Estimates of Methylmercury Exposure Based on Monitoring Data, Dietary Surveys and Mercury Residue Data

4.2.1 Non-Human Mammalian Species Exposures to Methylmercury

Mink (*Mustela vison*) and otter (*Lutra canadensis*) occupy top trophic positions in the aquatic foodweb and bioaccumulate mercury from food. The diet of mink varies with location, time of year, and available prey. Mink consume fish, small animals, crayfish, birds, and amphibians (Linscombe et al., 1982). Otters, by contrast, are much more consistently fish eaters whose diet consists of at least 95 percent fish (Toweill and Tabor, 1982). For both otter and mink, the mercury concentrations in these animals' tissues have been positively associated with mercury levels in prey (for example; fish, shellfish, crayfish) (Wren and Stokes, 1986; Foley et al., 1988; Langlois and Langis, 1995). Mink and otter accumulated about 10 times more mercury on a concentration basis than did predatory fishes from the same drainage areas (Kucera, 1983). These correlations were statistically significant (Foley et al., 1988) on the basis of mercury in the watershed because of the importance of fish, shellfish and crayfish to the minks' and otters' diets.

Case reports of clinical mercury poisoning exist for wild mink (Wobeser and Swift, 1976) and otter (Wren, 1985). Such reports are rare, but this would be expected given the rapid onset of symptomatology of methylmercury poisoning, and assuming that the wild mink exhibit the same progression of signs and symptoms observed in a laboratory setting. Under the experimental situation established by Wobeser (1973), the minks' conditions deteriorated from anorexia and ataxia to death within two or three days at exposures producing liver mercury concentrations in excess of approximately 20 μg/g. The short time-period between onset of gross signs and symptoms of methylmercury intoxication and death decreases the likelihood of observing in the wild clinically ill mink prior to death. Consequently assessment of mercury exposure to wildlife has been based on mercury concentrations in body organs such as liver, kidney and brain rather than an observation of gross clinical symptamology. The magnitude of the concentration in one organ for both mink and otter (for example, liver) is highly correlated with other organs (for example, kidney or brain); see reports of Wobeser (1973), Kucera (1983), Wren and Stokes (1986). Usually mercury concentrations in liver are used for comparison across studies.

Liver mercury concentrations in the range of 20 to 25 μg/gram fresh weight were associated with severe, clinically evident mercury poisoning in mink fed 1.8 μg/gram methylmercury in diet (Wobeser, 1973). Among animals that died during the experimental period, liver mercury concentrations averaged above approximately 25 μg/gram fresh weight (Wobeser, 1973). Using mink and otter trapped by fur traders or trappers, mercury concentrations have been reported for Quebec (Langlois and Langis, 1995), Ontario (Wren et al., 1986), Manitoba (Kucera, 1983), New York State (Foley et al., 1988); and Georgia (Halbrook et al., 1994). The range of concentrations reported in different geographic locations is substantial. Wild mink with liver mercury concentration as high as 20 μg/g were identified in northern Quebec (Langlois and Langis, 1995).

There are substantial region-to-region differences in mercury concentrations in tissues of mink and otters. There are also differences among individual animals trapped in a particular location. Consequently broad generalizations are difficult regarding how close liver mercury concentrations of wildlife are to liver mercury concentrations of experimentally poisoned mink. However, the upper range of liver mercury concentrations of mink from northern Quebec (Langlois and Langis, 1995), otters from Georgia (Hallbrook et al., 1994) and otters from Ontario (Wren et al., 1986) approximate those of clinically poisoned animals. Based on these reports, methylmercury poisoning sufficiently severe to be fatal to mink and otters can be projected at current mercury exposures in some geographic locations.

Sublethal effects on mink and otters can be projected to be more wide-spread with additional reports showing average liver mercury concentrations approximately one-third of those in moribund mink with experimental methylmercury poisoning. For example, in some geographic areas, average concentrations are about one-third those of mink with clinical mercury poisoning in a laboratory situation. Liver mercury concentrations of river otters from the lower coastal plain in Geogria averaged 7.5 μg/g (Hallbrook et al., 1994); this is approximately 33 percent of the concentrations associated with severe intoxication and/or death in a closely related specie, the mink (Wobeser et al., 1976a,b). In many geographic regions [e.g. Georgia (Halbrook et al., 1994), New York State (Foley et al., 1988)], mercury concentrations in mink and otters' tissues are 10 to 30 percent of concentrations associated with severe, clinically evident methylmercury poisoning in mink.

Average tissue mercury concentrations for mink and otter from multiple regions of North American are within an order of magnitude of tissue mercury concentrations of mink severely poisoned experimentally. For example, data showing mink liver mercury concentrations averaging 2 μg/g or higher were reported in several regions of New York State (Foley et al., 1988), Ontario (Wren

et al., 1986), and Manitoba (Kucera, 1983). Concentrations in excess of 20 μg/g occurred in mink dying of methylmercury poisoning (Wobeser, 1973; Wobeser et al., 1976a,b, 1979).

There may be other factors in addition to methylmercury concentration in the food supply of the mink and otter that are responsible for the association. Liver mercury concentrations in wild mink were not always predictably associated with proximity to long-term mercury contamination. For example, Wren et al., (1986) found that wild mink trapped in the English River system, severely contaminated by mercury discharge from a chloralkali plant 15 to 22 years earlier than the dates of mink trapping, had a range of 0.6 to 6.9 μg/g liver. By contrast mink trapped in the Turkey Lakes watershed, a region considered relatively pristine, had liver mercury concentrations ranging between 1.1 and 7.5 μg/gram fresh tissue (Wren et al., 1986). Another region of Ontario was substantially lower in mercury contamination; wild mink from Cambridge had average liver concentrations of 0.14 μg/g (fresh weight) (Wren et al., 1986).

4.2.2 Avian Species Exposure to Methylmercury

During the decades when seed-grains were treated with organo-mercurial fungicides huge numbers of wild birds were poisoned fatally with mercury. In the 1970s declining use of organo-mercurial fungicides greatly reduced the severity of mercury exposure. However, mercury residues either through natural or anthropogenic mercury sources remain. During the period 1990 through mid-1995 several reports of mercury concentrations in avian species have been published in the peer-reviewed literature (among others see Bowerman et al., 1994; Burger et al., 1993, 1994; Custer and Hohman, 1994; Spalding et al., 1994; Sundlof et al., 1994; Langlois and Langis, 1995; Lonzarich et al., 1992; Thompson et al., 1992). Considered with earlier information on mercury concentrations in tissues from avian wildlife, mercury is a common contaminant of avian tissues from diverse geographic locations. Mercury concentration in tissues have been reported for the following birds: seabirds from colonies in the Northeast Atlantic (Thompson et al., 1992); the common tern in Buzzards Bay, Massachusetts (Burger et al., 1994); the California clapper rail from the salt marshes of central and northern California (Lonzarich et al., 1992); canvasback ducks in Louisiana (Custer and Hohman, 1994); wading birds of Southern Florida (Sundlof et al., 1994; Spalding et al., 1994; Burger et al., 1993); loons in the Great Lakes regions and Ontario (Barr, 1986); and the Bald Eagle in the Great Lakes Region (Bowerman et al., 1994).

Feeding habits of particular avian species are a major predictor of risk of mercury toxicity in the 1990s. When seed-grains were treated with organo-mercurial fungicides herbivorous and omnivorous species were at risk of mercury toxicity, as were carnivorous birds. Because of the biomagnification of methylmercury in the aquatic foodweb, birds which feed on fish, crayfish or shellfish now have higher exposures to methylmercury than do non-fish eating birds. Birds, such as the heron, which consume large fish as their prey are predicted to be at greater risk of methylmercury poisoning than are birds consuming smaller fish (Spalding et al., 1994; Sundlof et al., 1994). When the quantity of fish consumed on a body weight basis is also considered smaller birds, such as the kingfisher, have been judged to be at elevated risk of methylmercury poisoning.

Several estimates exist in the published literature on quantities of mercury in soft tissues (liver, kidney, brain) associated with mercury poisoning in avian species. Experimental studies of survival and reproductive success of black ducks (*Anas rubripes*) by Findley and Stendell (1978) indicated that adult black ducks would tolerate liver mercury concentrations of 23 ppm and appear in good health. They found, however, that even though the black ducks fed methylmercury in diet appeared in good health that they had impaired reproductive success indicated by reduced hatchability of eggs and high duckling mortality. Findley et al. (1979) concluded that concentrations of mercury in excess of 20

µg/g fresh weight in soft tissues should be considered extremely hazardous to avian species. Scheuhammer (1991) in a review indicated that the major effects of methylmercury in avian species were neurological, developmental and reproductive. The neurological changes included weakness, walking or flying difficulties and inco-ordination which were associated with brain mercury concentrations of 15 µg/g (fresh weight), or liver or kidney mercury concentration of 30 µg/g (fresh weight). Schuehammer observed that generally significant reproductive impairment due to methylmercury occurs at about one-fifth the tissue concentrations required to produce overt neurotoxicity. Scheuhammer indicated that liver mercury concentrations of 2 to 12 µg/g (fresh weight) in adult breeding pheasants and mallard ducks were linked to decreased hatchability of eggs. Barr (1986) reported adult loons with total mercury concentrations in the brain as low as 2 ppm (fresh weight) showed aberrations in reproductive behavior, resulting in lowered incubation success and abandonment of territories. Both methylmercury and total mercury concentrations in liver and brain of the loon have correlation coefficients of 0.58 and 0.46, respectively. Barr (1986) noted that clinical signs of mercury poisoning, such as impaired vision and ataxia, had been found in several avian species (as reported by Evans and Kostyniak, 1972; Hays and Risebrough, 1972) at mercury concentrations lower than those present in the loons from one of the sites of Barr's investigations. Barr (1986) notes that impairment of vision or ataxia in a visual hunter such as loon would be likely to reduce its chances of procuring adequate food and defending a territory.

Mercury concentrations in livers of wading birds in Southern Florida (Sundlof et al., 1994; Spalding et al., 1994) and the merganser in northern Quebec (Lanlois and Langis, 1995) are in the range associated with adverse reproductive and neurological effects in other species of birds. Sundlof et al. (1994) reported that four great blue herons (*Ardea herodias*) collected from the central Everglades contained liver mercury at concentrations typically associated with overt neurological signs ($\geq$30 µg mercury/g fresh weight). Furthermore, these investigators found between 30 percent and 80 percent of the potential breeding-age birds collected in an area encompassing the central Everglades contained liver mercury at concentrations associated with reproductive impairment in ducks and pheasants. In a parallel study Spalding et al. (1994) determined the magnitude of mercury contamination associated with death of great white herons (*Ardea herodias occidentalis*). Birds that died of acute causes (e.g., trauma from collision with powerlines or vehicles) had much lower liver mercury concentrations (geometric mean 1.8 µg/g fresh weight, range 0.6 to 4.0 µg/g fresh weight) than did birds that died of chronic diseases (geometric mean 9.8 µg/g fresh weight, range 2.9 to 59.4 µg/g fresh weight).

The common merganser (*Mergus merganser*) and red-breasted merganser (*Mergus serrator*) were among wildlife species sampled in the Great Whale and Nottaway-Broadback-Rupert (NBR) hydroelectro projects in northern Quebec (Langlois and Langis, 1995). Liver mercury concentrations for these species were reported as mean ± standard deviation (SD) (shown in Table 4-1). Using standard statistical procedures it is estimated that 33.3 percent of the liver mercury concentrations for the respective species would be greater than the mean+one standard deviation. If the liver concentrations associated with neurological, reproductive and developmental effects in other avian species are applicable to the common and red-breasted merganser, adverse health and reproductive effects are associated with mercury exposures experienced by these avian species.

Table 4-1
Liver Mercury Concentration in Common Merganser, Red-Breasted Merganser and Herring Gulls from Northern Quebec (Langlois and Langis, 1995)

Mercury Concentration, liver (µg/g fresh weight)						
Species	Location					
	Great Whale			NBR		
	Mean ± SD	Mean + 1 SD 66.7th Percentile	Mean + 2 SD 95th Percentile	Mean ± SD	Mean + 1 SD 66.7th Percentile	Mean + 2 SD 95th Percentile
Common merganser	17.5 ±12.0	29.5	41.5	10.5±7.5	17.5	25.0
Red-breasted merganser	12.4±18.8	33.2	50.0	No values reported	--	--
Herring gull	2.9±2.4	5.3	7.7	3.6±2.5	6.1	9.7

Tissue mercury concentrations and population dynamics of the common loon (*Gavia immer*) in an area with mercury-contaminated waters in northwestern Ontario were reported by (Barr, 1986). Mercury concentrations for total and methylmercury for adults and chicks for liver, muscle, and brain are shown in Table 4-2. The concentration of total mercury residue in loon tissues decreased in the

Table 4-2
Mercury and Methylmercury Concentrations in Tissues (µg per Gram Fresh Weight) from the Common Loon in Northwestern Ontario (Barr, 1986)

	Liver			Muscle			Brain		
	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range
Adults Total mercury	12.95	11.67	1.64-47.71	2.33	2.07	0.16-6.87	0.86	0.89	0.31-4.61
Methyl-mercury	11.67	2.40	0.00-10.20	1.65	1.60	0.15-6.59	0.65	0.79	0.22-4.27
Chicks Total mercury	0.91	0.33	0.35-1.47	0.44	0.22	0.14-0.89	0.37	0.18	0.14-0.78
Methyl-mercury	0.80	0.29	0.32-1.36	0.37	0.20	0.09-0.80	0.37	0.17	0.14-0.75

sequence liver > muscle >brain, but the percentage of methylmercury increased from liver < muscle < brain. Barr (1986) found that almost 100 percent of the mercury transferred from adult loons through eggs to chicks was organic mercury with no net loss of methylmercury in chick tissue. Levels of

methylmercury in eggs and in the brain of newly hatched chicks frequently exceeded levels in the female parent's brains. There was a statistically significant correlation between total mercury levels in the brain of nesting females and their eggs (p=0.005).

The upper portion of the range of liver mercury concentrations for the loon was greater than mercury concentrations associated with overt clinical toxicity in other avian species. Barr (1986) reported finding loons that were emaciated, expected to accompany either anorexia or reduced ability to obtain prey. Barr's conclusions were than there was a strong negative correlation between successful use of territories by breeding loons and mercury contamination (Barr, 1986). Liver mercury concentrations (mean approximately 13 ppm, range approximately 2 to 48 ppm mercury) were higher than the range identified by Schuehammer as being associated with reproductive failure in other avian species: 2 to 12 ppm mercury (Scheuhammer, 1991). Scheuhammer concluded that results suggest a reduction in egg laying, and in nest and territorial fidelity at mercury concentration ranging from 0.3 to 0.4 ppm in prey and 2 to 3 ppm in adult loon brain and loon eggs. These data confirm earlier reports by Fimreite and Reynolds (1973) that the common loon may be particularly adversely affected by high levels of methylmercury accumulated from their diet.

4.2.3 Human Intake of Methylmercury Estimated Through Dietary Surveys and Mercury Residue Data

Food intake primarily from the ingestion of contaminated fish is the only significant source of methylmercury exposure to the general human population (Stern, 1993; Swedish EPA, 1991; WHO, 1990). Total mercury concentrations in meats and cereals often measure hundreds of times less than in fish (Swedish EPA, 1991). In most non-fish foodstuffs mercury concentrations are typically near detection limits and are comprised mainly of inorganic species (WHO, 1990). In contrast, most of the mercury in fish is methylated and fish methylmercury concentrations are typically above analytic detection limits.

Available techniques to estimate fish consumption include long-term dietary histories and questionnaires to identify typical food intake or short-term dietary recall techniques. Temporal variation in dietary patterns is an issue to consider in evaluation of short-term recall/record data. For epidemiological studies that seek to understand the relationship of long-term dietary patterns to chronic disease, typical food intake is the relevant measure to evaluate (Willett, 1990). Because methylmercury is a developmental toxin that may produce adverse effects following a comparatively brief exposure period (i.e., a few months rather than decades), comparatively short-term dietary patterns can have importance.

Estimates of fish consumption rely on dietary survey data that can be obtained using a variety of dietary survey techniques. Critical elements in any survey aimed at determining intake of methylmercury from fish are these:

- Species of fish or shellfish consumed;
- Concentration of methylmercury in the fish;
- Quantity of fish consumed.

The duration of fish consumption is also of importance; however, the time period of consumption that is relevant when conducting an assessment of risk depends on the health endpoint of concern. To illustrate, acute effects of certain fish contaminants (such as paralytic shell fish toxin or cigutara toxin) may result from eating as little as one meal of contaminated fish. By contrast, if one is interested in the benefits of consuming unsaturated fatty acids (e.g., omega 3 fatty acid) on prevalence

of cardiovascular disease, decades of exposure for a group of persons is typically required to establish whether or not an effect would occur. For a health endpoint such as developmental deficits associated with a particular period during gestation (e.g., adverse effects of maternal consumption of methylmercury from fish on the developing fetal nervous system), short-term consumption patterns during the critical weeks or months of gestation are considered the relevant period for the health endpoint.

Survey methods can broadly be classified into longitudinal methods or cross-sectional surveys. Typically long-term or longitudinal estimates of intake can be used to reflect patterns for individuals (e.g., dietary histories); or longitudinal estimates of moderate duration (e.g., month-long periods) for individuals or groups. Cross-sectional data are used to give a "snap shot" in time and are typically used to provide information on the distribution of intakes for groups within the population of interest. Cross-sectional data typically are for 24-hour or 3-day sampling periods and may rely on recall of foods consumed following questioning by a trained interviewer, or may rely on written records of foods consumed. Additional discussion of these issues are found on Appendix H to Volume III.

During the past decade reviewers of dietary survey methodology (for example, the Food and Nutrition Board of the National Research Council/National Academy of Sciences; the Life Sciences Research Office of the Federation of American Societies of Experimental Biology) have evaluated various dietary survey techniques with regard to their suitability for estimating exposure to contaminants and intake of nutrients. The Food and Nutrition Board of the National Research Council/National Academy of Sciences in their 1986 publication, *Nutrient Adequacy Assessment Using Food Consumption Surveys,* noted that dietary intake of an individual is not constant from day to day, but varies both in amount and in type of foods eaten (intraindividual variation). Variations between persons in their usual food intake averaged over time is referred to as interindividual variation. Among North American populations, the intraindividual (within person day-to-day) variation is usually regarded to be as large as or greater than the interindividual (person to person) variations. Having evaluated a number of data sets the Academy's Subcommittee concluded that 3 days of observation may be more than is required for the derivation of the distribution of usual intakes.

Major sources of data on dietary intake of fish used in preparing this report to Congress are the cross-sectional data from the USDA Continuing Surveys of Food Intake by Individuals conducted in the years 1989 through 1991 (CSFII 89/91) and the longer-term data on fish consumption based on recorded fish consumption for variable numbers of periods of one-month duration during the years 1973/1974. The SE data are from the National Purchase Diary (NPD 73/74) conducted by the Market Research Corporation.

The CSFII 89/91 data are cross-sectional data based on a 3-day sampling period. When appropriately weighted they can be used to estimate the food consumption patterns for the general United States population for the period 1989/1991 there were 11,706 respondents. The survey is designed to represent all seasons of the year and all days of the week. Because the food consumption records rely on standard coding of food intake and records of types of fish represented by a particular dietary record, it is possible to estimate quantities of particular types of fish that were consumed for the population as a whole and for subpopulations of interest. The portion size consumed by individuals is recorded, as is the person's self-reported body weight.

The CSFII 89/91 data on fish consumption have been used to estimate fish and methylmercury intake by various population subgroups. These calculations rely on values for the methylmercury concentrations in food supplied to the US EPA by the National Marine Fisheries Service. These data are presented in detail in Appendix H to Volume III.

4.2.3.1 Estimates of Human Intake of Methylmercury Based on Longitudinal Data

Estimates of fish consumption in the 1970s were determined by the NPD Research Inc., a market research and consulting firm that specializes in the analysis of consumer purchasing behavior as recorded in monthly diaries. That survey was funded by the Tuna Research Institute (TRI) as part of a study of tuna consumption. Later, the National Marine Fisheries Service (NMFS) received permission from TRI to obtain the data (SRI International Contract Report to U.S. EPA, 1980).

The NPD 73/74 data are based on a sample of 7,662 families (25,165 individuals) out of 9,590 families sampled between September 1973 and August 1974. Data recorded in the survey reflect the marketing nature of the survey design and have limitations with regard to quantities of fish consumed on a body weight basis. To illustrate, the fish consumption was based on questionnaires completed by the female head of the household in which she recorded the date of any meal containing fish, the type of fish (species), the packaging of the fish (canned, frozen, fresh, dried, or smoked, or eaten out), whether fresh fish was recreationally caught or commercially purchased, the amount of fish prepared for the meal, the number of servings consumed by each family member and any guests, and the amount of fish not consumed during the meal. Meals eaten both at home and away from home were recorded.

Use of these data to estimate intake of fish or mercury on a body weight basis are limited by the following data gaps.

1. This survey did not include data on the quantity of fish represented by a serving and information to calculate actual fish consumption from entries described as breaded fish or fish mixed with other ingredients. Portion size was estimated by using average portion size for seafood from USDA Handbook # 11. Table 10, page 40-41. The average serving sizes from this USDA source are shown in Table 4-3.

Table 4-3
Average Serving Size (gms) for Seafood from
USDA Handbook # 11 Used to Calculate Fish Intake by FDA (1978)

Age Group (years)	Male Subjects (gms)	Female Subjects (gms)
0-1	20	20
1-5	66	66
6-11	95	95
12-17	131	100
18-54	158	125
55-75	159	130
Over 75	180	139

2. There may have been systematic under-recording of fish intake; Crispin-Smith et al. noted that typical intakes declined 30% between the first survey period and the last

survey period among persons who completed four survey diaries (Crispin-Smith et al., 1985).

3. There have been changes in the quantities and types of fish consumed between 1973/1974 and present. To illustrate, the United States Department of Agriculture indicated (Putnam, 1991) that, on average, fish consumption increased 27% between 1970 and 1990. Whether or not this increase applies to the highest percentiles of fish consumption (e.g., 95th or 99th percentile) was not described in the publication by USDA.

4. An analyses of these data using the sample weights to project these data for the general United States population was prepared by SRI International under US EPA Contract 68-01-3887 in 1980. U.S. EPA was subsequently informed that the sample weights were not longer available. Consequently additional analyses with these data in a manner that can be projected to the general population appears no longer to be possible.

5. Body weights of the individuals surveyed do not appear in published materials. If body weights of the individuals participating in this survey were recorded these data do not appear to have been used in subsequent analyses.

Data on fish consumption from the NPD 73/74 survey have been published by Rupp et al., 1980 and analyzed by US EPA's contractor SRI International (1980). These data indicate that when a month-long survey period is used 94% of the surveyed population consumed fish. The species of fish most commonly consumed are shown in Table 4-4.

Table 4-4
Fish Species and Number of Persons Using the Species of Fish.
Adapted from Rupp et al., 1980

Category	Number of Individuals Consuming Fish Based on 24,652 Replies*
Tuna, light	16,817
Shrimp	5,808
Flounders	3,327
Not reported (or identified)	3,117
Perch (Marine)	2,519
Salmon	2,454
Clams	2,242
Cod	1,492
Pollock	1,466
Haddock	1,441
Herring	1,351
Oysters	1,239
Crab, other than King	1,168
Trout (freshwater)	970
Lobster, northern	575
Halibut	574
Scallops	526
Mackerel, other than jack	515
Whitefish	492
Snapper	490
Hake	372
Catfish (freshwater)	376
Lobster, spiny	350
Smelt	328
Bass	326
Perch (freshwater)	268
Bluegills	265
Crappie	228
Trout (marine)	220
Benito	148

* More than one species of fish may be eaten by an individual.

Rupp et al. also estimated quantities of fish and shellfish consumed by 12-18 year-old teenagers and by adults 18 to 98 years of age. These data are shown in Table 4-5. The distribution of fish consumption for age groups that included women of child-bearing ages are shown in Table 4-6.

Table 4-5
Fish Consumption from the NPD 1973/1974 Survey
(modified from Rupp et al., 1980)

Age Group	50th Percentile	90th Percentile	99th Percentile	Maximum
Teenagers aged 12-18 Years	1.88 kg/year	8.66 kg/year	25.03 kg/year or 69 grams/day	62.12 kg/year
Adults aged 18 to 98 Years	2.66 kg/year	14.53 kg/year	40.93 kg/year or 112 grams/day	167.20 kg/year

Table 4-6
Percent of Females By Age* Consuming Fish/Shellfish from SRI (1980)

Age Group (years)	47.6-60.0 gms/day	60.1-122.5 gms/day	over 122.5 gms/day
10-19	0.2%	0.4%	0.0%
20-29	0.9%	0.9%	0.0%
30-39	1.9%	1.7%	0.1%
40-49	3.4%	2.1%	0.2%

* The percentage of females in an age bracket who consume, on average, a specified amount (grams) of fish per day. The calculations in this table were based upon the respondents to the NPD survey who consumed fish in the month of the survey. The NPD Research estimates that these respondents represent, on a weighted basis, 94.0% of the population of U.S. residents (from Table 6, SRI Report, 1980).

4.2.3.2 Human Intake of Methylercury Estimated Through Cross-Sectional Dietary Surveys

General Population, All

Human methylmercury intake from fish for the general U.S. population was estimated in this Report by combining data on mercury concentrations in fish species (expressed as micrograms of mercury per gram fresh-weight of fish tissue) with the reported quantities and types of fish species consumed by fish eaters or "users" in the USDA's Continuing Surveys of Food Intake by Individuals (CSFII 89/91). When appropriately weighted they can be used to estimate the food consumption patterns for the general United States population for the period 1989/1991. Because the food consumption records rely on standard coding of food intake and records of types of fish represented by a particular dietary record it is possible to estimate how much of particular types of fish were consumed for the population as a whole and for subpopulations of interest. The portion size consumed by individuals is recorded, as is the person's self-reported body weight.

The dietary survey methodology consisted of an assessment of three consecutive days of food intake and selection of interviewees from probability samples for non-institutionalized United States

households. Survey respondents numbered 11,706 individuals who were surveyed across all four seasons of the year and all seven days of the week. Respondents also reported their body weights, and these data were utilized in Volume III to estimate fish consumption on a per body weight basis. Use of these survey data provides a nationally based estimate of fish intake by the general population of the United States.

Analysis of CSFII 89/91 data by U.S. EPA's Office of Water (personal communication from Helen Jacobs) determined confidence intervals around the various percentiles for total fish and shellfish consumed. The percentile confidence intervals were estimated using the percentile bootstrap methods with 1,000 bootstrap replications. These estimates are for the quantity of uncooked fish consumed by all 11,912 individuals who reported consumption data in the years 1989, 1990, and 1991 (see Table 4-7). Table 4-8 presents the daily average per capita estimates of fish consumption based on cooked fish.

Table 4-7
Daily Average Per Capita Estimates of Uncooked Fish Consumption from CSFII 89/91[a]

Percentile	Grams/person/day		
	Estimate	90% Interval	
		Lower Bound	Upper Bound
Mean	20.08	18.82	21.35
90th	70.11	65.37	74.20
95th	102.01	99.26	106.67
99th	173.18	162.80	176.52

[a] Based on uncooked fish and shellfish. Source of Analysis: OPPTS, U.S. EPA. Means are for total population of 11,912 individuals surveyed.

Table 4-8
Daily Average Per Capita Estimates of Cooked Fish Consumption
U.S. Population - Finfish and Shellfish

Habitat	Statistic	Grams/Person/Day		
		Estimate	90% Interval	
			Lower Bound	Upper Bound
Fresh/Estuarine	Mean	5.57	4.94	6.19
	50th %	0.00	0.00	0.00
	90th %	15.91	13.71	17.06
	95th %	39.42	37.48	41.64
	99th %	91.67	88.92	99.61

Table 4-8 (continued)
Daily Average Per Capita Estimates of Cooked Fish Consumption
U.S. Population - Finfish and Shellfish

Habitat	Statistic	Grams/Person/Day		
		Estimate	90% Interval	
			Lower Bound	Upper Bound
Marine	Mean	12.10	11.21	12.99
	50th %	0.00	0.00	0.00
	90th %	45.50	42.43	49.33
	95th %	69.70	66.98	73.91
	99th %	121.33	113.40	133.97
All Fish	Mean	17.66	16.58	18.75
	50th %	0.00	0.00	0.00
	90th %	61.47	58.47	65.33
	95th %	87.23	84.00	89.98
	99th %	152.36	146.38	160.65

* Percentile confidence intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 11,912 individuals to the U.S. population of 242,707,000 using 3-year combined survey weights.

Source of individual consumption data: combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFI).
The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for individual Food Intake Surveys.

The CSFII 89/91 survey design reflected known sources of variability in estimating dietary intakes in general. The extent to which comparatively short-term assessments of dietary intake predict long-term fish consumption patterns remains an uncertainty. Nutritional epidemiologists (among others see Willet, 1990) have observed that these surveys provide a cross-sectional view of dietary intake that better predicts central tendency than the extremes of the range of typical fish consumption behavior. In Volume III comparisons were made between quantities consumed and the upper quartile of the fish-consuming subpopulation of the general United States population and estimates of quantities of fish consumed by subpopulations of high fish-consuming Native American Tribes and anglers. Fish consumption rates reported by several tribes and by high fish-consuming anglers, corroborate the daily consumption rates of the extreme end of the distribution of the CSFII 89/91(see also Figure 4-5 in this volume). Since these individuals are part of the U.S. population, their consumption rates may be reflected in the CSFII 89/91. It should be noted that the angler and Native American fish consumption surveys utilize different types of survey methods; this further corroborates the high-end estimates of CSFII 89/91.

Among nationally representative weighted samples of individuals, 30.9 percent reported consumption of fish and/or combinations of fish, shellfish, or seafood with starches in a 3-day sampling period. Of individuals reporting fish consumption, approximately 98 percent consumed fish only once, and about 2 percent consumed fish in two or more meals during the 3-day survey period. For foods consumed by only a minority of the population, estimates of per capita consumption rates overestimate the consumption rate for the general population, but underestimate the consumption rate

among the portion of the population which actually consumes the food item. As a consequence, in this risk characterization fish consumption estimates are based on a "per consumer" basis.

Respondents in CSFII 89/91 who reported eating fish indicated the fish species and quantity of fish consumed. Fish consumption has been reported to be recalled with greater accuracy than other food groups (Karvetti and Knuts, 1985). Nevertheless, an uncertainty in these data is the ability of consumers to identify the species of fish consumed. The species of fish identified by the respondents were recorded as part of the dietary records of the survey. These fish species were identified and used to estimate dietary intake of methylmercury. The survey and results are described in Appendix H to Volume III.

Selection of a database for mercury residues in fish was determined by several factors. Because the dietary consumption data were nationally based, preference was given to fish residue data that included fish from widely diverse geographic areas. This choice aimed at avoiding data more appropriate for site-specific assessments that would result from the sampling of a very limited geographic area (e.g., a state-wide survey). In addition, the preferred database should include many individual types of fish to represent the consumed species; inclusion of many species types is considered to provide a better approximation of the estimate of central tendency from individual samples. A third preference was for data collected over a time period that approximated the years of the dietary survey. The third criteria was judged the least important in selection of the database because residues of mercury in soils and sediments continue to contribute mercury to the aquatic food-web and are considered to minimize year-to-year variability in mercury concentrations in fish tissues. Data describing methylmercury concentrations in marine fish were largely based on the National Marine Fisheries Service (NMFS) database, the largest publicly available database on mercury concentrations in marine fish. This NMFS database has been collected over the past two decades. Comparison of the values for central tendency (e.g., 50th percentile) in mercury concentrations between the NMFS database and FDA's compliance data on selected species (Carrington et al., 1995) indicated close agreement in mercury concentrations. Table 4-9 presents data on mercury concentrations in fish used in calculations for this report, as well as concentrations cited by FDA (1978) and by Stern et al. (1996.)

For freshwater fish, two publications reporting mercury concentrations in multiple species of fish were chosen. Data reported by Bahnick et al. (1994) and Lowe et al. (1985) were used to estimate average mercury concentrations in fresh-water finfish from across the United States. Both Lowe et al. (1985) and Bahnick et al. (1994) used nationwide surveys of freshwater fish. Both databases suffer from a limited number of samples at any one site; however, a strength of each data set is that many sites were sampled. These data are described in detail in Appendix H of Volume III. When average mercury concentration in fresh-water fish are compared, the results from Lowe et al. (1985) and Bahnick et al. (1994) differ by a factor of approximately two. Consequently separate analyses of methylmercury intake from fish were prepared to assess the impact of the database chosen for mercury residues.

Table 4-9
Summary of Mercury Concentrations in Fish Species
Micrograms Mercury per Gram Fresh Weight (µg Hg/g)

Data Used by USEPA[a] Mercury Study Report to Congress In Review		Data Used by US FDA[b] Report on the Chance of U.S. Seafood Consumers Exceeding "The Current Daily Intake for Mercury and Recommended Regulatory Controls" 1978			Data Used by State of New Jersey	
Fish Species	**Average (µg Hg/g)**	**Fish Species**	**Average (µg Hg/g)**	**Maximum (µg Hg/g)**	**Fish Species**	**Average (µg Hg/g)**
Abalone	0.016	Abalone	0.018	0.120	Not Reported (NR)	
Anchovies	0.047	Anchovies	0.039	0.210	NR	
Bass, Freshwater	Avgs.= 0.157 (Lowe et al., 1985) and 0.38 (Bahnick et al., 1994)	Bass, Striped	0.752	2.000	Bass, freshwater	0.41
Bass, Sea	Not Reported	Bass, Sea	0.157	0.575	Sea Bass	0.25
Bluefish	Not Reported	Bluefish	0.370	1.255	Bluefish	0.35
Bluegills	0.033	Bluegills	0.259	1.010	NR	
Bonito	Not Reported	Bonito (below 3197)	0.302	0.470	NR	
Bonito	Not Reported	Bonito (above 3197)	0.382	0.740	NR	
Butterfish	Not Reported	Butterfish	0.021	0.190	Butterfish	0.05
Carp, Common	0.093	Carp	0.181	0.540	Catfish, freshwater	0.15
Catfish (channel,large mouth, rock, striped, white)	0.088	Catfish (freshwater)	0.146	0.380	Clams	0.05
Catfish (Marine)	Not Reported	Catfish (Marine)	0.475	1.200	Cod/Scrod	0.15
Clams	0.023	Clams	0.049	0.260	See crab.	
Cod	0.121	Cod	0.125	0.590	Crab	0.15
Crab, King	0.070; Calculations based on 5 species of crab combined at 0.117	Crab, King	0.070	0.240	NR	

Table 4-9 (continued)
Summary of Mercury Concentrations in Fish Species
Micrograms Mercury per Gram Fresh Weight (µg Hg/g)

Data Used by USEPA[a] Mercury Study Report to Congress In Review		Data Used by US FDA[b] Report on the Chance of U.S. Seafood Consumers Exceeding "The Current Daily Intake for Mercury and Recommended Regulatory Controls" 1978			Data Used by State of New Jersey	
Crab	0.117	Crab, other than H1	0.140	0.610	NR	
Crappie (black, white)	0.114	Crappie	0.262	1.390	NR	
Croaker	0.125	Croaker	0.124	0.810	NR	
Dolphin	Not Reported	Dolphin	0.144	0.530	Dolphin (Mahi-mahi)	0.25
Drums, Freshwater	0.117	Drums	0.150	0.800	NR	
Flounders	0.092	Flounders	0.096	0.880	Flounder	0.10
Groupers		Groupers	0.595	2.450	NR	
Haddock	0.089	Haddock	0.109	0.368	Haddock	0.05
Hake	0.145	Hake	0.100	1.100	Hake	0.10
Halibut	0.250	Halibut 4	0.187	1.000	Halibut	0.25
Halibut	0.250	Halibut 3	0.284	1.260	Halibut	0.25
Halibut	0.250	Halibut 2H	0.440	1.460	Halibut	0.25
Halibut	0.250	Halibut 25	0.534	1.430	Halibut	0.25
Herring	0.013	Herring	0.023	0.260	Herring	0.05
Kingfish	0.100	Kingfish	0.078	0.330	Kingfish	0.05
Lobster	0.232	Lobster, Northern 11	0.339	1.603	Lobster	0.25
Lobster	0.232	Lobster Northern 10	0.509	2.310	Lobster	0.25
Lobster Spiny	0.232; Includes spiny (Pacific) lobster=0.210	Lobster,Spiny	0.113	0.370	Lobster	0.25
Mackerel	0.081; Averaged Chub = 0.081; Atlantic= 0.025; Jack=0.138	Mackerel, Atlantic	0.048	0.190	Mackerel	0.28
Mackerel	0.081	Mackerel, Jack	0.267	0.510	Mackerel	0.28

Table 4-9 (continued)
Summary of Mercury Concentrations in Fish Species
Micrograms Mercury per Gram Fresh Weight (µg Hg/g)

Data Used by USEPA[a] Mercury Study Report to Congress In Review		Data Used by US FDA[b] Report on the Chance of U.S. Seafood Consumers Exceeding "The Current Daily Intake for Mercury and Recommended Regulatory Controls" 1978			Data Used by State of New Jersey	
Mackerel	0.081	Mackerel, King (Gulf)	0.823	2.730	Mackerel	0.28
Mackerel	0.081	Mackerel, King (other)	1.128	2.900	Mackerel	0.28
Mackerel	0.081	Mackerel, Spanish 16	0.542	2.470	Mackerel	0.28
Mackerel	0.081	Mackerel, Spanish 10	0.825	1.605	Mackerel	0.28
Mullet	0.009	Mullet	0.016	0.280	Mullet	0.05
Oysters	0.023	Oysters	0.027	0.460	NR	
Perch, White and Yellow	0.110	Perch, Freshwater	0.290	0.880	Perch	0.18
Perch, Ocean	0.116	Perch, Marine	0.133	0.590	NR	
Pike, Northern	0.310 0.127	Pike	0.810	1.710	NR	
Pollock	0.150	Pollock	0.141	0.960	NR	
Pompano	0.104	Pompano	0.104	8.420	NR	
Rockfish	Not Reported	Rockfish	0.340	0.930	NR	
Sablefish	Not Reported	Sablefish	0.201	0.700	NR	
Salmon	0.035	Salmon	0.040	0.210	Salmon	0.05
Scallops	0.042	Scallops	0.058	0.220	NR	
Scup	Not Reported	Scup	0.106	0.520	NR	
Sharks	1.327	Sharks	1.244	4.528	Shark	1.11
Shrimp	0.047	Shrimp	0.040	0.440	Shrimp	0.11
Smelt	0.100	Smelt	0.016	0.058	Smelts	0.05
Snapper	0.25	Snapper,Red	0.454	2.170	Snapper	0.31
Snapper	0.25	Snapper, Other	0.362	1.840	Snapper	0.31
Snook	Not Reported	Snook	0.701	1.640	NR	
Spot	Not Reported	Spot	0.041	0.180	Spotfish	0.05

Table 4-9 (continued)
Summary of Mercury Concentrations in Fish Species
Micrograms Mercury per Gram Fresh Weight (μg Hg/g)

Data Used by USEPA[a] Mercury Study Report to Congress In Review		Data Used by US FDA[b] Report on the Chance of U.S. Seafood Consumers Exceeding "The Current Daily Intake for Mercury and Recommended Regulatory Controls" 1978			Data Used by State of New Jersey	
Squid	0.026	Squid and Octopi	0.031	0.400	Squid	0.05
Octopi	0.029	Squid and Octopi	0.031	0.400	NR	
Sunfish	Not Reported	Sunfish	0.312	1.200	NR	
Swordfish	0.95	Swordfish	1.218	2.720	Swordfish	0.93
Tillefish	Not Reported	Tillefish	1.607	3.730	NR	
Trout	0.149	Trout, Freshwater	0.417	1.220	Trout	0.05
Trout	0.149	Trout, Marine	0.212	1.190	Trout	0.05
Tuna	0.206; Averaged: Tuna, light skipjack=0.136 Tuna,light yellow=0.218; Albacore=0.264	Tuna, Light Skipjack	0.144	0.385	Tuna, fresh	0.17
Tuna	0.206	Tuna, Light Yellow	0.271	0.870	Tuna, fresh	0.17
Tuna	0.206	Tuna, White	0.350	0.904	Tuna, fresh	0.17
Whitefish	Not Reported	Whitefish	0.054	0.230	Whitefish	0.04
Other finfish		Other finfish	0.287	1.020	Finfish, other	0.17
Other shellfish	Not Reported				Shellfish, other	0.12
Fish Species (Freshwater) Not Reported by FDA, 1978						
Bloater	0.0.93					
Smallmouth Buffalo	0.096					
Northern Squawfish	0.33					
Sauger	0.23					

Table 4-9 (continued)
Summary of Mercury Concentrations in Fish Species
Micrograms Mercury per Gram Fresh Weight (μg Hg/g)

Data Used by USEPA[a] Mercury Study Report to Congress In Review		Data Used by US FDA[b] Report on the Chance of U.S. Seafood Consumers Exceeding "The Current Daily Intake for Mercury and Recommended Regulatory Controls" 1978			Data Used by State of New Jersey	
Sucker	0.114 (Lowe et al., 1985; 0.167 (Bahnick et al., 1994).					
Walleye	0.100 (Lowe et al., 1985) and 0.52 (Bahnick et al., 1994).					
Trout (brown, lake, rainbow)	0.149 (Lowe et al., 1985) and 0.14 (Bahnick et al., 1994 for brown trout).					
Fish Species Reported by the State of New Jersey and Not Reported by EPA or FDA						
Blowfish						0.05
Orange roughy						0.5
Sole						0.12
Weakfish						0.15
Porgy						0.55
Blackfish						0.25
Whiting						0.05
Turbot						0.10
Sardines						0.05
Tilapia						0.05

[a] From Appendix H, Volume III.
[b] FDA, 1978.
[c] Stern et al., 1996 - in press.

Findings of this evaluation based on dietary patterns for the general U.S. population and mercury residue data in fish were used to estimate mercury consumption from fish. Data on fish consumption (in grams per day) are shown for persons who reported consuming fish at least once in the three-day sampling period. These estimates are based on the total grams of fish or shellfish consumed within the 72-hour sampling period which is then averaged over the three 24-hour periods. For example, if a person reported consuming 30 grams of fish during the 72-hour period, this persons 24-hour average would be 10 grams. The mercury concentrations for particular fish and shellfish species used in these calculations is shown in Table 4-9 (columns under data used by U.S. EPA).

Consumption of methylmercury (expressed per kilogram self-reported body weight) from marine and freshwater finfish and shellfish for the general U.S. fish-consuming population were estimated; the data are shown in Tables 4-10 through 4-13. Tables 4-12 and 4-13 give estimated consumption of fish species designated as freshwater fish. For comparison, methylmercury intake from all fish and shellfish for the general U.S. population are shown in Tables 4-10 and 4-11. The most commonly consumed marine finfish for the general population is tuna. Use of the data of Bahnick et al. (1994) which reported overall higher mercury concentrations than those of Lowe et al. (1985) provided a range of estimates of methylmercury intake for the general U.S. fish-consuming population.

Methylmercury intakes calculated and shown in Appendix H of Volume III have been developed for a nationally based rather than a site-specific assessment. The CSFII 89/91 data from USDA was designed to be representative of the U.S. population. The concentrations of methylmercury in marine fish and shellfish were derived from a database that is national in scope and the data on fresh-water finfish were from two large studies that sampled fish at a number of sites throughout the United states. The applicability of these data to site-specific or region-specific assessments must be judged on a case-by-case basis.

Subgroups of General Population

In selection of sensitive subpopulations of humans, sensitivity may reflect inherent responsiveness of the subpopulation to the hazard (i.e., toxicity based) or reflect elevated exposures to the agent of concern. With respect to risks posed by methylmercury from fish, two subpopulations of humans are of particular interest in this risk characterization: women of child-bearing age and children. Women of child-bearing age are of concern because developmental effects following *in utero* exposures are the basis for the RfD and because the developing nervous system would be expected to be most vulnerable to methylmercury toxicity. Because 9.5 percent of women ages 15 through 44 years are pregnant in a given year, and the half-life of mercury averages 70 days, the entire population of women of child-bearing age is judged to be of concern.

Estimated methylmercury intake from finfish and shellfish of both marine and freshwater origin for women of child-bearing age are presented in Tables 4-10 and 4-11. The data of Bahnick et al. (1994) were used to calculate the estimates shown in Table 4-10. The estimated exposures in Bahnick et al. 1994 are generally higher in methylmercury concentration than are those of Lowe et al. (1985) which were used to present the estimates shown in Table 4-11. Because the quantities of freshwater fish consumed are a small part of the total fish intake for the general population, differences in average mercury concentrations between the data of Lowe et al. (1985) and Bahnick et al (1994) do not result in marked differences in average mercury intake from fish. Tables 4-12 and 4-13 present estimated methylmercury intakes from freshwater fish for U.S. women of child-bearing age.

Table 4-10

Consumption of All Fish & Shellfish (gms/day) and Methylmercury per Kg body weight from Fish among Respondents of the 1989-1991 CSFII Survey. Data for "Users" Only. Bahnick et al. estimates for fresh-water fish Methylmercury Concentrations[a]

Gender	Percentage	Aged 14 Years of Younger			Aged 15 through 44 Years			Aged 45 Years or Older			Total		
		N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$	N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$	N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$	N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$
Males	Min	380	1.9	< 0.01	646	1.9	< 0.01	556	2.5	<0.01	1582	1.9	< 0.01
	5th		3.5	0.01		9.3	0.01		9.3	0.01		7.0	0.01
	25th		14.2	0.09		24.6	0.04		22.7	0.03		20.4	0.04
	50th		23.0	0.16		45.5	0.08		40.3	0.07		37.8	0.09
	75th		45.0	0.25		73.3	0.16		64.5	0.13		65.3	0.17
	95th		80.6	0.84		124.5	0.33		127.2	0.38		120.8	0.45
	97.5th		104.5	0.94		153.3	0.46		172.8	0.71		149.2	0.64
	99th		132.4	1.33		177.9	0.60		203.1	0.95		177.2	0.94
	Max		139.4	1.51		312.0	1.98		388.9	1.57		388.9	1.98
Females	Min	340	1.0	< 0.01	864	1.3	< 0.01	828	1.9	< 0.01	2032	1.0	< 0.01
	5th		4.7	0.02		7.0	0.01		7.2	0.01		7.0	0.01
	25th		14.0	0.07		18.6	0.04		18.9	0.04		18.6	0.04
	50th		23.0	0.15		28.6	0.08		31.8	0.07		28.6	0.09
	75th		37.5	0.28		55.8	0.16		56.0	0.14		52.3	0.17
	95th		67.4	0.81		110.8	0.35		107.8	0.34		106.7	0.44
	97.5		112.1	0.90		132.8	0.48		134.1	0.55		127.4	0.60
	99th		113.8	1.29		174.6	0.74		159.0	0.63		161.3	0.90
	Max		153.5	1.69		461.0	2.76		250.2	1.67		461.0	2.76

[a] Data weighted to reflect U.S. population.

Table 4-11

Consumption of All Fish & Shellfish (gms/day) and Methylmercury per Kg body weight from Fish among Respondents of the 1989-1991 CSFII Survey. Data for "Users" Only. Lowe et al. estimates for fresh-water fish Methylmercury Concentrations[a]

Gender	Percentage	Aged 14 Years of Younger			Aged 15 through 44 Years			Aged 45 Years or Older			Total		
		N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$	N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$	N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$	N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$
Males	Min	380	1.9	< 0.01	646	1.9	< 0.01	556	2.5	< 0.01	1582	1.9	< 0.01
	5th		3.5	0.01		9.3	0.01		9.3	0.01		7.0	0.01
	25th		14.2	0.08		24.6	0.04		22.7	0.03		20.4	0.04
	50th		23.0	0.15		45.5	0.08		40.3	0.07		37.8	0.08
	75th		45.0	0.25		73.3	0.14		64.5	0.12		65.3	0.16
	95th		80.6	0.84		124.5	0.31		127.2	0.33		120.8	0.40
	97.5th		104.5	0.94		153.3	0.40		172.8	0.67		149.2	0.62
	99th		132.4	1.33		177.9	0.60		203.1	0.97		177.2	0.94
	Max		139.4	1.51		312.0	1.98		388.9	1.57		388.9	1.98
Females	Min	340	1.0	< 0.01	864	1.3	< 0.01	828	1.9	< 0.01	2032	1.0	< 0.01
	5th		4.7	0.02		7.0	0.01		7.2	0.01		7.0	0.01
	25th		14.0	0.07		18.6	0.04		18.9	0.03		18.6	0.04
	50th		23.0	0.12		28.6	0.08		31.8	0.07		28.6	0.08
	75th		37.5	0.27		55.8	0.15		56.0	0.13		52.3	0.16
	95th		67.4	0.68		110.8	0.32		107.8	0.32		106.7	0.41
	97.5		112.1	0.90		132.8	0.47		134.1	0.43		127.4	0.55
	99th		113.8	1.29		174.6	0.69		159.0	0.61		161.3	0.90
	Max		153.5	1.69		461.0	2.76		250.2	1.67		461.0	2.76

[a] Data weighted to reflect U.S. population.

Table 4-12

Consumption of Freshwater Fish (gms/day) and Methylmercury per Kg body weight from Fish among Respondents of the 1989-1991 CSFII Survey. Data for "Users" Only. Fish methylmercury concentrations based on Bahnick et al., (1994)[a]

Gender	Percentage	Aged 14 Years of Younger			Aged 15 through 44 Years			Aged 45 Years or Older			Total		
		N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$	N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$	N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$	N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$
Males	Min	60	4.0	0.04	80	7.6	0.03	82	3.1	0.01	222	3.1	0.01
	5th		8.8	0.07		19.0	0.06		18.1	0.04		12.7	0.05
	25th		17.2	0.15		42.9	0.11		23.4	0.09		26.0	0.10
	50th		26.2	0.19		58.5	0.16		43.0	0.11		44.7	0.16
	75th		37.5	0.24		77.1	0.24		63.7	0.17		72.4	0.24
	95th		57.0	0.55		140.6	0.50		147.6	0.35		134.0	0.46
	97.5th		78.7	0.68		224.4	0.52		172.9	0.45		172.9	0.55
	99th		86.4	0.77		224.4	0.55		388.9	0.71		224.4	0.71
	Max		96.5	0.77		247.8	0.64		388.9	0.71		388.9	0.77
Females	Min	46	1.0	0.02	109	8.8	0.02	115	2.0	0.01	270	1.0	0.01
	5th		2.5	0.05		18.1	0.05		13.8	0.04		10.7	0.04
	25th		13.8	0.12		23.4	0.08		22.4	0.07		21.4	0.08
	50th		14.1	0.16		37.5	0.11		34.0	0.12		31.2	0.13
	75th		37.5	0.19		56.9	0.19		67.5	0.2		56.2	0.19
	95th		43.7	0.64		178.3	0.68		102.0	0.39		118.9	0.55
	97.5th		63.3	0.65		178.3	0.68		172.9	0.55		172.9	0.65
	99th		71.0	0.87		213.2	0.71		172.9	0.55		178.3	0.68
	Max		71.0	0.87		217.8	0.73		222.1	0.55		222.1	0.87

[a] Data are weighted to be representative of the U.S. population.

Table 4-13

Consumption of Freshwater Fish (gms/day) and Methylmercury per Kg body weight from Fish among Respondents of the 1989-1991 CSFII Survey. Data for "Users" Only. Fish methylmercury concentrations based on Lowe et al., (1994)

Gender	Percentage	Aged 14 Years of Younger			Aged 15 through 44 Years			Aged 45 Years or Older			Total		
		N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$	N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$	N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$	N	Fish gms/day	Methyl-mercury $\mu g/kg_{bw}$
Males	Min	60	4.01	0.02	80	7.6	0.01	82	3.1	0.01	222	3.1	0.010
	5th		8.8	0.05		19.0	0.03		18.1	0.02		12.7	0.03
	25th		17.2	0.08		42.8	0.07		23.4	0.04		26.0	0.06
	50th		26.2	0.11		58.5	0.11		43.0	0.07		44.7	0.090
	75th		37.5	0.23		77.1	0.17		63.7	0.13		72.4	0.17
	95th		57.0	0.30		140.6	0.27		147.6	0.26		134.0	0.30
	97.5th		78.7	0.30		224.4	0.27		172.9	0.39		172.9	0.33
	99th		86.4	0.42		224.4	0.33		388.9	0.40		224.4	0.42
	Max		96.5	0.53		247.8	0.66		388.9	0.44		388.9	0.66
Females	Min	46	1.0	0.01	109	8.8	0.02	115	2.0	<0.01	270	1.0	<0.01
	5th		2.5	0.02		18.1	0.03		13.8	0.02		10.7	0.02
	25th		13.8	0.06		23.4	0.04		22.4	0.04		21.4	0.05
	50th		14.1	0.07		37.5	0.09		34.0	0.07		31.2	0.07
	75th		37.5	0.16		57.9	0.13		67.5	0.13		56.2	0.13
	95th		43.7	0.33		178.3	0.29		102.0	0.25		118.9	0.29
	97.5th		63.3	0.36		178.3	0.30		172.9	0.30		172.9	0.30
	99th		71.0	1.06		213.2	0.40		172.9	0.31		178.3	0.36
	Max		71.0	1.06		217.8	0.69		222.1	0.33		222.1	1.06

[a] Data are weighted to be representative of the U.S. population.

The second subpopulation identified in this risk characterization to be of concern consists of children aged 14 years and younger. Although it would be of interest to have subdivided the groups of children into at least two groups (e.g., ages 6 and younger; ages 7 through 14 years), data on children ages 14 and younger are presented as a whole. No age-based subdivision was calculated because of the limitations in the size of various categories. The basis for concern about children is that intake of methylmercury from fish is greater than for adults when expressed on a per kilogram body weight basis. When the methylmercury intake is expressed on a per kilogram body weight basis, the exposure for children aged 14 years and younger is approximately two-to-three times that of the adult. These data for children are presented in Tables 4-10 through 4-13. The higher estimated exposure to methylmercury is the result of the higher intake of food on a per kilogram weight basis among children. A major uncertainty identified in this risk characterization is the absence of data to assess health hazards of methylmercury for children who have low methylmercury exposures *in utero*.

One strength of the data from CSFII 89/91 is that individual body weight data were available and were utilized in calculation of dietary intakes on a per kilogram body weight basis. Consequently actual body weights rather than default values were utilized to estimate methylmercury exposure per kilogram body weight. The methylmercury intakes of adult males and females are comparable on a body weight basis. The maximum intakes on a per kilogram body weight basis are also provided for each group considered. The intakes for the high-end fish consumer (the maximum reported in each group of adults) is at least four times the intake for the individual at the 95th percentile.

Methylmercury intake from fish estimated in this way does not permit attribution to the anthropogenic or "natural" sources of mercury. Because of the magnitude of anthropogenic, ambient mercury contamination, the estimates of methylmercury from fish do not provide a "background" value. "Background" values imply an exposure against which the increments of anthropogenic activity could be added. This is not the situation due to release of substantial quantities of mercury into the environment through human activities and to recycling of this previously released mercury.

4.3 Estimates of Sizes of At-Risk Populations

4.3.1 Human Populations

4.3.1.1 Number of Human Subjects in At-Risk Subpopulations in the United States

The number of human subjects potentially at risk of adverse effects from exposure to methylmercury depends on the health-based endpoint(s) used in the risk assessment, and characteristics of exposure to methylmercury (e.g., quantity of fish consumed, concentration of mercury in the fish consumed). If paresthesias are the health-based endpoint of concern any adult male or female can be considered potentially at-risk depending on the quantity and type of fish consumed. The total population of the United States aged 15 years or greater is approximately 194,858,000 based on the 1990 United States Census data. The male population in these age groups numbers approximately 93,669,000. The female population in these ages numbers approximately 101,187,000. Approximately 30% of the adult population in the U.S. consumes fish on a regular basis.

The risk of paresthesia for children is difficult to estimate because of serious limitations of data on effects of methylmercury exposure among children who were not exposed *in utero*. Initial epidemiology investigations in Minamata and Niigata, Japan, where chronic exposure to methylmercury contaminated fish was the source of mercury exposure, indicated that the highest frequency of disease was observed among subjects ages 20-59 years. Fish consumption among subjects in the age category birth to 10 years of age was lower than for older subjects (see page 64,

Tsubaki and Irukayama, 1977). Cases of fatal Minamata disease, however, included six children (ages 2.5,4.5, 5.0, 6.4, 7 and 8 years) among 38 cases (pages 132-133, Tsubaki and Irukayama, 1977). Because the methylmercury contamination in Minamata area existed for a number of years clear separation of prenatal from postnatal exposure is not possible. Harada (1977, page 220 in Tsubaki and Irukayama, 1977) provided an analysis of the frequency of occurrence of various symptoms and signs in Minamata disease. Adults had a 100 percent incidence of paresthesia. Occurrence of paresthesia among congenital cases and children was considered not clear, but Harada noted that all patients had a sensation of pain.

Children were also affected by methylmercury poisoning in the Iraq epidemic. Rustam and Hamdi (1974) included the age groups "birth through 10 years" and "11 through 20 years" in the patients they evaluated in a neurological study of methylmercury poisoning in Iraq. The pediatric patients were not cases of *in utero* exposure because the youngest of this group was identified as 5 years of age. In their discussion of individual variation in response to mercury, Rustam and Hamdi observed that "in general, younger patients suffered heavier damage than the older ones" (page 509, Rustam and Hamdi, 1974).

Exposure patterns for children (see Volume III and Section 4.7 of Volume VI) suggest that their exposure to methylmercury on a "per kilogram body weight" basis is much higher compared with adult exposures. Neuronal migration, a process specifically affected by methylmercury, begins at about six weeks *in utero*, and that process continues until five months after birth (Chi et al., 1977). Considering the broad-based impairment of nervous system metabolism that can be produced by methylmercury (among others see Atchison and Hare, 1994); that nervous system development continues post-natally through at least the third to fourth year of life [visual connections are complete around 3 to 4 years of age (Hohman and Creutzfeld, 1975)]; and that the human brain is not fully mature in form until approximately age 20 (Rodier, 1994) children may be more sensitive to adverse sensory-motor effects of methylmercury than are adults. If children are arbitrarily defined as persons aged less than 15 years, the U.S. population is approximately 53,853,000 based on 1990 census data (Table 4-14).

Table 4-14
Resident Population of the United States and Divisions, April 1, 1990 Census by Gender and Age; in Thousands, including Armed Forces Residing in Region

Division/Gender	Total	<15 Years of Age	15-44 Years of Age	≥45 Years of Age
United States	248,710	53,853	117,610	77,248
Male	121,239	27,570	58,989	34,680
Female	127,471	26,284	58,620	42,567
Percent Female	51.3	48.8	49.8	55.1

Developmental endpoints have also been used to establish the critical effects for methylmercury. Estimates of the size of the population of women of reproductive age, number of live

births, number of fetal deaths, and number of legal abortions can be used to predict the percent of the population and number of women of reproductive age who are pregnant in a given year. This methodology has been previously used in the Agency for Toxic Substances and Disease Registry's (ATSDR's) Report to Congress on *The Nature and Extent of Lead Poisoning in Children in the United States* (Mushak and Crocetti, 1990). To estimate the size of this population on a national basis *Vital and Health Statistics* data for number of live births (National Center for Health Statistics of the United States, 1990; Volume I, Natality, Table 1-60, pages 134-140), and fetal deaths (National Center for Health Statistics of the United States, 1990; Volume II, Mortality; Table 3-10, pages 16, 18, and 20). The incidence of fetal wastage, that is, spontaneous abortions prior to 20 weeks of gestation was not considered since no systematically collected, nationally based data exist.

The estimate of number of women of child-bearing age includes some proportion of women who will never experience pregnancy. However, substitution of the number of pregnancies in a given year provides some measure of assessing the size of the surrogate population at risk. Estimates of the size of the population were based on "Estimates of Resident Population of the United States Regions and Divisions by Age and Sex" (Byerly, 1993). The Census data for 1990 were grouped by age and gender. The sizes of these populations for the contiguous U.S. are shown in Table 4-15.

Women ages 15 through 44 are the age group of greatest interest in identifying a subpopulation of concern for the effects of a developmental toxin such as methylmercury. This population consisted of 58,222,000 women living within the contiguous United States (Table 4-15). This population was chosen rather than for the total United States (population 58,620,000 women ages 15 through 44 years) because the dietary survey information from CSFII/89-91 did not include Hawaii and Alaska. Based on estimates of fish consumption data for Alaska by Nobmann et al. (1992) the quantities of fish eaten by Alaskans exceeds those of the contiguous U.S. population. It is also estimated that residents of the Hawaiian Islands have fish consumption patterns that differ from those of the contiguous United States.

The number of women of child-bearing age (15 through 44 years) in Alaska is estimated to be approximately 138,000 and in Hawaii, the approximate number is 284,000 women. The percentage of pregnant women for ages 15 through 44 eyars in Alaska was 9.7 percent, and in Hawaii this percentage was also 9.7 percent.

Table 4-15
Resident Population of the Contiguous United States, April 1, 1990 Census by Gender and Age; in Thousands, including Armed Forces Residing in Region

Division/Gender	Total	<15 Years of Age	15-44 Years of Age	≥45 Years of Age
Contiguous United States	247,052	53,462	116,772	76,817
Male	120,385	27,369	58,548	34,467
Female	126,667	26,094	58,222	42,348
Percent Female	51.3	48.8	49.9	55.1

The number of pregnancies per year was estimated by combining the number of live births, number of fetal deaths (past 20 weeks of gestation) and the number of legal abortions. The legal abortion data were based on information published by Koonin et al. (1993) in Morbidity and Mortality Weekly Report. These totals are presented in Table 4-16. As noted in this table, the total of legal abortions includes those with unknown age which were not included in the body of each table entry. There were 2,929 such cases for the United States in 1990 or 0.2 percent of all legal abortions. Another complication in the legal abortion data was for the age group 45 and older. The available data provide abortion data for 40 years and older only. To estimate the size of the population older than 45 years, the number of legal abortions for women age 40 years and older were allocated by using the proportions of Live Births and Fetal Deaths for the two age groups 40-44 and 45 and older.

Table 4-16
Pregnancies by Outcome for Resident Females by Divisions and States, U.S. 1990, by Age[a]

		Total[b]	<15 Years	15-44 Years	≥45 Years[c]
United States	Females	127,471,000	26,284,000	58,620,000	42,567,000
	Live births	4,158,212	11,657	4,144,917	1,638
	Fetal deaths	31,386	174	31,176	36
	Legal abortions	1,429,577	11,819	1,413,992	837
	Total pregnancies	5,619,175	23,650	5,590,085	2,511
	Percent Pregnant	--	--	9.5	--
Contiguous United States	Females	126,667,000	26,094,000	58,222,000	42,348,000
	Live births	4,125,821	11,615	4,112,579	1,627
	Fetal deaths	31,183	173	30,974	36
	Legal abortions	1,423,340	11,765	1,407,830	833
	Total pregnancies	5,580,344	23,553	5,551,383	2,496
	Percent Pregnant	--	--	9.5	--

[a] Data sources: Byerly ER, State Population Estimates by Age and Sex: 1980-1992, U.S. Bureau of the Census. National Center for Health Statistics of the U.S. Vol. I. Natality, Vol. II. Mortality, 1990. Koonin et al. Abortion Surveillance - US, 1990: MMWR 42:29-57, 1993.
[b] Total of legal abortions includes those with unknown age which are not included in the body of each table entry. There were 2929 such cases for the U.S. or 0.2 percent of all legal abortions.
[c] Cited sources provided abortion data for 40 years and older only. These were allocated by using the proportion of live births and fetal deaths for the two age groups 40-44 and 45 and older.

It was estimated that within the contiguous United States 9.5 percent of women ages 15 through 44 years were pregnant in a given year. The total number of live births reported in 1990 for

this age group was 4,112,579 with 30,974 reported fetal deaths and 1,407,830 reported legal abortions. The estimated number of total pregnancies for women ages 15 through 44 years was 5,551,383 in a population of 58,222,000 women (Table 4-16).

4.3.1.2 Populations Associated with High Consumption of Fish

Exposure to methylmercury depends on quantities of fish consumed, mercury concentrations in the fish chosen, and duration of these consumption patterns. Three types of data were used to predict the size of the adult female population potentially at-risk. In Section 5.3 of this Volume, comparison are made between exposures and recommendations by the World Health Organization that women consuming 100 grams or more of fish per day should be evaluated for the extent of methylmercury exposures.

Estimated Population Based on Longitudinal Data from NPD, Inc. 1973/74

Using data from NPD, Inc. obtained in 1973 and 1974, it was estimated that 94% of women consumed fish or shellfish at least once in a one-month period. If 9.5% of the female population is pregnant every year, then from these data it is estimated that 8.9% of pregnant women consume fish at least once per month. Among these consumers the 99th percentile consumption was 112 grams/day for adult men and women between the ages 18 and 98 years (Rupp et al., 1980). For female subjects estimated intake of fish at the upper ranges of intakes is shown in Table 4-17.

Table 4-17
Number of Pregnant Women Consuming Fish
at Various Intake Levels Based on Data from NPD,Inc. 1973/74
and 1990 U.S. Census Data

Estimated Quantity of Fish Consumed	Estimated Number of Pregnant Women
> 60 grams/day	55,785
At the 99th Percentile or 112 grams of fish and shellfish per day	51,867
> 120 grams/day	1,484

Estimated Population Based on Cross-Sectional Data

The number of women of child-bearing age in the United States estimated to consume fish in excess of 100 grams per day can be obtained by inference from the general U.S. population dietary surveys (e.g., United States Department of agriculture's CSFII 89/91). Intake of fish and shellfish for the general U.S. population (estimated by CSFII 89/91 data described in Appendix H, Volume III) based on "users" only was estimated to be 110 grams per day at the 95th percentile among women ages 15 through 44 years. Female children (aged 14 years or younger) consumed 112 grams of fish per day, at the 95th percentile while the overall intake at the 95th percentile among female subjects regardless of age was 107 grams per day. Estimates of the number of women of child-bearing age (ages 15 through 44 years) and the number of children (ages birth through 14 years) within the United States population is shown in Table 4-18.

Table 4-18
Estimated United States Population Consuming Fish, Excluding Alaska and Hawaii
Estimates Based on the 1990 U.S. Census and the Continuing Surveys of Food Intake
by Individuals, 1989/1991

Population Group	Estimated Number of Persons
Total U.S. Population	247,052,000
Total Female Population Aged 15 through 44 Years	58,222,000
Total Population of Children Aged <15 Years	53,463,000
Percent of Respective Group Reporting Fish Consumption during the 3-Day Dietary Survey Period in CSFII 89/91[a]	
Total Population	30.9 percent
Females Aged 15 through 44 Years	30.5 percent
Children Aged <15 Years	24.9 percent
Number of Persons Predicted to Consume Fish Based on Percentage Consuming Fish in CSFII 89/91	
Total Estimated Population	76,273,000
Total Estimated Number of Females Aged 15 through 44 Years	17,731,000
Total Estimated Number of Children Aged <15 Years	13,306,000
Number of Persons in Highest 5 Percent of Estimated Population that Consumes Fish	
Total Estimated Population	3,814,000
Total Estimated Female Population Aged 15 through 44 Years	887,000
Total Estimated Child Population	665,000
Estimated Number of Adult Pregnant Women in Highest 5 Percent Of Estimated Population that Consumes Fish	
Number of Females Aged 15 through 44 Years x Percentage of Women Pregnant in a Given Year	84,300

[a] Rounded to three significant figures.

The estimated number of women of child-bearing age (ages 15 through 44 years) in the contiguous 48 states is approximately 17,731,000. It is estimated that in a given year 9.5% of women in this age group are pregnant. The estimated number of women ages 15 through 44 years in the highest 5 percent of consumers identified in a cross sectional survey with a 3-day sampling window is 887,000. The estimated number of pregnant women in that highest 5 percent of fish consumers is estimated to be approximately 84,300; this is the number of pregnant women expected to consume an average of 100 g fish/day The type of fish consumed and the amount of mercury in those fish will affect the over all mercury exposure.

Specific Subpopulations of Anglers and Subsistence Fishers

Specific subpopulations of anglers and subsistence fishers ingest fish substantially in excess of the consumption by the general population. Fish consumption by these groups, by comparison to the general U.S. population, is shown in Figure 4-5. For example, Puffer et al. (1981) in a study of anglers in Los Angeles, California found a mean intake was 37 grams per day, but the 90th percentile for this group was 225. grams per day. Orientals and Samoans had mean fish intakes of 70.6 grams/day (Puffer et al., 1981). Alaskan Natives from 11 communities averaged 109 grams of fish/day (Nobbman et al., 1992). Wolfe and Walker identified a very high fish consumption rate among persons living in remote Alaskan communities. The Columbia River Intertribal Fish Commission (1994) reported that during the two months of highest average fish consumption average intake was 108 grams per day. The Tribes of Puget Sound reported (Toy et al., 1995) an average intake of 73 grams per day with a 90th percentile intake of 156 grams/day. West et al. (1989) found a mean intake of approximately 22 grams/day, but a reported maximum value over 200 grams/day. Peterson et al. 91994) in a study of Chippewa tribes found that 2 percent of 323 respondents ate at least one fish meal each day. In these individual tribal and angler studies, data were generally not separately reported for women of child-bearing age.

Estimated Exposure to Methylmercury from Fish

The extent to which elevated fish consumption by adult women (e.g., highest 1 to 5% of female consumers with sustained consumption of fish resulting in intakes of 100 grams per day or greater) is associated with increased exposure to methylmercury depends on the concentration of mercury in the type of fish as well as the total quantity consumed. Detailed analysis of the NPD, Inc. 1973/74 data were not conducted because of changes in the quantity and types of fish consumed between 1973/74 and the present; and because these data were not designed to be representative of the United States population. Using the cross-sectional data from CSFII 89/91 the fish consumed were analyzed to assess the top 25 species of fish consumed. These fish species and the average mercury concentration used to calculate mercury exposures are shown in Table 4-18. These species represent approximately 95% of the fish reported to be consumed by people surveyed in CSFII 89/91. When weighted by the frequency of consumption, the mean mercury concentration was 0.134 micrograms per gram wet weight of fish. Consumption of a 100 gram portion of fish with the mixture of fish species shown in Table 4-19 at mean mercury concentrations is estimated at 13.4 micrograms of mercury.

The CSFII 89/91 data were analyzed to determine broad categories of fish consumed for three groups: all persons in the survey who reported consuming fish or shellfish; persons who reported consuming fish or shellfish at 100 grams per day or greater; persons whose exposure to mercury was estimated to be 1 microgram/kg body weight/day or greater. These data are shown in Table 4-20 for all consumers, Table 4-21 for women of child-bearing age, and 4-22 for children ages 14 and younger. For adults, comparison of the types of fish consumed indicates that mercury exposures of 1 μg/kg bw/day and higher are associated with much higher consumption of swordfish, shark and barracuda than is seen for all adult consumers. For children, the basis for mercury exposures of 1 μg/kg bw/day or higher is not intake of swordfish, shark, or barracuda. Based on the analysis of the CSFII 89/91 the basis for mercury exposures of 1 μg/kg bw/day or higher is generally higher intake of fish relative to body size.

Among anglers and members of some Native American Tribes intakes of fish higher than those of the general population have been reported. Detailed descriptions of these studies have been presented in Volume III of this Mercury Study Report to Congress. Figure 4-5 summaries the higher end fish/shellfish consumers. The level of mercury exposure for these groups depends on the mercury

Figure 4-5
Distribution of fish Consumption Rates
of Various Populations

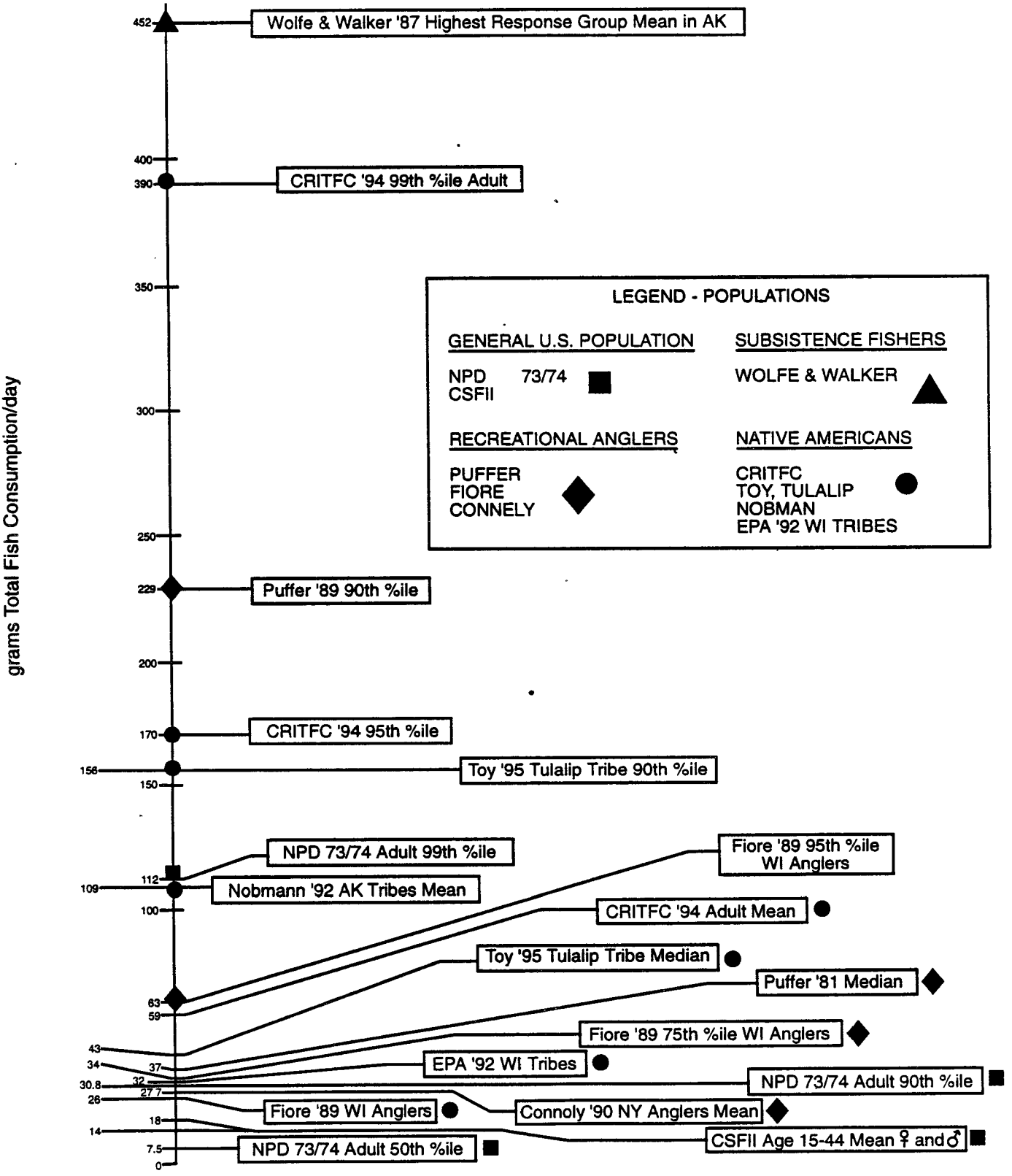


Table 4-19
Fish Species by Percent of Consumption in CSFII 89/91,
Mean Mercury Concentration and Mercury Levels in 100 gram Servings of Fish

Fish/Shellfish Species	Percent of Overall Fish or Shellfish Reported as Consumed by Respondents in CSFII 89/91	µg Hg/Gram of Fish or Shellfish on a Wet Weight Basis	µg Hg/100 Gram Serving of Fish or Shellfish
Tuna	31.88	0.206	6.567
Shrimp	10.71	0.047	0.503
Flatfish	10.55	0.144	1.519
Cod	6.51	0.121	0.788
Catfish	4.23	0.035	0.148
Salmon	4.21	0.035	0.147
Pollock	4.01	0.150	0.602
Perch	3.58	0.110	0.394
Clams	3.42	0.121	0.414
Crab	3.33	0.117	0.390
Haddock	2.56	0.089	0.228
Trout	2.04	0.149	0.304
Ocean Perch	1.58	0.116	0.183
Scallops	1.30	0.042	0.055
Oysters	1.06	0.023	0.024
Sardines	0.90	0.050	0.045
Whiting	0.780	0.050	0.039
Mackerel	0.5558	0.081	0.047
Pompano	0.52	0.104	0.054
Mullet	0.38	0.009	0.004
Herring	0.34	0.013	0.004
Swordfish	0.28	0.95	0.27
Squid	0.28	0.026	0.01
Croaker	0.24	0.125	0.03
Anchovies	0.24	0.047	0.01

Table 4-20
Percent of Dietary Intake by Species-Category of Fish/Shellfish
for Persons Consuming Fish or Shellfish (from CSFII 89/91)

Type of Fish	All Persons Consuming Fish or Shellfish (%)	Persons Consuming Fish or Shellfish at 100 grams/day or more (%)	Persons Consuming Fish or Shellfish at 1 µg Hg/kg body weight or more (%)
Finfish (Except as listed below)	40.6	34.7	23.0
Tuna	25.8	12.3	24.0
Shellfish	16.9	27.6	19.0
Swordfish, Shark and Barracuda	0.7	1.2	27.6
Freshwater Fish	16.0	23.8	6.4
Total Fish	to 100.0	to 100.0	to 100.0

Table 4-21
Percent of Dietary Intake by Species-Category of Fish/Shellfish by Women of Child-Bearing Age (from CSFII 89/91)

Type of Fish/Shellfish Consumed	All Women of Child-Bearing Age Who Reported Consuming Fish/Shellfish (%)	Women Consuming 100 grams or more Fish/Shellfish per Day (%)	Women with Mercury Exposure of 1 µg/kg body weight/day or higher (%)
Finfish (Except as listed below)	40.3	37.3	19.7
Tuna	26.1	10.5	9.1
Shellfish	16.7	27.9	14.6
Swordfish, Shark and Barracuda	0.8	1.9	45.7
Freshwater Fish	15.6	22.5	10.8
Total Fish and Shellfish	to 100.0	to 100.0	to 100.0

Table 4-22
Percent of Dietary Intake by Species-Category of Fish/Shellfish by Children Ages 14 Years and Younger (from CSFII 89/91)

Type of Fish/Shellfish Consumed	All Children Reporting Fish Consumption	Children Consuming > 100 grams/day	Children with Mercury Exposures > 1 µg/kg body weight/day or more
Finfish *	43.8	35.0	22.4
Tuna	32.3	23.2	42.5
Shellfish	11.0	37.2	28.6
Swordfish, Shark or Barracuda	0	0	0
Freshwater Fish	12.9	4.7	6.5
Total Fish and Shellfish	to 100.0	to 100.0	to 100.0

* Except as listed below.

mercury/gram fresh weight identified from the mix of fish reported in CSFII 89/91) with individual fish species provides an estimate for specific groups. If fish such as salmon with a mercury concentration of 0.035 µg mercury/gram fresh weight or shellfish (scallops and oysters averaging 0.055 and 0.024 µg mercury/gram fresh weight, respectively) are chosen, mercury exposure would be lower than that predicted for the general diet. However, if fish species with substantially higher mercury concentrations are chosen mercury intake will be increased above that predicted for the general diet.

Recreational anglers and members of Native American Tribes consume fish from the general food supply as well as self-caught fish. For example, Fiore et al. (1989) reported mean, 75th and 95th percentile consumption of fish among licensed anglers in Wisconsin. A comparison of total fish intake and daily intake of sports-fish is shown in Table 4-23. Sports-fish comprised less than 50% of the intake of fish among this group of anglers. Toy et el. (1995) reported on fish and shellfish consumption among the Tulalip and Squaxin Island Tribes living near Puget Sound. Both tribes rely on commercial fishing as an important part of tribal income. Subsistence fishing and shell-fishing are significant parts of tribal members economies and diets. Among consumers of anadromous fish, local waters (i.e., Puget Sound) supplied a mean of 80% of the fish consumed. Survey respondents from the Tulalip Tribes purchased approximately two-thirds of fish from grocery stores or restaurants, while among the Squaxin Island Tribe, the source of fish was about 50% self-caught and 50% purchased from grocery stores or restaurants.

Table 4-23
Total Fish Intake and Intake of Sports-fish by Licensed Wisconsin Anglers as Reported by Fiore et al., 1989

Level of Fish Consumption	Intake of Sports-fish grams/day	Total Fish Intake gms/day
Mean	12.3	26.1
75th Percentile	15.5	34.2
95th Percentile	37.7	63.4

Data on fish purchases by members of Native American Tribes and by anglers indicate that persons who "subsist" on self caught fish also purchase fish commercially. The National Academy of Sciences-National Research Council report Seafood Safety indicated that approximately 20% of fish and shellfish are obtained outside of commercial sources (NAS/NRC, 1990).

Using age-specific data on the number of women predicted to be pregnant in a given year, the number of pregnant women consuming fish at various levels is shown in Table 4-24.

Table 4-24
EstimatedNumber of Pregnant Women Consuming Fish at Various Intake Levels Based on Data from NPD,Inc. 1973/74 and 1990 U.S. Census Data

Estimated Quantity of Fish Consumed	Estimated Number of Pregnant Women
> 60 grams/day	55,785
At the 99th Percentile or 112 grams of fish and shellfish per day	51,867
> 120 grams/day	1,484

concentration of the fish consumed. Comparison of the estimated average mercury concentration for a broad mixture of fish species (e.g., 0.13 to 0.14 μg).

4.3.2 Estimates for the Size of the Piscivorous Wildlife Population

Five wildlife species were considered in the exposure and ecological risk Volumes of this assessment. The five species were selected because they consumed fish. The selected species consisted of three avian species (the bald eagle, osprey and belted kingfisher) and two mammalian species (the river otter and mink). Estimates of the sizes of these populations in the U.S. are presented as part of the risk characterization. These population size estimates are uncertain; generally a range or an imprecise estimate is presented. For most of these population estimates, there is no good method for corroboration. It should also be noted that these piscivorous wildlife populations are not the only species potentially exposed through the fish consumption route.

4.3.2.1 Bald Eagle

An estimated 10,000 to 12,000 bald eagles inhabit the lower 48 United States. This total represents combined estimates of the total number of breeding pairs and immature eagles. U.S. Fish and Wildlife Service (1994) estimated that there are 4,016 breeding pairs in the lower 48 states. The Peregrine Fund, Inc. estimates that there are several thousand sexually immature eagles dwelling in the same geographic area (Petit, 1995).

4.3.2.2 Osprey

The size of the U.S. osprey population is estimated to be between 10,000 and 20,000 individuals. This estimate is based on a compilation of individual state population size estimates reported in the literature (Petit, 1995).

4.3.2.3 Belted Kingfisher

Population estimates for small birds such as the belted kingfisher have a larger degree of uncertainty because they are based on species density estimates and it is not possible to assess the accuracy of such predictions. Petit (1995) presents a rough estimate of approximately 170,000 belted kingfishers in the lower 48 states. This estimate is the product of estimated kingfisher densities from the breeding bird survey and total land area of the lower 48 United States.

4.3.2.4 Mink

The National Geographic Society (1960) estimated that approximately 1,000,000 mink are trapped each year on the North American continent. The source of this information is clearly dated. If one assumes that 10 percent of the population is snared each year, then, roughly 10,000,000 mink live on the North American Continent (Petit, 1995). There is a great deal of uncertainty in this estimate.

4.3.2.5 River Otter

Although the original otter range encompassed all the U.S. states on the North American continent, the species range is presently more limited. Otter populations are considered stable across the United States (Jenkins, 1983), although they are listed as endangered species in several states.

The book *Wild Mammals of North America Biology, Management, and Economics* edited by Chapman and Feldhamer (1982) reports that otters are extremely difficult to count noting the questionable accuracy of most index techniques. The book notes that most states base otter population estimates on the reports of trapper and furbuyers. Jenkins (1983) estimated that, in a one-year period over 1978 and 1979, 29,000 otters were harvested in the United States. Using the crude estimation that 10 percent of the total population is eliminated by trapping in a given year, there are roughly 300,000 otters inhabiting the United States.

5. INTEGRATIVE ANALYSIS FOR METHYLMERCURY

5.1 Characterization of Risk: Quantitative Integration of Human and Wildlife Exposure and Dose-Response

5.1.1 Introduction

In this chapter findings from the exposure analyses are integrated with those from the dose-response assessments for both humans and wildlife. This integration is done only for methylmercury, as the exposure assessment indicates this is the form to which the greatest exposure is likely. The quantitative dose-response measures used for methylmercury are these: the human RfD of $1x10^{-4}$ mg/kg-day and the benchmark dose from which it was derived; the individual wildlife criteria and the wildlife RfDs, LOAELs and NOAELs on which they were based.

The purpose of Section 5.2 was to determine which of the species considered to consume fish from the hypothetical water body (developed in Volume III) is expected to be adversely affected by the lowest methylmercury concentrations in fish (that is, individuals of which species are expected to be the most at risk from methylmercury concentrations in fish). Comparisons of the fish consumption rate assumptions for humans and the five wildlife species considered (presented in Volumes III and V) and the health endpoint data (developed in Volumes IV and V) for the species considered are presented. Assumptions employed to estimate the transport of mercury through the aquatic food chain model (developed in Volumes III and V) are described to illustrate the impact of selected uncertainties underlying the assumptions. The fish consumption rate assumptions and the health endpoint data were then integrated to assess which species is most at risk from methylmercury in fish.

The aim of Section 5.3 was to compare quantitative dose-response estimates or recommendations with measured mercury levels in fish and to determine the numbers of individuals estimated to consume those mercury levels. This comparison gives an indication of the size of the population that is not likely to be impacted by mercury. Comparisons with the total population numbers gives an indication of the size of the "at risk" population.

5.1.2 Description of Subsistence Fishers

The term "subsistence fishers" has been used to describe various persons who rely on fish as a major source of protein. "Subsistence fishers" are not defined by whether the fish/shellfish are self-caught or obtained for money. Groups with high fish intake are typically determined by social, economic, ethnic, and geographic characteristics. An additional group of people consume high levels of fish in response to numerous health-based messages that have promoted the consumption of fish to reduce the likelihood of disease, particularly of the cardio-vascular system. Further, there are large numbers of people who simply prefer fish and shellfish as a source of protein. Consequently in the following analyses, "high-end fish consumers" include these groups: anglers; members of some Native American Tribes; members of ethnic groups who consume higher than typical intakes of fish; persons who preferentially select fish for health-promotion purposes; individuals who relish the taste of fish; and persons who rely on self-caught fish from local sources because of limited money to buy food.

Although humans have a degree of choice on their source of protein, the wildlife described have much more restricted choices on protein sources because they are confined spatially or territorially. Consequently all consumption by wildlife has been assumed to be locally caught, although the highest predators in the aquatic food web cover wide territories.

5.2 Integration of Modeled Methylmercury Exposure Estimates for Humans and Wildlife with the Dose-Response Assessments

5.2.1 Methylmercury Intake by Humans and Wildlife Based on Modeling of Fate and Transport of Mercury and Patterns of Fish Intake

A comparison of pollutant exposure levels across the species in an ecosystem requires, among other things, a knowledge of the environmental fate and transport of the pollutant (including chemical transformation of the pollutant in the environment), the contact medium of interest, as well as the contact rates and body weights of the wildlife species and the human subpopulations of interest in the ecosystem.

Although methylmercury is found in other media and biota, it accumulates to the highest concentrations in the muscle tissues of fish, particularly piscivorous fish. This conclusion is based upon both the measurement data and the results of the modeling presented in the Volume III of this Report. Methylmercury remains essentially unchanged in fish tissue, when subjected to human preparation methods (i.e., cooking). Although methylmercury exposure may occur through other routes (for example, the ingestion of methylmercury-contaminated drinking water and the consumption of food sources other than fish such as amphibians or reptiles, the inhalation of atmospheric methylmercury, and dermal uptake through contact with soil and water), the fish consumption pathway dominates these other methylmercury exposure pathways in piscivores. This is clearly the result of the bioaccumulation of methylmercury in their food source, fish, and because this compound is highly bioavailable from fish. Other forms of mercury are also toxic, but since they are not known to accumulate in commonly eaten foods, and since they are not as bioavailable in most media, they are not of as great a concern. Consequently, the following comparison of methylmercury contact rates is based solely on the daily ingestion rate of fish and assumptions pertaining to the transport of methylmercury through the aquatic food chain.

The piscivores selected for analysis were these: human recreational angler, human high-end local fish consumer (or subsistence fisher), child of a high-end local fish consumer, bald eagle, osprey, kingfisher, mink and otter. All species were assumed to consume fish from the same lake and the same concentrations of methylmercury were assumed to exist in the fish of the same trophic level. The piscivore's estimated methylmercury contact rate from fish consumption was based on two important factors: the methylmercury concentration in the contaminated fish and the daily amount of fish eaten.

The methylmercury concentration in fish was estimated by multiplying the total dissolved mercury concentration in water by a bioaccumulation factor (BAF). The predicted ranges and patterns of mercury concentrations in surface waters at hypothetical locations near the hypothetical mercury sources (the model plants) and under other deposition assumptions have been described in Volume III. The type of model plant is predicted to be the most critical factor affecting mercury concentrations in surface waters. Local water bodies in proximity to anthropogenic sources emitting substantial levels of divalent mercury or close to sources with low stack heights or slow stack exit gas velocities were predicted to be more highly impacted by stack mercury releases than those water bodies near sources emitting lower levels of mercury or having higher effective stack heights. Based on the modeling presented in Chapter 6 of Volume III, the closer a water body is to a mercury emissions source, the higher the resulting mercury concentrations in the water body. (See the related discussion in Chapter 6 of Volume III.) This also assumes that the size of the watershed and transport of mercury in the

watershed of each lake is the same. It is also important to remember that this modeling was conducted assuming flat terrain surrounding the model plants.

For locations that are assumed to be influenced only by long-range atmospheric mercury transport, the concentrations of mercury in surface waters were a function of overall proximity to anthropogenic sources, increased soot and ozone levels in the atmosphere and elevated rainfall. (See the related discussion in Chapter 5 of Volume III.)

The concentrations of methylmercury in fish are also influenced by the fishes' diets. (The bioaccumulation model is described in Volume V). Briefly, in the four-tier trophic food chain model used in this effort, fish are assumed to feed at two levels: trophic level 3 fish were assumed to feed on plankton which have lower levels of methylmercury, and trophic level 4 fish were assumed to feed on trophic level 3 fish, which, due to bioaccumulation, had higher methylmercury concentrations than the plankton upon which they feed. The bioaccumulation factor (BAF) (66,200) for trophic level 3 fish was estimated based on several sets of collected data. The BAF for trophic level 4 (335,000) was estimated by applying a predator-prey factor (of approximately 5) to the bioaccumulation factor estimated for trophic level 3 fish.

The BAF model assumed that the higher the dissolved total mercury concentrations in the local waters, the proportionally greater the methylmercury concentration in the fish; and, as a consequence, the higher the methylmercury exposure of the piscivores. The biomagnification of methylmercury as modeled through the aquatic food web significantly impacts the exposure of piscivores. Those piscivores consuming a diet primarily consisting of trophic level 3 fish would be predicted to receive approximately 5 times less (20 percent) methylmercury per gram of fish eaten than those eating trophic level 4 fish from the same site. Humans, which are assumed to eat only trophic level 4 fish, will have a greater methylmercury exposure per gram of fish consumed than ospreys and kingfishers, which are assumed to consume only trophic level 3 fish from the same water bodies. Similarly, otters, which are assumed to consume an 80/20 mix of trophic level 3 and 4 fish will have a greater methylmercury exposure per gram of fish consumed than minks, which are assumed to eat only trophic level 3 fish.

The ratio of grams fish consumed per day to piscivore body weight is also important in estimating methylmercury exposure on a g/kg bw/day basis. The greater this ratio the higher the resulting methylmercury exposure assuming methylmercury concentrations in consumed fish are constant. For example, osprey and kingfishers each consume trophic level 3 fish only. Since kingfishers daily consume 50 percent of their body weights in fish and osprey roughly 20 percent of their body weights in fish of the same trophic level, the resulting average daily methylmercury intake in g/kg body weight will be higher among the kingfisher population.

Assuming that these piscivorous birds and mammals and the human fish-eating subpopulations consume fish from the same lake, the estimates of daily consumption rates, the trophic level of the fish consumed and the body weight of the animal all contribute significantly to methylmercury exposure when expressed on a per kg of body weight basis. For example, the daily fish consumption of the otter is approximately 16 percent of body weight and that of mink is 20 percent. Trophic level 4 fish are assumed to make-up roughly 20 percent of the otter's total fish consumption with the other 80 percent consisting of trophic level 3 fish; on the other hand, minks are assumed to eat exclusively trophic level 3 fish. As a result of percent of daily body weight consumed as fish and the trophic level of fish consumed, otters will have a higher methylmercury contact rate than mink.

By using the relationship for methylmercury described by the four-tier trophic food chain model (i.e., the different bioaccumulation factors for fish in trophic levels 3 and 4), the estimates of the daily fish consumption rates from each trophic level and the body weight of the animal, the rates of methylmercury exposure (in mg/kg bw/day) for the animals in this hypothetical environment can be ranked. To illustrate this, assume that for a lake at a given location all trophic level 3 fish are contaminated with 0.1 μg methylmercury/g fish tissue; the trophic level 4 fish would be predicted to have methylmercury concentrations of 0.5 μg/g. Eagles at this lake daily consume (370 g/day x 0.1 μg methylmercury/g fish tissue) + (90 g/day x 0.5 μg methylmercury/g fish tissue)= 82 μg methylmercury/day; given the body weight estimate 4.5 kg, the rate of exposure is estimated as 18 μg/kg bw/day.

Continuing the example exposure estimates for the other species: ospreys at this lake: 0.1 μg/g x 300g/day/1.5 kg bw = 20 μg/kg bw/day; kingfishers at this lake: 0.1 μg/g x 75/0.15 = 50 μg/kg bw/day; otters at this lake consume both trophic level 3 and 4 fish: (0.1 μg/g x 976 g/day + 0.5 μg/g x 244 g/day)/7.4 =30 μg/kg bw/day; mink at this lake: 0.1 μg/g x 160.2 g/day/0.8 = 20 μg/kg bw/day; and high-end fish-eating humans at this lake: 0.5 x 60 g/day/70 = 0.4 μg/kg bw/day.

From the modeling standpoint the methylmercury levels in the trophic level 3 fish or the total dissolved mercury concentration in the water is irrelevant to the rank; only the relationship between the aquatic trophic levels is critical. Using this model and the assumptions in Tables 5-1, 5-2 and 5-3, the predicted piscivore exposure ranking from highest to lowest is: kingfisher > otter > osprey, mink > bald eagle > human.

Table 5-1
Assumed Human Fish Consumption Rates and Body Weights Used in the Exposure Modeling

Subpopulation	Assumed Body Weight (kg)	Assumed Local Fish Consumption Rate ($g_{wet\ weight}$/day)
Adult High-End Fish Consumer	70	60
Child High-End Fish Consumer	17	20
Adult Recreational Angler	70	30

Table 5-2
Assumed Fish Consumption Rates and Body Weights of Piscivorous Birds and Mammals Used in the Exposure Modeling

Animal	Body Weight	Total Ingestion Rate ($g_{wet\ weight}$/day)	Percent of Diet Consisting of Trophic Level 3 Fish	Percent of Diet Consisting of Trophic Level 4 Fish	Percent of Non-Aquatic Foods in Diet
Bald Eagle	4.6	500	74	18	8
Osprey	1.5	300	100	0	0
Kingfisher	0.15	75	100	0	0
River Otter	7.4	1220	80	20	0
Mink	0.8	178	90	0	10

Table 5-3
Assumed Fish Consumption Rates of Piscivorous Birds and Mammals Used in the Exposure Modeling

Animal	Trophic Level 3 Fish Ingestion Rate (g/day)	Trophic Level 4 Fish Ingestion Rate (g/day)
Bald Eagle	370	90
Osprey	300	0
Kingfisher	75	0
River Otter	976	244
Mink	160.2	0

The ranking demonstrates the importance of the trophic level of the fish which the piscivore consumes, the daily consumption rate, and the ratio of daily fish consumption rate to body weight. Despite consuming a comparatively small amount of trophic level 3 fish, the kingfisher ranked first in this exposure ranking scheme; these birds consume large amounts of fish on a daily basis by comparison to their body weights. This use of this method also illustrates that within this hypothetical ecosystem the human methylmercury contact rate based on fish consumption is much lower than that of these piscivorous wildlife.

5.2.2 Comparison of Dose-Response Estimates Across Species

The second step for ranking species at risk from fish-related methylmercury exposure entails a comparison of the health endpoints and the associated dose-response across species. The chemical species of mercury (i.e., methylmercury) and the route of exposure (i.e., fish consumption) are the same for all wildlife and human species. For the comparisons across health endpoints to be valid, the health effects must be judged to be of similar concern for the species considered.

Methylmercury (as described in Volumes IV and V of this Report) has deleterious effects on the chordate nervous system. Methylmercury also efficiently passes through the intestinal walls of chordates and into the blood. Once in the blood, methylmercury may cross the blood brain and placental barriers and impact the potentially affected neuronal tissues.

The human health endpoint of concern is developmental neurotoxicity. The health endpoints of concern for the avian wildlife species are reproductive and behavioral deficits and for the mammalian quadrupeds are neurological effects. For more details see Volumes IV and V.

Assuming that the effects are of similar concern for the well-being of individuals within a species, the NOAELs, LOAELs and the human and wildlife WCs for these health endpoints can then be compared across species.

U.S. EPA has on two occasions published RfDs for methylmercury which have represented the Agency consensus for that time. These are described in the sections below. At the time of the generation of the Mercury Study Report to Congress, it became apparent that considerable new data on the health effects of methylmercury in humans were emerging. Among these are large studies of fish or fish and marine mammal consuming populations in the Seychelles and Faroes Islands. Smaller scale studies are in progress which describe effects in population s around the U.S. Great Lakes. In addition, there are new evaluations of published work described in section 3.3.1.1 of Volume IV, including novel statistical approaches and application of physiologically based pharmacokinetic models.

As the majority of these new data are either not yet published or have not yet been subject to rigorous review, it was decided that it was premature for U.S. EPA to make a change in the methylmercury RfD at this time. An interagency process, with external involvement , will be undertaken for the purpose of review of these new data, evaluations of these data and evaluations of existing data. An outcome of this process will be assessment by U.S.EPA of its RfD for methylmercury to determine if change is warranted.

The neurotoxicity of methylmercury in children exposed *in utero* has been determined to be the critical effect for the human RfD. The RfD was based on a statistical analysis of data from human subjects exposed to methylmercury through the ingestion route in Iraq (Marsh et al., 1987). (See Volume IV and Chapter 2 of this volume.) The RfD for humans was estimated to be $1x10^{-4}$ mg/kg-day or 0.1 μg/kg bw/day. To compare methylmercury dose-response in the observed response range, human NOAELs and LOAELs were estimated from the Marsh et al. (1987) data by using the hair-mercury concentration groupings given in the *Seafood Safety* report from NAS/NRC (NAS, 1991; see Table 5-4). In this report each of the maternal-child pairs were assigned to one of five hair-mercury concentration groups. The geometric means of each of the hair-mercury concentration groups were 1.4, 10.0, 52.5, 163.4 and 436.5 ppm. The incidence of combined developmental effects (late walking, late talking, mental symptoms, seizures or neurological score greater than 3) in each of the groups was

18.5 percent, 21.4 percent, 46.2 percent, 66.7 percent and 93.3 percent for the 1.4, 10.0, 52.5, 163.4 and 436.5 ppm groups, respectively. The combined developmental effects incidence was determined from Marsh et al. (1987) by scoring an individual as a responder if one or more of the developmental effects was observed, summing the responders across each group and dividing by the number of individuals in each group. These concentration groupings and incidence of combined developmental effects were used in the calculation of the benchmark dose for the derivation of the methylmercury RfD. The benchmark dose of 11 ppm mercury in hair was operationally equivalent to a NOAEL in the derivation of the methylmercury RfD. A LOAEL of 52.5 ppm mercury in hair was estimated for this risk characterization from inspection of data in Table 5-4. The NOAEL of 11 ppm mercury in hair and the LOAEL of 52.5 ppm mercury in hair correspond to ingestion levels of 1 μg/kg-day and 5.3 μg/kg-day, respectively; these dose conversions were made by applying the methods for converting hair mercury concentrations to ingestion levels used in the derivation of the RfD in Volume IV of this Report.

Table 5-4
Incidence of Effects in Iraqi Children by Exposure Group[a]

Effect	Dose (ppm) Mercury in Hair				
	1.37	10	52.53	163.38	436.60
Late walking	0	2	2	3	12
Late talking	2	1	3	4	11
Mental symptoms	1	0	1	3	4
Seizures	0	0	1	2	4
Neurological scores >3	3	1	4	3	9
Neurological scores >4	0	1	2	2	6
All endpoints	4	3	6	8	14
N (sample size)	27	14	13	12	15

[a] From Table 6-11 of Seafood Safety; dose is geometric mean

The RfDs for avian and mammalian wildlife are derived in Volume V of this Report. The avian RfD was based on the data from a series of studies by Heinz and collaborators (Heinz, 1974, 1975, 1976a,b, 1979). Heinz and collaborators fed mercury contaminated grain to mallard ducks. A NOAEL could not be identified. The estimated LOAEL, based on reproductive and behavioral effects, was 64 μg/kg bw/day. The avian RfD was estimated by dividing the LOAEL by the uncertainty factors.

The estimation of the RfD for the avian species utilized the following formula: $RfD = TD \times [1/(UF_A \times UF_S \times UF_L)]$, where

RfD = 64 μg/kg bw/day x [1/(3 x 1 x 3)]

RfD = 7.1 μg/kg bw/day

where: TD - tested dose; here equal to the LOAEL of 64 μg/kg bw/day.

UF_A - an uncertainty factor to indicate the uncertainty in applying a dose-response derived for one species to another. A factor of 3 was applied.

UF_S - an uncertainty factor which accounted for extrapolation from a subchronic dose-response study to a chronic exposure. As the duration of the Heinz studies was for the animals' lifetime, a factor of 1 was applied.

UF_L - an uncertainty factor employed to indicate uncertainty around the toxic threshold. A factor of 3 was applied.

Note that in Volume V for the calculation of the Wildlife Criteria, the composite uncertainty factor (UF_L x UF_A) was rounded to 10.

The mammalian RfD was based on the data from a series of studies by Wobeser and collaborators (Wobeser, 1973; Wobesser et al., 1976a,b). Wobeser and collaborators fed methylmercury to ranch mink. A NOAEL of 55 μg/kg bw/day was estimated from these studies. The estimated LOAEL, based on damage to the nervous system and liver, was 180 μg/kg bw/day. The mammalian RfD was estimated by dividing the NOAEL by the uncertainty factors. The uncertainty factors utilized included: UF_L-an uncertainty factor employed to indicate uncertainty around the toxic threshold, UF_A-an uncertainty factor to indicate the uncertainty in applying a dose-response derived for one species to another, and UF_S- an uncertainty factor which accounted for extrapolation from a subchronic dose-response study to a chronic exposure.

The estimation of the RfD for the mammalian species utilized the following formula:

$RfD = TD \times [1/(UF_A \times UF_S \times UF_L)]$

RfD = 55 μg/kg bw/day x [1/(1 x 10 x 1)]

RfD = 5.5 μg/kg bw/day

where: TD - tested dose; here equal to the LOAEL of 55 μg/kg bw/day.

UF_A - an uncertainty factor to indicate the uncertainty in applying a dose-response derived for one species to another. A factor of 1 was applied. Mink and otter are considered to be similar.

UF_S - an uncertainty factor which accounted for extrapolation from a subchronic dose-response study to a chronic exposure. The Wobeser studies were judged to be subchronic, and factor of 10 was applied.

UF_L - an uncertainty factor employed to indicate uncertainty around the toxic threshold. Since a NOAEL was estimated a factor of 1 was applied.

Based on the data developed for the health assessment, the human LOAEL and RfD are orders of magnitude lower than the corresponding LOAELs and RfD of the other animals (Table 5-5). There

is a great deal of uncertainty in this comparison. It must be noted that the effects in humans are based on the RfD definition of a critical effect; that is the most sensitive reported adverse effect or indicator of adverse effect. The effects reported for mammals (i.e., neurologic damage in the mink) and birds (i.e., reproductive effects in mallards) would be considered frank effects in the human RfD methodology. The observations in laboratory animals indicate that it would be reasonable to expect more subtle and less damaging effects of methylmercury to occur at lower doses than the wildlife LOAEL AND NOAEL.

Table 5-5
Animal and Human Health Endpoints for Methylmercury in µg/kg bw/day

Animal	NOAEL	LOAEL	Health Effect Related to LOAEL	RfD or Wildlife WC	Health Effect Related to RfD or Wildlife WC
Human	1.0	5.3	Neuro-developmental effects in children	0.1	Neuro-developmental effects in children
Mammalian Quadrupeds	55	180	Neurological damage	5.5	Neurological damage
Avian	--	64	Behavioral and reproductive effects	7.1	Behavioral effects

5.2.3 Integration of Modeled Methylmercury Intake Through Consumption of Fish for Hypothetical Humans and Wildlife with Dose-Response Data

In this section the dose-response and exposure estimates are integrated to predict concentrations of methylmercury in fish tissue which correspond to various health endpoints when consumed by the piscivore. The methylmercury body burdens in fish which correspond to piscivore health endpoints are estimated by dividing the product of the piscivore body weight (kg) and the human or wildlife WC (µg/kg/day), or LOAEL (µg/kg/day) by the daily rate of fish consumption (g/day). The units that result are expressed on the basis of fish muscle concentration (µg methylmercury/g fish muscle tissue). The corresponding fish muscle concentrations could also account for the differences in bioaccumulation between trophic level 3 and 4 fish. This was accomplished by converting the concentrations calculated for consumers of trophic level 4 fish to the values expected in trophic level 3 fish in the same lake and vice versa. The difference in BAF 3 and BAF 4 is approximately a factor of 5 and is based on the predator-prey factor. (See Volume V for more details).

Table 5-6 shows that the RfDs for humans and wildlife are estimated to result from fish concentration at least nine times lower than those for the estimated LOAELs. The RfD is, by definition, a protective endpoint. There is predicted to be no risk at this level of exposure. The risks posed by exceedance of this value cannot be estimated from the available data. The LOAEL, on the other hand, is the lowest observed effect level. Exposure at the LOAEL is predicted to cause adverse effects in some members of the populations. Since an avian NOAEL could not be estimated from the data, an additional comparison of fish methylmercury concentrations not expected to adversely affect

the health of the piscivores was not done. The use of the human and wildlife WC was the only basis for estimating the fish methylmercury concentrations not expected to have adverse effects on the health of the piscivores.

Table 5-6
The Concentrations of Methylmercury in Trophic Level 3 and Trophic Level 4 Fish Which, If Consumed at the Assumed Rates on a Daily Basis, Result in Exposure at the RfD or the LOAEL

Population	Methylmercury Concentration in Trophic Level 3 Fish at RfD (μg/g)	Methylmercury Concentration in Trophic Level 4 Fish at RfD (μg/g)	Methylmercury Concentration in Trophic Level 3 Fish at LOAEL (μg/g)	Methylmercury Concentration in Trophic Level 4 Fish at LOAEL (μg/g)
Eagle	0.04	0.20	0.36	1.8
Osprey	0.036	0.18	0.32	1.6
Kingfisher	0.014	0.07	0.13	0.64
Mink	0.027	0.135	0.90	4.49
Otter	0.019	0.093	0.61	3.04
Adult Human Recreational Angler	0.05	0.23	2.47	12.4
Adult Human High-End Fish Consumer	0.02	0.12	1.24	6.18
Child of High-End Fish Consumer	0.02	0.08	0.90	4.51

Based on the results presented in Table 5-6, the most susceptible species can be determined. The species with the lowest estimated fish methylmercury concentration which corresponds to a LOAEL level is predicted to be the most susceptible to methylmercury concentrations in fish. The kingfisher is the most susceptible species considered in this analysis based on either the LOAEL or the Wildlife WC. This susceptibility is a function of the large amount of fish per body weight consumed by this species.

Comparing both the human and wildlife WCs, the high-end fish-consuming humans and the otter follow the kingfisher; mink, osprey, eagle, and human recreational angler follow on this basis. It is interesting to note that fairly low concentrations of methylmercury in trophic level 3 fish are predicted to result in wildlife and human exposure at the RfD or Wildlife WC. The predicted fish methylmercury concentrations also exhibit a fairly narrow range; the range is from 0.01 to 0.05 μg methylmercury/g fish tissue.

If the LOAEL is the basis for comparison, the kingfisher is followed by the osprey, eagle, otter then mink and child and, finally, adult high-end human fish consumers. The piscivorous wildlife are, on the basis of the LOAEL, generally more sensitive than the humans.

Note both the range between the RfD and the LOAEL for these organisms and the differences in severity of the health end points. Changes in this range (e.g., a reduction of the mammalian quadruped LOAEL) may change the predicted ranking. New avian and mammalian studies which examine the effects of lower dietary methylmercury levels on neuronal tissues may provide a more appropriate comparison for the human health data.

Both modeled and measured methylmercury concentrations result in exceedence of the LOAEL for all the wildlife species considered (See Volume III Chapters 2 [measured concentrations in fish], and 5 and 6 [predicted concentrations in fish]). Measured methylmercury concentrations in fish which would result in exceedence of the LOAEL for humans have been reported. These values are also predicted to occur in a few combinations in the modeling exercise; for example, when the long range transport and the predicted concentrations based on the local atmospheric modeling of the large municipal waste combustor are combined for hypothetical locations in the Eastern United States.

Table 5-6 shows the fish methylmercury concentrations that are predicted to be protective of selected wildlife species and the three hypothetical humans. Selection of the human RfD (based on an estimate of 60 grams of fish consumption per day) as a protective basis for any risk management action is expected to be protective of all wildlife considered except for the kingfisher.

There is a great deal of uncertainty in this comparison. The uncertainty includes the uncertainty and variability in the health endpoints and fish consumption rates. For example, there are reports of fish consumption by persons in the U.S. in exceedance of 60 grams/day; these are documented in Appendix H of Volume III. There is also a great deal of variability pertaining to the transport of mercury from the water body and sediments through the aquatic food chain. See related discussions in Volume III and Volume V.

For mercury the form or species of most concern for chordates in this assessment is methylmercury (see Volumes IV and V of this Report). Although methylmercury is found in other media and biota, it accumulates to the highest levels in the muscle tissues of fish, particularly piscivorous fish. This is based upon both the measurement data and the modeling data also presented in the Exposure Volume (Volume III). Methylmercury remains essentially unchanged in fish tissue, when subjected to human preparation methods (i.e., cooking). Methylmercury also efficiently passes through intestinal walls into the blood. Other forms of mercury are also toxic, but since they are not known to accumulate in commonly eaten foods, and since they are not as bioavailable in most media, they are not as great a concern.

5.3 Potential Effects of Mercury Emission Sources on Local Fish Consumers

In the hypothetical sites constructed in Volume III of this Report, some of the mercury emitted from local sources is predicted to deposit on local watersheds and water bodies. The fate and transport of the atmospheric mercury in the local area around the sources (within 50 Km) was modeled with a modified version of the COMPDEP model. Since mercury emissions are also thought to be transported across great distances, the RELMAP model was used to estimate the impacts of all mercury sources in the continental U.S. The RELMAP model predicted a range of mercury air concentrations and mercury deposition rates across the U.S. The U.S. was divided into Eastern and Western halves. The

hypothetical local sites were placed at the 50th and 90th percentiles for the RELMAP-predicted mercury air concentration and total deposition in both the Eastern and Western halves of the U.S. Some of the mercury emitted from continental U.S. sources is also predicted to deposit on local watersheds and water bodies.

The results of both the RELMAP and COMPDEP models are associated with some degree of uncertainty. The uncertainties have been described in Volume III. It is important to note that the dry deposition of divalent vapor-phase mercury, one component of the total mercury deposition, is highly uncertain. The deposition velocity associated with this form was derived from that of a surrogate compound with a similar Henry's Law Coefficient.

The movement of mercury through the environment is very complex. The deposited mercury is predicted to be transported to the water body, and some of the total mercury that is dissolved in the water column is predicted to be incorporated into the aquatic food chain. The amount of mercury that is incorporated into the aquatic life at each trophic level is predicted through a bioaccumulation factor (BAF). Uptake of dissolved mercury is highly variable, and there appears to be a great deal of variability among water bodies. A number of factors, such as pH, appear to affect bioaccumulation. The BAFs were derived from measured data; the uncertainty analysis presented in Volume V indicates the range of values that can be associated with the BAF.

Piscivorous human or animal exposure to mercury results from the consumption of fish. Essentially all the mercury in fish appears to be in the form of methylmercury. The uncertainties in the modeling results were large and, as a result, only qualitative conclusions were derived. The consequences of the predictions at these hypothetical sites can be examined.

5.3.1 Humans

Three types of human consumers were modeled: the adult subsistence fisher, the child of the subsistence fisher and the adult recreational angler. The fish consumption rates associated with these three hypothetical individuals was 60, 20 and 30 grams/day, respectively.

The fish consumption rates for the subsistence anglers was that reported as the mean consumption by Columbia River Intertribal Fish Commission (1995). Mean daily consumption for females was 56 g and for males, 63 g. These values are corroborated by data from other studies. Fish consumption studies such as those of Nobmann, 1992 (mean fish consumption of 3 Alaskan Tribes), Fiore et al., 1989 (95th percentile of Wisconsin Anglers), Toy et al., 1996 (90th percentile fish consumption rate for the Tulalip tribe) and Wolfe and Walker, 1987 (group mean of the highest response group) report similar or higher fish consumption rates than those modeled. The CSFII 89/91 reports the 95th and 99th percentiles of fish consumption rates for estuarine and freshwater fish (the types most likely consumed by subsistence anglers) as 47.3 and 113 g/day, respectively. Clearly, there are individuals who consume high levels of fish, and they comprise a small percentage of the U.S. population.

Given these fish consumption rates, the issue then becomes the concentrations of methylmercury in the fish. The subsistence-level consumers modeled were assumed to derive all fish consumed from a single or small number of geographically proximal water bodies. The water bodies modeled were assumed to be a series of small lakes. Humans were assumed to consume trophic level 4 fish. Although the methylmercury concentrations of trophic level 4 fish are known to vary, measurements near or exceding one ppm are not uncommon. As the predicted fish concentrations

exceed 1 ppm in trophic level 4 fish and at daily fish consumption rates modeled, exposure to methylmercury through fish consumption approaches or exceeds the product of 10 times RfD for the high end consumer.

In the hypothetical Eastern site, when the 50th percentile RELMAP results and the results of the local emission sources (i.e., model plants) are combined, two scenarios are predicted to result in fish mercury concentrations greater than 1 ppm: the trophic level 4 fish in lakes at 2.5 Km from the chlor-alkili plant (CAP) and the primary lead smelter (PLS) (See Table G-1 from Volume III). At 2.3 and 1.9 ug mercury/g, fish a daily consumption rate of 60 g and a body weight of 70 Kg results in predictions of 2.0 and 1.6 ug methylmercury/Kg bw/day, respectively. In the hypothetical Eastern site, when the 90th percentile RELMAP results and the results of the local emission sources (i.e., model plants) are combined, five combinations are predicted to have fish mercury concentrations greater than 1 ppm: the trophic level 4 fish in lakes at 2.5 Km from the chlor-alkali plant (CAP), the primary lead smelter (PLS), the large municipal waste combustor (large MWC) and the small municipal waste combustor (Small MWC) and the trophic level 4 fish in lakes at 10 Km from the large MWC mercury (See Table G-1 from Volume III). See Table 5-7.

Table 5-7
Predicted Methylmercury Concentrations in Fish in the Eastern U.S. combining 90th percentile RELMAP Estimates and Local Source Estimates and the Resulting Human Exposure Estimates.

Combination	Predicted Trophic Level 4 Fish Concentration (ug mercury/g fish)	Estimated Human Intake ug mercury/Kg bw/day
Large MWC 2.5 Km	4.9	4.2
Small MWC 2.5 Km	1.1	0.94
CAP 2.5 Km	2.6	2.2
PLS 2.5 Km	2.1	1.8
Large MWC 10 Km	1.1	0.94

In the hypothetical Western site, when the 50th percentile RELMAP results and the results of the local emission sources (i.e., model plants) are combined, two combinations are predicted to have fish mercury concentrations greater than 1 ppm: the trophic level 4 fish in lakes at 2.5 Km from the large MWC and the CAP (See Table G-2 from Volume III). At 1.9 and 2.1 ug mercury/g fish, a daily consumption rate of 60 g and a body weight of 70 Kg results in predictions of 1.6 and 1.8 ug methylmercury/Kg bw/day, respectively. In the hypothetical Western site, when the 90th percentile RELMAP results and the results of the local emission sources (i.e., model plants) are combined, the same two combinations are predicted to have fish concentrations greater than 1 ppm: the trophic level 4 fish in lakes at 2.5 Km from the large MWC and the CAP (See Table G-2 from Volume III). The predicted exposure estimates 1.7 and 1.9 ug/ Kg bw/day, respectively.

The predicted methylmercury concentrations in trophic level 4 fish occur generally in the high end combinations (e.g., 90th percentile RELMAP results combined with results predicted at 2.5 Km from a local source). The local sources either have low effective stack height or emit vapor-phase

divalent mercury. Given the current understanding of the atmospheric fate and transport of emitted mercury, qualitatively these results appear plausible.

The quantitative accuracy of the predicted fish methylmercury concentrations can not be assessed with the available mercury monitoring data. The predicted value is on the high end of the measured data as is expected given the modeling construct (i.e., 90th percentile RELMAP results in the eastern half of the U.S. and 2.5 Km downwind from a large MWC). The measured freshwater fish mercury concentrations in the U.S. range from <0.01 ug mercury/g fish to 8.94 ug mercury/g fish (NJDEP, 1994); typical values are between 0.11 and 0.26 ug mercury/g (Lowe et al., 1985; Bahnick et al., 1994). If the predicted results are accurate (and again there are no data to conclusively demonstrate or refuel this) then individuals who consume 60 grams of the fish at the predicted levels in Table 5-7 or more per day may be adversely impacted from mercury emissions from the identified sources.

For the anglers who are assumed to consume a smaller quantity of local fish per day (i.e., 30 grams), the number of combinations from which they are potentially adversely impacted is fewer: 1) in the Eastern U.S. the 50th percentile RELMAP and 2.5 Km from the CAP; 2) the 90th percentile RELMAP and 2.5 Km from the large MWC and CAP; and 3) in the Western U.S. the 90th percentile RELMAP results and 2.5 Km from the CAP.

Two issues must be considered for the freshwater anglers. The data of Fiore et al ., 1989 indicate that some members of the population consume both locally-caught freshwater fish and commercial fish. This additional source of methylmercury exposure should be considered. If the individuals are eating a variety of fish in commerce then the additional exposure will probably be modest. If the individuals are consuming a more limited selection of commercial fish, (e.g., fish at the apex of marine food web), which may have higher concentrations of mercury, these additional exposures may result in adverse impacts. This again depends on the quantity and types of fish consumed both from local waters and commercial.

The second issue for anglers is that they are assumed to fish from a variety of water bodies. Several studies indicate that many anglers may travel extended distances to fish. These individuals who consume fish from a variety of sources again probably decrease their chances of exposure to methylmercury at toxicologically significant doses. There are a limited number of these mercury emission sources and a limited number of locations predicted to be at or above the 90th percentile for deposition of mercury.

5.4 Comparison with Other Recommendations

Recommended limits on methylmercury exposure have been expressed in these units: µg/kg body weight/day; concentrations of mercury in tissues such as blood, hair, feathers, liver, kidney, brain, etc.; grams of fish per day; number of fish meals per time interval (e.g., per week).

Reference values for mercury concentrations (expressed as total mercury) in biological materials commonly used to indicate human exposures to mercury were published by the WHO/IPCS (1990). The mean concentration of mercury in whole blood is approximately 8 µg/L, in hair about 2 µg/g, and in urine approximately 4 µg/L. Wide variation occurs about these values (WHO/IPCS, 1990).

Methylmercury exposures for general populations are reflected by hair mercury levels. Because fish are the primary exposure pathway for methylmercury there is a broad-based scientific

literature associating increases in hair mercury concentrations with increases in fish consumption (among other see: Abe et al., 1995; Akagi et al., 1995; Airey et al., 1983; Barbosa et al., 1995; Chai et al., 1994; Girard and Dumont, 1995; Oskarsson et al., 1990; Wheatley and Paradis, 1995). The WHO/IPCS (1990) evaluation and the U.S. EPA RfD of 0.1 μg/kg bw/day were based on neurotoxicity to the fetus as hazard endpoint. Consequently the predictability of fetal mercury exposure from maternal hair mercury concentrations is critical to the assessment of fetal risk from maternal exposures. Maternal hair mercury concentrations predict mercury concentrations in fetal brain (Cernichiari et al., 1995); fetal blood (Cernichiari et al., 1995); umbilical cord blood (Wheatley and Paradis, 1995; Girard and Dumont, 1995) and newborn hair (Chai et al., 1994).

There are no biological monitoring data to estimate mercury exposures (specifically hair mercury concentrations) based on a survey that can be extrapolated to the general population of the United States ~~do not yet exist~~. To adequately predict methylmercury exposure for the general United States population the data should be obtained from subjects who are chosen based on a sampling strategy that can be extrapolated to the United States population, and must include appropriate quality assurance/quality control procedures. There are some data available on hair mercury concentrations from persons living in the United States including reports by the following: Creason et al., 1978a, 1978b, 1978c; Lasora and Citterman, 1991; and Crispin-Smith et al., 1985.

Although data on hair mercury concentrations from a sample representative of the United States population with adequate documentation of quality assurance/quality control do not exist, results from individual studies conducted within the United States are shown in Table 5-8. These surveys were conducted in widely diverse geographic areas within the United States. Overall, the mean hair mercury concentrations identified for subjects in these studies are typically under 1 μg/g or 1 ppm. For a number of the surveys the detection limit was greater than 1 ppm indicating that a substantial number of zero or trace values were included in the mean concentration. Calculating mean concentrations when the analytical method has a detection limit near the overall mean presents difficulties that have been treated with a variety of strategies. Although these approaches may present a way to calculate a mean from existing data, the preferred approach is an analytical method sufficiently sensitive and precise to provide data in the appropriate range.

The maximum values reported in these individual surveys range from 2.1 to 15.6 ppm. The highest maximum value (15.6 ppm) was reported by Fleming et al. (1995) from a study that specifically focussed on persons from the Florida Everglades who consumed wildlife from this area. Until appropriate survey data for the general United States population exist, the overall pattern of hair mercury concentrations for the United States remains unclear.

Although not from a United States population, hair mercury concentrations have been monitored among Canadian aboriginal peoples. Girard and Dumont (1995) summarized data on hair mercury concentrations among the Cree Indians of Quebec sampled between 1983 and 1991. Of 626 hair samples, 112 had hair mercury concentrations greater than 2.5 ppm. In 1983 21% of mothers had hair mercury concentrations > 6 ppm. Between 1983 and 1991 the prevalence of hair mercury concentrations> 6 ppm decreased to 2%. Wheatley and Paradis (1995) reported on hair mercury concentrations in Canadian Aboriginal Peoples providing cumulative results between 1970 and 1992. During that period, 24.5% of people had hair mercury concentrations > 6 ppm, and 1.5% had hair mercury concentrations > 10 ppm. Data were reported on 71,842 tests with regions including these: Atlantic Provinces, Quebec, Ontario, Manitoba, Saskatchewan, Alberta, British Columbia, Northwest Territories, and Yukon. The highest prevalence of hair mercury concentrations > 6 ppm was in

Table 5-8
Hair Mercury Concentrations (μg Hg/gram hair or ppm)
from Residents of Various Communities in the United States

Study	Community	Mean Concentrationppm	Maximum Concentration ppm	Additional Information on Study
Creason et al., 1978a	New York Metropolitan Area'	Children (n=280), 0.67 Adults (n=203), 0.77	Children, 11.3 Adults, 14.0	Survey conducted in 1971 and 1972
Creason et al., 1978b	Four communities in New Jersey (Ridgewood, Fairlawn, Matawan and Elizabeth)	Children (n=204), 0.77 Adults (n=117) 0.78	Children, 4.4 Adults, 5.6	Survey conducted in 1972 and 1973
Creason et al., 1978c	Birmingham, Alabama and Charlotte, North Carolina	Children (n=322), 0.46; Adults (n=282), 0.47	Children, 5.4; Adults, 7.5	Survey conducted in 1972 and 1973
Airey, 1983	USA Data cited by Airey, 1983. Community not identified	1. Males (n=22), 2.7 ppm; 2. Females (n=16), 2.6 ppm; 3. Males and Females (24 subjects), 2.1 ppm; 4. Males and Females (31 subjects), 2.2 ppm; 5. Males and Females (24 subjects), 2.9 ppm; 6. Males and Females (79 subjects), 2.4 ppm;	1. 6.2 ppm 2. 5.5 ppm 3. 5.6 ppm 4. 6.6 ppm 5. 7.9 ppm 6. 7.9 ppm	
Airey, 1983	USDA Data cited by Airey, 1983. Community identified: LaJolla-San Diego	1. 2.4 ppm (13 males) 2. 2.7 ppm (13 females); 3. 2.3 ppm (8 subjects including males and females); 4. 2.9 ppm (17 subjects including males and females); 5. 2.6 ppm (5 subjects including males and females); 6. 2.7 ppm (30 subjects including males and females)	1. 6.2 ppm 2. 5.5 ppm 3. 4.5 ppm 4. 6.6 ppm 5. 6.2 ppm 6. 6.6 ppm	

Table 5-8
Hair Mercury Concentrations (μg Hg/gram hair or ppm)
from Residents of Various Communities in the United States

Study	Community	Mean Concentrationppm	Maximum Concentration ppm	Additional Information on Study
Airey, 1983	USA Data cited by Airey, 1983. Area identified: Maryland	1. 1.8 ppm (11 subjects, males and females); 2. 1.5 ppm (11 subjects, males and females); 3. 2.3 ppm (11 subjects, males and females); 4. 1.9 ppm (33 subjects, males and females)	1. 3.8 ppm 2. 3.9 ppm 3. 4.5 ppm 4. 4.5 ppm	
Airey, 1983	USA data cited by Airey, 1983. Community identified: Seattle.	1. 33 ppm (9 males); 2. 2.2 ppm (3 females) 3. 2.6 ppm (5 subjects, males and females); 4. 1.5 ppm (3 subjects, males and females); 5. 3.8 ppm (8 subjects, males and females); 6. 3.0 ppm (16 subjects, males and females).	1. 5.6 ppm 2. 4.1 ppm 3. 5.6 ppm 4. 2.1 ppm 5. 7.9 ppm 6. 7.9 ppm	
Crispin-Smith et al., 1985	USA, communities and distribution not identified.	0.48 ppm (1431 individuals); 0.52 (1009 individuals reporting some seafood consumption).	Maximum values in this survey: 6.3 ppm	The 1009 individuals are a subset of the 1431 individuals.
Lasora et al., 1991	Nome, Alaska	(80 females of child-bearing age)	Maximum value: 15.2 ppm	
Lasora et al., 1991	Sequim, Washington	0.70 ppm (7 females of child-bearing age)	Maximum value: 1.5 ppm	
Fleming et al., 1995	Florida Everglades	1.3 ppm (330 male and female subjects)	Maximum value: 15.6 ppm	To be included in the survey subjects had to have consumed wildlife from the Florida Everglades.

Northwest Territories where 42.6% of total population of 2273 had hair mercury concentrations > 6 ppm and, of those, 3.0% had hair mercury concentrations > 10 ppm. this study illustrates regional or ethnic differences in hair mercury levels.

5.4.1 Human Populations and Subpopulations

Cross-comparisons of limits on methylmercury exposure by various organizations are facilitated by the work of Airey (1983) (Table 5-9) who analyzed mercury concentrations in 559

Table 5-9
Association Between Hair Mercury and Frequency of Fish Ingestion

Assocation of Hair Mercury Concentration (μg mercury/gram hair) with Frequency of Fish Ingestion by Adult Male and Female Subjects Living in 32 Locations within 13 Countries (Airey, 1983)		
Frequency of Fish Meals	**Arithmetic Mean**	**Range**
Once a month or less	1.4	0.1 - 6.2
Twice a month	1.9	0.2 - 9.2
Every week	2.5	0.2 - 16.2
Every day	11.6	3.6 - 24.0

samples of human hair from 32 locations in 13 countries. The United States averaged 2.4 μg mercury/gram hair; compared with the lowest mean reported from Germany (0.5 μg mercury/gram) and the highest from Japan (3.9 μg mercury/gram hair), Mean hair content of mercury varied with the frequency of reported fish consumption.

5.4.1.1 Comparison with World Health Organization Recommendations

Grams of Fish per Day

The World Health Organization's International Programme for Chemical Safety (WHO/IPCS) recommended as a preventive measure, that in populations that consume large amounts of fish (e.g., 100 gram/day) hair levels of methylmercury in women of child-bearing age should be monitored. The number of women of child-bearing age in the United States estimated to consume fish in excess of 100 grams per day can be obtained by inference from the general U.S. population dietary surveys (e.g., United States Department of Agriculture's CSFII 89/91). Intake of fish and shellfish for the general US population (estimated by CSFII 89/91 data described in Appendix H, Volume III) based on "users" only was estimated to be 110 grams per day at the 95th percentile among women aged 15 through 44 years. Female children (aged 14 years or younger) consumed 112 grams of fish per day, the 95th percentile (Table 22, Appendix H, Volume III), while the overall intake at the 95th percentile among female subjects regardless of age was 107 grams per day. Estimates of the number of women of child-bearing age (ages 15 through 44 years) and the number of children (ages birth through 14 years) within the United States population are shown in Table 5-10.

The number of women of child-bearing age consuming fish and/or shellfish in excess of 100 grams per day was also estimated from the NPD, Inc. 1973/74 data that recorded fish consumption for a one-month period. Within this sample, 94% of people reported consuming fish or shellfish at least once in a one month period. Within this sample, the 99th percentile consumers reported an average fish/shellfish intake of 112 grams/day. Using the population size estimates for women of child-bearing age from the 1990 United States Census described above estimates of the number of women of child-bearing age (ages 15 through 44 years) and the number of children (ages birth through 14 years) within the United States population are shown in Table 5-11.

Table 5-10
Estimated United States Population Consuming Fish, Excluding Alaska and Hawaii Estimates Based on the 1990 U.S. Census and the Continuing Surveys of Food Intake by Individuals, 1989/1991

Population Group	Estimated Number of Persons
Total U.S. Population	247,052,000
Total Female Population Aged 15 through 44 Years	58,222,000
Total Population of Children Aged <15 Years	53,463,000
Percent of Respective Group Reporting Fish Consumption during the 3-Day Dietary Survey Period in CSFII 89/91[a]	
Total Population	30.9 percent
Females Aged 15 through 44 Years	30.5 percent
Children Aged <15 Years	24.9 percent
Number of Persons Predicted to Consume Fish Based on Percentage Consuming Fish in CSFII 89/91	
Total Estimated Population	76,273,000
Total Estimated Number of Females Aged 15 through 44 Years	17,731,000
Total Estimated Number of Children Aged <15 Years	13,306,000
Number of Persons in Highest 5 Percent of Estimated Population that Consumes Fish[b]	
Total Estimated Population	3,814,000
Total Estimated Female Population Aged 15 through 44 Years	887,000
Total Estimated Child Population	665,000
Estimated Number of Adult Pregnant Women in Highest 5 Percent Of Estimated Population that Consumes Fish	
Number of Females Aged 15 through 44 Years x Percentage of Women Pregnant in a Given Year	84,300

[a] Rounded to three significant figures.
[b] Persons who consume an average 100 g or more of fish/day.

Table 5-11
Estimated Fish-Consuming Population
in the United States, excluding Alaska and Hawaii
Estimates Based on the 1990 U.S. Census and the
National Purchase Diary Inc., 1973/74 Data on Fish/Shellfish Consumption

Population Group	Estimated Number of Persons
Total U.S. Population	247,052,000
Total Female Population Aged 15 through 45 Years	58,222,000
Total Population of Children Aged < 15 Years	53,462,000
Percent of Respective Group Reporting Fish Consumption during the One-Month Survey period in NPD, Inc. 1973/64 Survey	
Total Population	94%
Females Aged 15 through 45 Years	94%
Children Aged < 15 Years	94%
Number of Persons Predicted to Consume Fish Based on Percentage Consuming Fish or Shellfish in NPD, Inc. 1973/74	
Total Estimated Population	232,229,000
Total Estimated Number of Females Aged 15 through 45 Years	54,729,000
Total Estimated Number of Children Aged < 15 Years	50,254,000
Number of Persons in Highest One Percent of Estimated Fish-Consuming Population[a]	
Total Estimated Population	2,322,000
Total Estimated Adult Female Population	547,000
Total Estimated Child Population	503,000
Estimated Number of Adult Pregnant Women in Highest One Percent of Estimated Fish-Consuming Population	
Number of Adult Females x Percentage of Women Pregnant in a Given Years	51,900

[a] Persons who consume an average 100 g or more or fish/day.

The estimated number of women of child-bearing age (ages 15 through 44 years) in the contiguous 48 states is approximately 17,731,000. It is estimated that in a given year 9.5 percent of women in this age group are pregnant. The groups of concern are women of child-bearing age who are pregnant and children. Using consumption of 100 grams of fish/shellfish per day or more as a screen for concern for mercury exposure estimates have been made of the number of women and children whose fish/shellfish intake is at or above 100 grams/day. Within the CSFII 89/91 cross-sectional data that identified 30.5% of females of child-bearing age consuming fish/shellfish at 100 grams or more in the 3-day sampling window, the number of persons with these consumption patterns were identified. The estimated number of women ages 15 through 44 years in the highest 5 percent of fish consumers (those consuming 100 g or more of fish per day) is approximately 887,000 based on CSFII 89/91 data. The estimated number of pregnant women in that highest 5% of fish consumers is estimated to be approximately 84,300.

Whether or not a 3-day sampling window adequately projects longer-term fish consumption has been raised as a question. Data are available from the National Purchase Diary, Inc. 1973/94 sample that recorded fish/shellfish consumption for a month-long period. Within these data, 94% of people reported ingesting fish at least once during the period. Within these 94%, the 99th percentile intake was reported (Rupp et al., 1980) to be 112 grams/day. Using this top 1% of consumers the size of the population of women of child-bearing age and children consuming 100 grams of fish/shellfish per day or more was estimated. The estimated number of pregnant women consuming 100 grams of fish/shellfish per day or more was estimated to be 51,900.

The USDA reports that overall fish/shellfish consumption in the United States has increased by 26% between 1970 and 1990. The estimated number of pregnant women who consume 100 grams/day or more of fish is, thus, likely greater than 51,900. If the general increase of 26% applies at the extremes of the distribution, the projected number of women would be approximately 65,000 women.

Local point sources for emissions of mercury can be most clearly linked to localized deposition of mercury. An analysis of the CSFII 89/91 data by personnel from US EPA's Office of Prevention, Pesticides, and Toxic Substances (personal communication, Helen Jacobs) determined that at the mean 33% of total fish/shellfish intake identified in this survey came from freshwater and estaurine fish and shellfish. Subpopulations of anglers and subsistence fishers have been assumed to obtain most of their self-caught fish and shellfish from these local and estaurine sources.

Specific subpopulations of anglers and subsistence fishers and other high end fish consumers ingest fish substantially in excess of the general population. Figure 4-5 (p. 4-41) summarizes grams of fish consumed among specific subpopulations and highlights high end consumption. For example, Puffer et al. (1981) in a study of anglers in Los Angeles, California found that mean intake was 37 grams per day, but the 90th percentile for this group was 225 grams per day. Orientals and Samoans had mean fish intakes with a mean of 70.6 grams/day (Puffer et al. 1981). Alaskan Natives from 11 communities averaged 109 grams of fish/day (Nobbman et al., 1992). Wolfe and Walker identified a very high fish consumption rate among persons living in remote Alaskan communities. The Columbia River Intertribal Fish Commission (1994) reported that during the two months of highest average fish consumption average intake was 108 grams/day. The Tribes of Puget Sound reported (Toy et al., 1995) an average of 73 grams/day with a 90th percentile of 156 grams/day. West et al. (1989) found a mean intake of approximately 22 grams/day, but a reported maximum value over 200 grams/day. Peterson et al (1994) in a study of Chippewa tribes found that 2 percent of 323 respondents ate at least one fish meal each day. In these individual tribal and angler studies, data were generally not separately reported for women of child-bearing age.

Micrograms of Methylmercury per Day

The WHO/IPCS cited (WHO/IPCS, 1990) a reanalysis of the Iraqi data by Nordberg and Strangert (1976, 1978, 1982 as cited in WHO/IPCS, 1990). This analysis included consideration of inter-individual variation in mercury half-life and assumed a continuous distribution of individual thresholds superimposed on a background frequency of symptoms such as paresthesia. These calculations indicate that an intake of 50 μg methylmercury per day in an adult will not result in any adverse effects to adults. A long term methylmercury intake of 3 to 7 μg/kg body weight/day would adversely effect nervous system function as manifested by <5 percent increase in incidence of paresthesia in adults. Hair mercury concentrations would be approximately 50 to 125 μg/gram at this exposure. For the general population of the United States (Appendix H, Volume III), among women of child-bearing age, the 97th percentile ingestion level of methylmercury was estimated to be approximately 0.48 μg/kg body weight/day. The intakes at the 95th percentile of methylmercury by children ages 14 years or younger was 0.84 μg/kg/day for males and 0.81 μg/kg body weight/day for females, based on the freshwater methylmercury concentration data of Bahnick et al. (1985). Using the freshwater fish mercury concentration data of Lowe et al. (1994), the 95th percentile exposures were 0.84 μg mercury/kg bw for males and 0.68 μg/kg bw for females ages 14 years and younger.

Micrograms of Mercury per Gram of Hair

Biological monitoring based on hair, blood and/or concentrations in other tissues has been used as an index of body burden of mercury. These concentrations are used as a surrogate for mercury concentrations in tissues proximate to the site of effect (e.g., mercury concentrations in nervous system tissue). The WHO/IPCS has concluded (1990) that the general population does not face a significant health risk from methylmercury. When fish consumption is high enough for groups to attain a blood methylmercury level of about 200 μg/L (corresponding to 50 μg/g hair) a low (5 percent) risk of neurological damage will occur. In 1995 Kinjo et al. reported threshold values hair mercury based on logit and hockey stick analyses for calculated maximum hair mercury concentrations from human subjects in the Niigata epidemic of Minamata disease in Japan. Male adults were calculated to have threshold values (μg/g hair) (95 percent CI) of 46.5 (30,71) and 43.0 (27,67) depending on whether or not patients with estimated maximum hair mercury concentrations of less than 20 μg mercury/gram hair were included. Calculated threshold values for adult women were 24.7 (20,30) or 49.3 (30,64) with and without inclusion of patients with estimated maximum values of less than 20 μg/g. [Exclusion of hair mercury concentrations less than 20 μg mercury/gram hair was based on unreliability of the analytical method (dithizone colorimetric techniques) at these concentrations]. Of the 986 subjects reported by Kinjo et al. (1995) 26 had hair mercury concentrations less than 20 μg mercury/gram hair.

Clinical observations in Iraq suggest that women during pernancy are more sensitive to the effects of methylmercury with fetuses at particularly increased risk. The World Health Organization/International Programme for Chemical Safety (1990) indicated, based on analysis of the Iraqi data, a 30 percent or higher risk of abnormal neurological signs when maternal hair mercury concentrations were above 70 μg/g. These abnormal neurological signs were the following: increased muscle tone in the leg and exaggerated deep tendon reflexes, often accompanied by ataxia together with a history of developmental delays. The WHO/IPCS (1990) evaluation indicated that data from the Iraqi epidemic do not permit conclusions about risk of adverse effects below this level. However, using statistical methods for biological modeling by Cox et al. (1989) and other data, WHO calculated that a maternal hair concentration of 10 to 20 μg/g implies a 5 percent risk of neurological disorder.

Extrapolation of these data to lower mercury concentrations is uncertain, but psychological and behavioral testing of subjects may identify subclinical effects.

5.4.1.2 Comparison with U.S. EPA's RfD and Benchmark Dose

The RfD and benchmark dose for methylmercury were based on the Iraqi data. Dose-conversion calculations were used to convert data on hair mercury concentration to estimates of blood mercury concentration and dietary intake (μg/day) of methylmercury. The RfD/RfC Work Group chose a benchmark (lower bound for 10 percent risk) based on modeling of all nervous-system effects in children. The 10 percent risk level was 11 ppm hair concentration for methylmercury. A dose-conversion equation was used to estimate a daily intake of 1.1 μg methylmercury/kg body weight/day that when ingested by a 60 kg individual is predicted to maintain a blood concentration of approximately 44 μg/L or a hair concentration of 11 μg mercury/gram hair (11 ppm).

The benchmark dose can be compared with other recommended limits and with data on methylmercury exposure via fish. The benchmark dose of 11 μg methylmercury/gram of hair compares closely with the arithmetic mean of hair mercury concentration (Airey, 1983) for people from many different communities who eat fish every day (11.6 μg mercury/gram hair). If a 100 gram portion size for fish is assumed, this corresponds with quantities of fish eaten by approximately the 95th percentile fish consumer among persons who reported consuming fish in the CSFII 89/91. Expressed another way the benchmark dose (see also Volume VI, Chapter 2, pg. 10) is 1.1 μg/kg body weight/day assuming a 60 kg body weight individual. The benchmark dose was used as an estimate of a NOAEL.

Comparison with the General Population

Among women of child-bearing age in the general U.S. population (as estimated from CSFII 89/91 food consumption data and fish mercury concentrations presented in Appendix H, Volume III), only women reporting greater than 99th percentile consumption would exceed the benchmark dose for methylmercury intake from fish, when methylmercury intake is expressed on a per kilogram body weight basis.

Two issues need to be noted regarding these comparisons. Estimated dietary intakes at the 99th percentile and higher are at the extremes of the distribution. Short-term dietary intakes based on three-days food consumption records are known to be quite subject to variability at the extremes of the distribution. Consequently these data must be interpreted with caution until they can be confirmed or repudiated with additional exposure assessments.

It must be noted that the benchmark was calculated to be a lower-bound on an effect level: occurrence of neurological effects associated with prenatal exposure to methylmercury at a 10 percent risk level. By contrast the RfD is an exposure level that is assumed to be protective against known adverse effects for all members of the population including sensitive subpopulations. The RfD for methylmercury is 0.1 μg/kg body weight/day. The RfD may be considered the midpoint in an estimate range of about an order of magnitude. This range reflects variability and uncertainty in the estimate.

Comparison with Populations Consuming Large Amounts of Fish

In the review of published data on fish-consumption among subpopulations who consume fish more frequently than the general population, a number of reports were identified who consume substantially higher quantities of fish than among the general population. These groups were identified when the recommendation to monitor populations consuming one fish-meal a day (or 100 grams of fish per day) was evaluated. Most of these reports do not provide a clear identification of the age and gender of their subjects. However, to the extent that these subjects are women of reproductive age (15 through 44 years) the likelihood that they will exceed the benchmark dose for methylmercury depends on the methylmercury concentration of the fish consumed.

Depending on whether or not the fish obtained by a high-end fish consumer come from one source (e.g., a small lake or local river) or from simply more of the general food supply, the mercury concentration of the fish obtained may or may not be site-specific. Assuming a high-end fish consumer obtains a broad mixture of fish sources, the mean mercury concentration of the fish consumed is estimated to be about the mean or median value for the fish mercury concentrations used in the estimates for Appendix H of Volume IV. More precise estimates of mercury intake for these subpopulations will require site-specific determinations of mercury in the fish consumed.

5.4.2 Wildlife Species

The Great Lakes Water Quality Initiative Criteria (GLWQI Criteria) were described in Volume IV (Section 4.2) of this Mercury Study Report to Congress. The evaluation of data and calculation of water concentrations (WC) in the Mercury Study Report to Congress was done in accordance with the methods and assessments published in the draft GLWQI (U.S. EPA 1993a). Availability of additional data and differences in interpretation of those data led to differences in the calculated values of the WC in this Report and those published in the final GLWQI (U.S. EPA, 1995b). Both evaluations used the same methodology which was described in Section 4.2.1 of Volume IV. These two evaluations relied on the same experimental studies as the basis for the WC calculation: for birds, the three generation reproduction study in mallards (Heinz, 1974, 1975, 1976a,b, 1979); and for mammals the subchronic dietary studies in mink (Wobeser et al., 1976a,b). In addition to these studies, the authors of the Mercury Study Report to Congress were able to obtain Wobeser's dissertation (Wobeser, 1973); this provided some additional information that was augmented by discussions with the author.

A comparison between the species-specific Wildlife Criteria Calculated in the Great Lakes Water Quality Initiative and the Mercury Study Report to Congress was presented in Volume IV (Table 4-3, pg. IV-15, repeated here as Table 5-12).

Table 5-12
Comparison of Wildlife Criteria Calculated by Great Lakes Water Quality Initiative and by the Mercury Study

Species	Wildlife Criterion (pg/L)	
	GLWQI	MSRC
Mink	2880	415
Otter	1930	278
Kingfisher	1040	193
Osprey	Not done	483
Eagle	1920	538

All of the WC calculated in this Report are lower (more conservative) than those published in the GLWQI. All species-specific WC, however, differ less than an order of magnitude from one another. Range in differences is from nearly 4-fold lower for the WC in this Report (eagle) to 7-fold lower (mink and otter). Variation in the calculated WC are from two sources: evaluation of effects in wildlife and evaluation of exposure to wildlife.

Details of differences between the GLWQI and this Report on evaluation of effects in birds and piscivorous mammals have been presented in Volume V. For birds the GLWQI used a different rate of food consumption 0.156 kg/kg-d compared with 0.128 kg/kg-d in this Report) and different uncertainty factors than did the Mercury Study Report to Congress. In the effects assessment for piscivorous mammals both the GLWQI and this Report used data on mink administered mercury in the diet from the studies of Wobeser (1976a,b).

The Report also obtained the doctoral thesis of Wobeser (Wobeser, 1973). The GLWQI identified a NOAEL of 1.1 ppm. At this dietary exposure there were changes in the liver, lesions in the central nervous system and axonal degeneration; moreover, two of the animals in this treatment group were observed at the end of the treatment of move slowly by comparison to other mink. The study authors reported their opinion that mink treated at 1.1 ppm in the diet for longer than the study (93 days) would be expected to show clinical signs of nervous system damage. Mink treated at the next higher dose, 1.8 ppm, were observed with anorexia, ataxia and increased mortality. Based on these considerations, this Report considered 1.1 ppm to be the LOAEL, and as described in Section 4.2.2 of Volume IV, used data from the first part of the study to identify a NOAEL of 0.33 ppm. This Report used data from Wobeser (1973) to establish the weights of female mink and kits used in these experiments; this results in slight differences in conversion of dose in ppm diet to μg/kg bw/day.

Another difference between the GLWQI and the Mercury Study Report to Congress was through assessment of exposure to birds through consumption of prey. The GLWQI made assessments specific to the Great Lakes region. Because the Mercury Study Report to Congress is a national

assessment use of region-specific assumption was not considered appropriate. Additional information on these differences is found in Volume IV (Section 4.2).

5.5 Risk Characterization Issues

The results of this risk characterization method pose a series of questions applicable to discussion of management of potential risk.

1. Should environmental mercury concentrations be managed based on the risks estimated for humans that eat fish or for wildlife that each fish?

2. If potential piscivorous wildlife risks are the basis selected, then the risk manager must determine which wildlife species are present and which wildlife species health endpoints to protect.

3. If potential risks to humans are the basis selected, then the risk manager must determine the level of consumption of local fish by humans and which human health endpoints to protect.

4. What level of uncertainty can be tolerated for a given situation?

Table 5-9 shows that the RfD or Wildlife Criteria Values are reached at fish concentration at least nine times lower than for the estimated LOAELs for the wildlife species and humans. The RfD is, by definition, a protective endpoint. The risks posed by exceedance of this value are uncertain. The LOAEL, on the other hand, is the lowest observed effect level. Exposure at the rate of the LOAEL is predicted to cause adverse effects in some members of the populations.

Table 5-9 shows that selection of the Wildlife Criteria Value for kingfisher protects for the Wildlife Criterion Values of all other selected species and the human RfD, as well as the LOAEL at the modeled rates for human local fish consumption. Similarly selection of the human RfD based on an estimate of 60 grams of fish consumption per day is expected to be protective of all wildlife considered at the Wildlife Criteria Values except for the kingfisher, as well as for the LOAELs. Selection of any LOAEL is not protective for the human RfD or Wildlife Criteria Values. These are decisions of risk management.

6. CONCLUSIONS

The following conclusions are presented in approximate order of degree of certainty in the conclusion, based on the quality of the underlying database. The conclusions progress from those with greater certainty to those with lesser certainty.

- There is a plausible link between methylmercury concentrations in freshwater fish and anthropogenic mercury emissions. The degree to which this linkage occurs cannot be estimated quantitatively at this time.

- Among humans and wildlife that consume fish, methylmercury is the predominant chemical species contributing to mercury exposure.

- Methylmercury is known to cause neurotoxic effects in humans via the food chain.

- The human RfD for methylmercury is calculated to be $1x10^{-4}$ mg/kg body weight/day. While there is uncertainty in this value, there are data and quantitative analyses of health endpoints that corroborate and support a reference dose within a range of an order of magnitude. A quantitative uncertainty analysis indicates that the human RfD based on observation of developmental neurotoxicity in children exposed to methylmercury *in utero* is likely to be protective of human health.

- The RfD is a confident estimate (within a factor of 10) of a levels of exposure without adverse effects on those human health endpoints measured in the Iraqi population exposed to methylmercury from grain. These included a variety of developmental neurotoxic signs and symptoms. The human RfD is for ingested methylmercury; no distinction was made regarding the food in or other media serving as the ingestion vehicle.

- U.S. EPA calculates that members of the U.S. population ingest methylmercury through the consumption of fish at quantities of about 10 times the human reference dose. This amount of methylmercury is equivalent to the benchmark dose used in the calculation of the reference dose; the benchmark dose was taken to be an amount equivalent to the NOAEL. The NOAEL was an ingested amount of 1.1 μg per kg body weight per day. Consumption of mercury equivalent to the NOAEL is predicted to be without harm for the majority of a population. Individual risks cannot be determined from the available data.

- Prediction of risk cannot be made for ingestion of methylmercury above the benchmark dose, given the currently available data in humans.

- Concentrations of mercury in the tissues of wildlife species have been reported at levels associated with adverse health effects in laboratory studies in the same species.

- Dietary survey data indicate that approximately 30 percent of the general U.S. population consumes fish at least once during a three-day period. Among this group of fish consumers roughly 50 percent are predicted to consume methylmercury at the RfD. Consuming methylmercury at levels equal to the RfD is equated to be without harm.

- Dietary intake data from cross-sectional surveys indicate that approximately 30 percent of the general U.S. population consumes fish at least once during a three-day period. Among this

group of fish consumers the majority are predicted to consume methylmercury at or below the RfD. Consuming methylmercury at levels equal to the RfD is expected to be without harm.

- Based on longer-term data survey data that recorded fish consumption for a one-month period, approximately 94% of the population consumes fish at least once during that period.

- Using both the longitudinal and cross-sectional survey data, it is estimated that 1 to 2 percent of women of child-bearing age regularly consume fish and shellfish at average intakes of 100 grams per day or greater. Whether or not methylmercury intakes are elevated above the estimated NOAEL depends on the concentration of methylmercury in the fish and shellfish consumed.

- U.S. EPA estimates that approximately one-third of fish and shellfish consumed are from freshwater/estaurine habitats that may be affected by local sources of mercury.

- Case reports in the literature document that sick and/or dying animals and birds with seriously elevated tissue mercury concentrations have been found in the wild. These wildlife have mercury concentrations elevated to a level documented in laboratory studies to produce adverse effects in these species. for a specific case report concurrent exposure to other sources of ill health cannot be excluded.

- Modeled estimates of mercury concentration in fish around hypothetical mercury emissions sources predict exposures at the wildlife WC. The wildlife WC, like the human RfD, is predicted to be a safe dose over a lifetime. It should be noted, however, that the wildlife effects used as the basis for the WC are gross clinical manifestations or death. Expression of subtle adverse effects at these doses cannot be excluded.

- Data are not sufficient for calculation of separate reference doses for children, *in utero* exposure and the aged.

- Comparisons of dose-response and exposure estimates through the consumption of fish indicate that certain species of piscivorous wildlife are more exposed on a per kilogram body weight basis than are humans. The implications for wildlife health are uncertain.

There are many uncertainties associated with this analysis. The sources of uncertainty include the following:

- There is considerable uncertainty and apparent variability in the movement of mercury from the abiotic elements of the aquatic system through the aquatic food chain.

- U.S. EPA has developed a BAF in an attempt to quantify the relationship between dissolved mercury concentrations in the water column and methylmercury concentrations in fish. This BAF was developed using a four-tier food chain model and extant field data. A quantitative uncertainty analysis of the BAF and the variability of the BAF was examined.

- There is considerable uncertainty in atmospheric processes that affect emitted mercury. U.S. EPA has attempted to predict the fate and transport of mercury through the use of atmospheric models. The results of these models are uncertain. For the regional (RELMAP) modeling,

predicted mercury concentrations are corroborated by measured data for certain areas of the United States.

- A quantitative uncertainty analysis and qualitative considerations lead to the conclusion that paresthesia in adults is not the most reliable endpoint on which to base a quantitative dose-response assessment. A quantitative uncertainty analysis and qualitative considerations also indicate that late walking in children is less reliable than combined developmental effects in children exposed *in utero*.

- Total sources of exposure for selected populations may include occupational exposure primarily to mercury vapor. Exposures from dental amalgam are expected to contribute to the overall body burden of mercury. The association, however, between overall body burden of mercury from these sources and methylmercury from the aquatic food chain is not established.

- Data estimating body burden of mercury based on biological monitoring of hair and blood mercury levels among the general U.S. population have not been published. Such information would permit firmer estimates of the risk of mercury toxicity in the general U.S. population.

- Data on body burden of mercury among populations that consume large quantities of fish are also very limited. Such information would permit firmer estimates of risk of mercury toxicity for these specific high-risk populations.

To improve the risk assessment for mercury and mercury compounds, U.S. EPA would need the following:

- A monitoring program to assess either blood mercury or feather/hair mercury of piscivorous wildlife; particularly those in highly impacted areas. This program should include assessment of health endpoints including neurotoxicity and reproductive effects.

- Collection of additional monitoring data on hair or blood mercury and assessment of health endpoints among women of child-bearing age and children. This study should focus on high-end fish consumers and on consumption of fish from contaminated water bodies.

- There is a need for improved data on effects that influence survival of the wildlife species as well as on individual members of the species.

- There is a need for controlled studies on mercury effects in intact ecosystems.

- Monitoring data sufficient to validate or improve the local impact exposure models are needed.

7. RESEARCH NEEDS

The primary purpose of the Mercury Study Report to Congress was to assess the impact of U.S. anthropogenic emissions on mercury exposure to humans and wildlife. The size of some populations of concern have been estimated: namely women of child-bearing age and children who eat fish. In the general population, people typically obtain their fish from many sources. The question on whether or not the impact of mercury from anthropogenic ambient emissions can be proportioned to the overall impact of methylmercury on wildlife is a much more difficult issue.

As with environmental monitoring data, information on body burden of mercury in populations of concern (blood and/or hair mercury concentrations) are not available for the general U.S. population. Data on higher-risk groups are currently too limited to discern a pattern more predictive of methylmercury exposure than information on quantities of fish consumed. The selenium content of certain foods has been suggestive as a basis for modifying estimates of the quantities of methylmercury that produce adverse effects. Currently, data on this mercury/selenium association form an inadequate basis to modify quantitative estimates of human response to a particular exposure to mercury.

Available data for human health risk assessment have limitations as described in the Report and in this summary. Studies of human fish-consuming populations in the Seychelles and Faroes Islands address some of these limitations; they are expected to be published within a year of release of this Report. Additional studies on U.S. populations who consume fish from the Great Lakes are in progress. Public health agencies of the U.S. government as well as the U.S. EPA will evaluate these new data when they are available. Risk management decisions beyond the ongoing activities specified in the Clean Air Act Amendments of 1990 will be based on consideration of all human data including results of these new studies.

The benchmark dose methodology used in estimating the RfD required that data be clustered into dose groups. Most data on neurologically based development endpoints are continuous; that is, not assigned to dose groups. For example, scoring on scales of IQ involves points rather than a "yes/no" type of categorization. Measurements on the degree of constriction of the visual field involve a scaling rather than a "constricted/unconstricted" type of variable. Although arbitrary scales can be constructed, these groupings have generally not been done in current systems. Use of alternative dose groupings (as described in Volume IV) had no significant effect on calculated benchmark doses. An additional difficulty occurs in estimation of benchmark dose for multiple endpoints that have been measured. Further research on appropriate methods for mathematical modeling is needed. For some situations such information is known, but for methylmercury exposure and multiple endpoints assessing the same system (i.e., developmentally sensitive neurological, neuromotor and neuropsychological effects) the time-course/dose-response of such changes have not been clearly established. Development of the mathematical models needs to be accompanied by understanding the physiological/pathological processes of methylmercury intoxication.

Research to decrease the above uncertainties and to address characterization limitations include the following:

- A monitoring program to assess either blood mercury or feather/hair mercury of piscivorous wildlife; particularly those in highly impacted areas. This program should include assessment of health endpoints including neurotoxicity and reproductive effects.

- Collection of additional monitoring data on hair or blood mercury and assessment of health endpoints among women of child-bearing age and children. This study should focus on high-end fish consumers and on consumption of fish from contaminated water bodies.

- There is a need for improved data on effects that influence survival of the wildlife species as well as on individual members of the species.

- There is a need for controlled studies on mercury effects in intact ecosystems.

- Monitoring data sufficient to validate or improve the local impact exposure models are needed.

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