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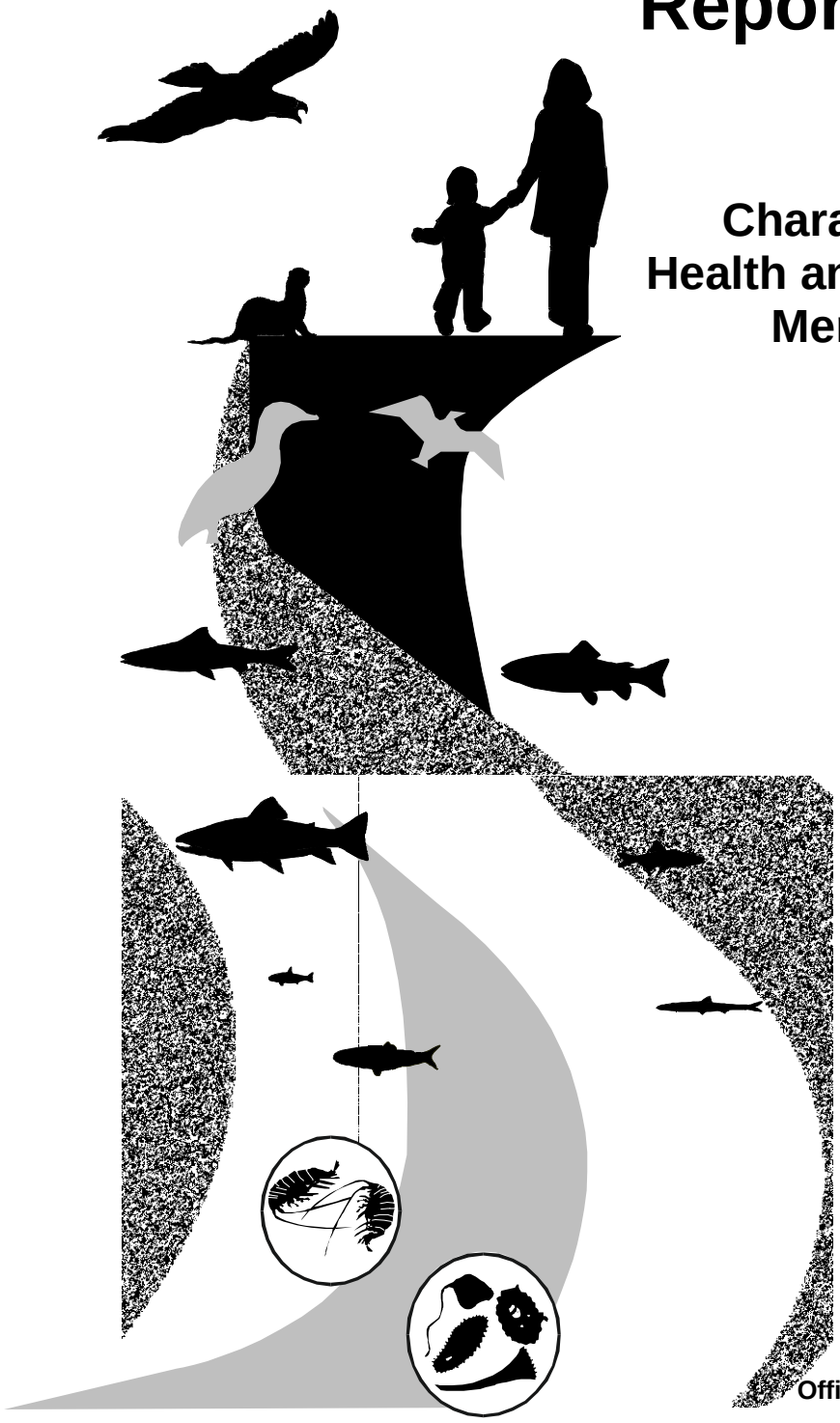

Volume VII: Characterization of Human Health and Wildlife Risks from Mercury Exposure in the United States

Office of Air Quality Planning & Standards
and
Office of Research and Development

MERCURY STUDY REPORT TO CONGRESS

VOLUME VII:

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

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Office of Air Quality Planning and Standards
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U.S. Environmental Protection Agency

TABLE OF CONTENTS

TABLE OF CONTENTS (continued)

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LIST OF TABLES

LIST OF TABLES (continued)

LIST OF FIGURES

LIST OF SYMBOLS, UNITS AND ACRONYMS

AC	Activated carbon
APCD	Air pollution control device
ASME	American Society of Mechanical Engineers
CAA	Clean Air Act as Amended in 1990
CaS	Calcium sulfide
cf	Cubic feet
CFB	Circulating fluidized bed
cm	Cubic meter
CRF	Capital recovery factor
dscf	Dry standard cubic feet
dscm	Dry standard cubic meter
ESP	Electrostatic precipitator
DSI	Dry sorbent injection
EPRI	Electric Power Research Institute
FFDCA	Federal Food, Drug, Cosmetic Act
FFs	Fabric filters
FGD	Flue gas desulfurization
FIFRA	Federal Insecticide, Fungicide, Rodenticide Act
FWS	U.S. Fish and Wildlife Service
GACT	Generally available control technology
GLFCATF	Great Lakes Fish Consumption Advisory Task Force
GLNPO	Great Lakes National Program Office
g	Gram
gr	Grains
HAPs	Hazardous air pollutants
HCl	Hydrochloric acid
Hg	Mercury
HgCl	Mercuric chloride
HgI	Mercuric iodide
HgO	Mercuric oxide
HgS	Mercuric sulfide
HgSe	Mercuric selenite
HMTA	Hazardous Materials Transportation Act
HVAC	Heating, ventilating and air conditioning
IDLH	Immediately dangerous to life and health
INGAA	Interstate Natural Gas Association Of America
kg	Kilogram
kW	Kilowatt
MACT	Maximum achievable control technology
MB	Mass burn
MCL	Maximum contaminant level
Mg	Megagram
MSW	Municipal solid waste
MW	Megawatt
MWCs	Municipal waste combustors
MWIs	Medical waste incinerators

LIST OF SYMBOLS, UNITS AND ACRONYMS (continued)

NaCl	Sodium chloride
NaOH	Sodium hydroxide
ng	Nanogram
NIOSH	National Institute for Occupational Safety and Health
Nm^3	Normal cubic meter
NOAA	National Oceanic and Atmospheric Administration
NPDES	National Pollutant Discharge Elimination System
NSP	Northern States Power
NSPS	New source performance standard
OAQPS	Office of Air Quality Planning and Standards (U.S. EPA)
OECD	Organization for Economic Co-operation and Development
O&M	Operation and maintenance
OSHA	Occupational Safety and Health Administration
PCBs	Polychlorinated biphenyls
PELs	Permissible exposure limits
PM	Particulate matter
ppm	parts per million
ppmv	parts per million by volume
RQ	Reportable quantity
SARA	Superfund Amendments and Reauthorization Act
scf	Standard cubic feet
scm	Standard cubic meter
SD	Spray dryer
SDAs	Spray dryer absorbers
TCC	Total capital cost
TCLP	Toxicity characteristic leaching procedure
TMT	Trimercapto-s-triazine
tpd	Tons per day
TRI	Toxic Release Inventory
µg	Microgram
UNDEERC	University of North Dakota Energy and Environmental Research Center
WS	Wet scrubber
WW	Waterwall

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 an eight-volume Mercury Study: Report to Congress. The seven volumes are as follows:

I. Executive Summary
II. An Inventory of Anthropogenic Mercury Emissions in the United States
III. Fate and Transport of Mercury in the Environment
IV. An Assessment of Exposure to Mercury in the United States
V. Health Effects of Mercury and Mercury Compounds
VI. An Ecological Assessment for Anthropogenic Mercury Emissions in the United States
VII. Characterization of Human Health and Wildlife Risks from Mercury Exposure in the United States
VIII. 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^o), 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 V. A brief characterization of endpoints other than systemic toxicity is given in Chapter 2 of Volume V.

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 (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 V, Chapter 5.) 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 et al., 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 population s around the U.S. Great Lakes. In addition, there are new evaluations of published work described in Chapter 3 of Volume V, 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 IV and is summarized in Chapter 3 of Volume VII. 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 Chapter 6 of Volume V, 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 V, Chapter 6. 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 V, Chapter 6.

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.

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

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

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

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). 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:

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

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 and is discussed in detail in a report on the benchmark dose by U.S. EPA's Risk Assessment Forum (U.S. EPA, 1995).

Uncertainty Factors

An uncertainty factor is a numeric reduction of an effect or no effect dose which is used to account for a lack of data or for known areas of variability or uncertainty in any step in the calculation of a RfD. U.S. EPA defines uncertainty factors in five areas of data extrapolation:

1. When effect data in humans are used, to account for the likelihood of susceptible subpopulations;
2. When animal data are used, to account for uncertainty in extrapolating to humans;
3. When less-than-lifetime studies are used, to account for uncertainty in applying data to chronic exposure;
4. When no NOAEL is identified, to account for uncertainty in the actual no effect dose; and
5. When there are no results from certain long-term studies (e.g., a two-generation reproductive assay), to account for uncertainty in choice of critical effect.

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

Modifying Factors

Modifying factors (MF) are similar to uncertainty factors in that they are used to adjust the no adverse effect dose in calculating an RfD. They may be applied to account for known areas of uncertainty not covered by the adjustments above.

A composite uncertainty factor (UF) 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:

$$RfD \quad \frac{Benchmark\ Dose}{UF\ x\ MF}$$

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

$$1\ x\ 10^{-4}\ mg/kg-day$$

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. 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. Kinjo 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 associated with the lowest adverse effect level of exposure 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. Children are a second subpopulation of interest. There is general agreeement that the nervous system continues development in post-natal life and that methylmercury can adversely affect the developmental processes. The major uncertainty in this area is the absence of dose response data to quantitatively establish a separate RfD for children.

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 Minamata 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 bio-toxicity 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 et al., 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 (Bakir et al., 1972). 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. 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 are known.

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 Minamata 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 (Tamashiro 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 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 (see Volume V) 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 presented in Volume V.

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 $0.7x10^{-4}$ mg/kg-day (described in Stern, 1993) compared to U.S. EPA's RfD of $1x10^{-4}$ 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. (1995) 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. (1987). 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 Volume V, show considerable uncertainty in thresholds estimated from the data on late walking.

Late walking, as assessed in the exposed Iraqi population (Marsh et al., 1987) 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 Marsh et al. (1987) 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 Volume V 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 ws 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. Marsh et al. (1995) showed no effects of methylmercury based on endpoints similar to those assessed among 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 separate "developmental toxicity" RfD is needed for methylmercury in addition to the RfD. The primary difference between these tow approaches to RfDs is the duration of exposure. 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) and is discussed in Volume V. 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 Volume V. 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 Volume V.

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 39th and 91st 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 1st percentile for all developmental effects, with only a 5 percent chance that it was as high as the 16th 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 5th and 95th 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 5th and 95th 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. RISK CHARACTERIZATION FOR WILDLIFE

3.1 Scope of the Risk Assessment

As described in Chapter 2 of Volume VI, mercury bioconcentrates, bioaccumulates and biomagnifies in aquatic food chains. These processes result in mercury residues in fish that are much higher than concentrations in the water in which they live, thereby providing an enriched contaminant source for piscivorous avian and mammalian wildlife. Existing data permit a general treatment of mercury exposure and effects on such populations. A more accurate assessment of the risk posed by mercury to a specific group of animals occupying a given location requires the collection of necessary supporting information such as food habits, migratory behavior, breeding biology, and mercury residues in preferred
prey items.

The scope of the present Report was intended to be national in scale. It was determined, therefore, that any effort to assess the risk of mercury to a given species living in a defined location would be inappropriate. Instead, an effort was made to compare mercury exposure and effects in a general way using data collected from throughout the country and in so doing to develop qualitative statements about risk.

Consistent with this broader-scale approach, an effort was made to derive a wildlife criterion (WC) level for mercury that is protective of piscivorous wildlife. This WC is defined as the concentration of mercury in water that, if not exceeded, protects avian and mammalian wildlife populations from adverse effects resulting from ingestion of surface waters and from ingestion of aquatic life taken from these surface waters. The health of wildlife populations may, therefore, be considered the assessment endpoint of concern. Although not generally derived for the purpose of ecological risk assessment, WC values incorporate the same type of exposure and effects information used in more standard approaches. Such calculations also provide for a simple assessment of risk in any given situation, i.e., by determining whether the concentration of mercury in water exceeds the criterion value.

Calculation of a WC for mercury is 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 this criterion value are based on those described in the Proposed Great Lakes Water Quality Guidance for the Great Lakes Water Quality Initiative (U.S. EPA, 1993c) and implemented in the final Water Quality Guidance for the Great Lakes System (U.S. EPA, 1995b), henceforth referred to as the "Proposed Guidance" and "Final Guidance," respectively. When originally implemented in support of the Great Lakes Water Quality Initiative (GLWQI), this approach yielded a single measurement endpoint, which was the total mercury concentration in water that was believed to be protective of piscivorous wildlife. In this report, an effort was made to update the WC for mercury by calculating its value using data for methylmercury. It should be noted that a methylmercury-based WC can still be related to total mercury residues in fish or water through the use of appropriate conversion factors. By convention, mercury concentrations in environmental media (and in dosing solutions) are usually expressed as μg/g of elemental mercury, regardless of the identity of the mercury species. This convention is retained throughout this chapter.

3.2 Exposure of Piscivorous Wildlife to Mercury

Exposure was characterized in a progressive manner, with varying reliance on computer models for mercury deposition and fate. The objective of this analysis was to characterize the extent to which piscivorous wildlife are exposed to mercury originating from airborne emissions. Details on exposure assessment inputs, methods and results can be found in Volumes III and IV of this Report. Three general approaches were used, which are described in the following sections.

3.2.1 Estimation of Current Average Exposure to Piscivorous Wildlife on a Nationwide Basis

The first analysis was conducted without computer models. Estimates of current mercury exposure to selected piscivorous wildlife species were calculated as the product of the fish consumption rate and measured mercury concentrations in fish. This analysis was not intended to be a site-specific analysis, but rather to provide national exposure estimates for piscivorous wildlife. This analysis used mean total mercury measurements from two nationwide studies of fish residues and published fish consumption data for the selected wildlife species. The relative ranking of exposure in μg/kg bw/d of selected wildlife species was as follows: kingfisher > river otter > loon =osprey = mink $\geq$ bald eagle.

3.2.2 Estimation of Mercury Deposition on a Regional Scale (40 km grid) and Comparison of These Deposition Data with Species Distribution Information

The second type of analysis was carried out on a regional scale. A long-range atmospheric transport model (RELMAP) was used in conjunction with the mercury emissions inventory provided in Volume II of this Report to generate predictions of mercury deposition across the continental U.S. Ecosystems subject to high levels of mercury deposition will be more exposed to mercury than ecosystems with lower levels of mercury deposition. The pattern of mercury deposition nationwide, therefore, will influence which ecoregions and ecosystems might be exposed to hazardous levels of mercury. Thus, predictions of mercury deposition were compared with the locations of major lakes and rivers, national resource lands, threatened and endangered plant species and the distributions of selected piscivorous wildlife species. Volume VI contains maps of these distributions. Additionally, mercury deposition data were superimposed onto a map of surface waters impacted by acid deposition, because it has been shown that low pH values are positively correlated with high levels of mercury in fish. The extent of overlap of selected species distributions with areas receiving high rates of deposition (>5 $\mu g/m^2$) was characterized.

Avian wildlife considered in this analysis included piscivorous species with habitats that are widely distributed (kingfishers) and narrowly distributed (bald eagles), as well as birds whose range fell within areas of high mercury deposition (ospreys and common loons). All the birds selected were piscivores that feed at or near the top of aquatic food chains and are therefore at risk from biomagnified mercury. Two of the mammals selected for this analysis (mink and river otters) are piscivorous and widely distributed. The other mammal selected, the Florida panther, is not widely distributed but is listed as an endangered species. The Florida panther lives in an environment known to be contaminated with mercury and preys upon small mammals (such as raccoons), which may contain high tissue burdens of mercury. Results for each avian and mammalian species are summarized in Table 3-1.

Approximately 29% of the kingfisher's range occurs within regions of high mercury deposition. On a nationwide basis, mercury does not appear to be a threat to this species. However, kingfishers consume more mercury on a body weight basis than any other wildlife species examined.

Although a recovery in the population of bald eagles in some areas has resulted in a status upgrade from "endangered" to "threatened" in five states (Michigan, Minnesota, Oregon, Washington and Wisconsin), bald eagle populations are still depleted throughout much of their historical range. Bald eagles can be found seasonally in large numbers in several geographic locations, but most of these individuals are transient, and the overall population is still small. Historically, eagle populations in the lower 48 states have been adversely impacted by the effects of bioaccumulative contaminants (primarily DDT and perhaps also PCBs). Approximately 34% of the bald eagle's range overlaps mercury regions of high mercury deposition. Areas of particular concern include the Great Lakes region, the northeastern Atlantic states and south Florida.

Table 3-1
Percent of Species Range Overlapping with Regions of High Mercury Deposition

Species	Percent of Range Impacted
Kingfisher	29%
Bald Eagle	34%
Osprey	20%
Common Loon	40%
Florida Panther	100%
Mink	35%
River Otter	38%

Nationwide, approximately 20% of the osprey's total range overlaps regions of high mercury deposition; however, a much larger fraction of the osprey's eastern population occurs within these regions. The osprey diet consists almost exclusively of fish. Their position at the top of the aquatic food chain places ospreys at risk from toxins that bioaccumulate. Osprey populations underwent severe declines during the 1950s through the 1970s due to widespread use of DDT and related compounds.

Nearly 40% of the loon's range is located in regions of high mercury deposition. Limited data from the study of mercury point sources showed that loon reproductive success was negatively correlated with exposure to mercury in a significant dose-response relationship. Mercury residues in fish collected from lakes used as loon breeding areas may, in some cases, exceed levels that, on the basis of other information, are associated with reproductive impairment. Loons frequently breed in areas that have been adversely impacted by acid deposition. An assessment of mercury’s effects on loon populations is complicated by the fact that decreases in surface water pH have been associated with both increased mercury residues in fish and declines in the available forage base.

All (100%) of the panther’s range falls within an area of high mercury deposition. Mercury levels found in tissues obtained from dead panthers are similar to levels that have been associated with frank toxic effects in other feline species. The State of Florida has taken measures to reduce the risk to panthers posed by mercury. Existing plans include modification of surface vegetation to increase the number of deer available as prey in order to reduce the reliance of panthers on raccoons. Raccoons frequently feed at or near the top of aquatic food webs and can accumulate substantial tissue burdens of mercury. An evaluation of the risk posed by mercury to the Florida panther is complicated by the possible impacts of other chemical stressors, habitat loss, and inbreeding.

Approximately 35% of the range of mink habitat coincides with regions of high mercury deposition nationwide. Mink occupy a large geographic area and are common throughout the U.S. Given the opportunity, mink will prey on small mammals and birds. Many subpopulations, however, prey almost exclusively on fish and other aquatic biota. Due to allometric considerations, mink may be exposed to more mercury on a body weight basis than larger piscivorous mammals feeding at higher trophic levels. Mercury residues in wild-caught mink have been shown in several cases to be equal to or greater than levels associated with toxic effects in the laboratory.

River otter habitat overlaps regions of high mercury deposition for about 14% of the range for this species. River otters occupy large areas of the U.S., but their population numbers are thought to be declining in both the midwestern and southeastern states. The river otter's diet is almost exclusively of aquatic origins and includes fish (primarily), crayfish, amphibians and aquatic insects. The consumption of large, piscivorous fish puts the river otter at risk from bioaccumulative contaminants including mercury. Like the mink, mercury residues in some wild-caught otters have been shown to be close to, and in some cases greater than, concentrations associated with frank toxic effects.

3.2.3 Estimation of Mercury Exposure on a Local Scale in Areas Near Emissions Point Sources

A final analysis was conducted using a local-scale air atmospheric fate model (GAS-ISC3), in addition to the long-range transport data and an indirect exposure methodology, to predict mercury concentrations in water and fish under a variety of hypothetical emissions scenarios. GAS-ISC3 simulated mercury deposition originating from model plants representing a range of mercury emissions source classes. The four source categories were selected based on their estimated annual mercury emissions or their potential to be localized point sources of concern. The categories selected were these: municipal waste combustors (MWCs), medical waste incinerators (MWIs), utility boilers, and chlor-alkali plants. To account for the long-range transport of emitted mercury, the 50th percentile RELMAP atmospheric concentrations and deposition rates were included in the estimates from the local air dispersion model. To account for other sources of mercury, estimates of background concentrations of mercury were also included in this exposure assessment.

These data were used to estimate the contributions of different emission source types to mercury exposure of selected wildlife species. It was concluded from this analysis that local emissions sources have the potential to increase significantly the exposure of piscivorous birds and mammals to mercury. Important factors related to local source impacts include quantity of mercury emitted by the source, species and physical form of mercury emitted, and effective stack height. The extent of this local contribution depends, in turn, upon watershed characteristics, facility type, local meteorology, and terrain. The exposure of a given wildlife species is also highly dependent upon the fish bioaccumulation factor, the trophic level(s) at which it feeds and the amount of fish consumed per day.

The accumulation of methylmercury in fish tissues appears to be highly variable across bodies of water; field data were determined to be sufficient to calculate representative means for different trophic levels. The variability can be seen in the distribution of the methylmercury bioaccumulation factors (BAF) for fish in trophic levels 3 and 4. These values, summarized in Table 3-2 below, were derived from field studies. These means are believed to be better estimates of mercury bioaccumulation in natural systems than values derived from laboratory studies.

Table 3-2
Percentiles of the Methylmercury Bioaccumulation Factor

Parameter	Percentile of Distribution				
	5th	25th	50th	75th	95th
Trophic 3 BAF	4.6×10^5	9.5×10^5	1.6×10^6	2.6×10^6	5.4×10^6
Trophic 4 BAF	3.3×10^6	5.0×10^6	6.8×10^6	9.2×10^6	1.4×10^7

3.3 Effects Assessment for Mercury

Due to the broad range and extent of mercury emissions throughout the United States, many potential ecological effects could have been considered. Neither the available data nor existing methodology supported evaluation of all possible effects.

The ecosystem effects of mercury are incompletely understood. No applicable studies of the effects of mercury on intact ecosystems were found. The ecological risk assessment for mercury did not, therefore, address effects of mercury on ecosystems, plant and animal communities or species diversity. Effects of methylmercury on fish and other aquatic biota were also not characterized, although there is evidence of adverse impacts on these organisms following point source releases of mercury and in aquatic environments affected by urban runoff.

Data on methylmercury effects in wildlife suitable for dose-response assessment are limited to what are termed "individual effects" in the U.S. EPA Framework for Ecological Risk Assessment (U.S. EPA, 1992a). A reference dose (RfD), defined as the chronic NOAEL, was derived for avian species from studies by Heinz (1975, 1976a,b, 1979) in which three generations of mallard ducks (*Anas platyrhychos*) were dosed with methylmercury dicyandiamide. The lowest dose, 0.5 ppm (64 µg/kg bw/d), resulted in adverse effects on reproduction and behavior and was designated as a chronic LOAEL. A chronic NOAEL was estimated by dividing the chronic LOAEL by a LOAEL-to-NOAEL uncertainty factor of 3. Calculated in this manner, the RfD for avian wildlife species is 21 µg/kg bw/d.

The RfD for mammalian species was derived from studies involving subchronic exposures with mink (Wobeser, 1973, 1976a,b), in which animals were dosed with mercury in the form of mercury-contaminated fish. The dose of 0.33 ppm (55 µg/kg bw/d) was selected as the NOAEL for subchronic exposure. As this was less than a lifetime exposure, the subchronic NOAEL was divided by a subchronic-to-chronic uncertainty factor of 3. Calculated in this manner, the RfD for mammalian wildlife species is 18 µg/kg bw/d.

3.4 Risk Assessment for Mercury

As discussed in Section 3.1, an effort was made to derive a WC value for mercury that is protective of piscivorous wildlife. In general, selections of wildlife species for WC development were based on the following factors: (1) exposure to bioaccumulative contaminants; (2) relevance to establishing species of concern on a national basis; (3) availability of information with which to calculate criterion values; and (4) evidence for bioaccumulation and/or adverse effects. The species selected were

piscivorous birds and mammals. Avian species were the bald eagle (*Haliaeetus leucocephalus*), the osprey (*Pandion haliaetus*), common loon (*Gavia immer*) and the belted kingfisher (*Ceryle alcyon*). Mammalian species were the mink (*Mustela vison*) and the river otter (*Lutra canadensis*).

Because this assessment depends to a large extent on the assignment of BAFs for mercury in fish at trophic levels 3 and 4, an effort was made to review published field data from which these BAFs could be estimated. A Monte Carlo analysis was then performed to characterize the variability around these estimates. The results of this effort are reported in Appendix D of Volume III and are summarized in Table 3-2.

A WC value for mercury was estimated as the ratio of an RfD, defined as the chronic NOAEL (in µg/kg bw/d), to an estimated mercury consumption rate, referenced to water concentration using a BAF. Individual wildlife criteria are provided in Table 3-3. This approach is similar to that used in non-cancer human health risk assessment and was employed previously to estimate a WC for mercury in the Water Quality Guidance for the Great Lakes System (GLWQI). The present effort differs, however, from that of the GLWQI in that the entire analysis was conducted on a methylmercury basis. Additional differences resulted from the availability of new data, including measured residue levels in fish and water, and a re-evaluation of the toxicity data from which RfD estimates were derived. In this Report, a more sensitive endpoint was selected for mammalian species, with the goal of assessing the full range of effects of mercury. These changes reflect the amount of discretion allowed under Agency Risk Assessment Guidelines.

Table 3-3
Wildlife Criteria for Mercury

Organism	Wildlife Criterion (pg/L)
Mink	57
River otter	42
Kingfisher	27
Loon	67
Osprey	67
Bald eagle	82

Species-specific WC values for mercury were estimated for selected avian and mammalian wildlife (identified above). A final WC was then calculated as the lowest mean of WC values for each of the two taxonomic classes (birds and mammals). The final WC for mercury was based on individual WC values calculated for avian species, and was estimated to be 50 picograms (pg) methylmercury/L water.

The WC for methylmercury can be expressed as a corresponding mercury residue in fish though the use of appropriate BAFs. Using the BAFs presented in Table 3-2 (50th percentile), a WC of 50 pg/L

corresponds to methylmercury concentrations in fish of 0.077 µg/g and 0.346 µg/g for trophic levels 3 and 4, respectively. In addition, a WC for total mercury can be calculated using an estimate of methylmercury as a proportion of total mercury in water. Based upon a survey of speciation data, the best current estimate of methylmercury as a proportion of total was determined to be 0.078. Using this value, a methylmercury WC of 50 pg/L corresponds to a total mercury WC of 641 pg/L.

3.5 Risk of Mercury from Airborne Emissions to Piscivorous Avian and Mammalian Wildlife

3.5.1 Lines of Evidence

Barr (1986) found that 0.3 ppm of mercury in trophic level 3 fish caused adverse effects on reproduction in common loons. In this Report, an effort was made to calculate a WC for mercury which, if not exceeded, would be protective of piscivorous birds and mammals. The mercury residue in trophic level 3 fish that corresponds to this WC is 0.077 ppm, or about one-fourth the effect level identified by Barr (1986). Based upon a review of two national surveys, the average value for trophic level 3 fish in the continental U.S. was estimated to be 0.052 ppm; however, these surveys may have overestimated the true national average due to a bias toward waters receiving municipal and industrial waste. Nevertheless, recent surveys of lakes that do not receive point source loadings have yielded residue values in forage fish exceeding 0.077 ppm, particularly in regions already impacted by acid deposition (see for example Gerstenberger et al., 1993; Simonin et al., 1994; Driscoll et al., 1994; Lange et al., 1993; Cabana et al., 1994). Although it is difficult to precisely determine an adverse effects level for mercury in forage fish consumed by piscivorous wildlife, this value appears to lie in the range 0.077-0.30 ppm. The exact level may also vary to some degree depending upon the species in question and specific environmental factors.

The effects data, though limited, are remarkable for their consistency; RfDs derived for birds and mammals (mink and domestic cats) are essentially identical. Very few uncertainty factors were used in these calculations, and the uncertainty factor values were small. In addition, the estimated value of UF_L (used to adjust the TD for avian species) was supported by several sources of data. Finally, it should be noted that all wildlife RfDs are greater than the RfD for human health by a factor of about 200 (RfD for human health = 0.1 µg/kg bw/d; see Volume IV). As noted previously, the human health assessment differs from the wildlife assessment in its consideration of subtle cognitive impacts. The possibility also exists that humans are more sensitive than piscivorous wildlife on a delivered dose basis, perhaps due to differences in ability to detoxify methylmercury. Nevertheless, the WC for mercury is unlikely to be grossly “overprotective” (i.e., too low) and may, in some instances, be “underprotective.”

3.5.2 Risk Statements

Given the national-scale scope of this Report, quantitative estimates of risk are not possible or appropriate. It is notable, however, that hazard quotients derived by other authors for mink (Giesey et al., 1994) and great egrets (Jurczck, 1993) ranged from 1.2 to 6.6. Such calculations suggest the possibility of local impacts on these two highly exposed populations. As indicated previously, fish residues in some areas exceed calculated WC values for trophic levels 3 and 4. It should be emphasized that these WC values were calculated using geometric mean BAF values; thus, BAFs were higher in approximately half of the systems for which field-data were available. For this reason, and given the small difference between effect (0.3 ppm) and no-effect (0.077 ppm) residue levels, it is likely that individuals of some highly exposed subpopulations (birds and mammals) are consuming fish at or very near adverse effect levels. Additional work is required to establish whether and to what extent impacts

are occurring, and what effect local-scale impacts may have on larger species populations. Existing data are insufficient to speculate on the spatial or temporal scale of these possible adverse effects or the potential for recovery. However, the risk of adverse effects is great enough to warrant intensified study of highly exposed wildlife subpopulations, particularly in areas near mercury emissions point sources. Finally, the data suggest that special attention should be given to the possibility that mercury acts in concert with other bioaccumulative contaminants (e.g., PCBs, TCDD) to produce toxic effects at residue levels that, when evaluated separately, would not indicate a problem.

4. CHARACTERIZATION OF FATE OF ENVIRONMENTAL MERCURY

Measured mercury data collected around U.S. anthropogenic sources are described in Volume III of this Report. The lack of key data, such as data describing chemical reactions of emitted mercury in the local atmosphere, as well as of the lack of more comprehensive data collections around specific sources, resulted in a decision by U.S. EPA to employ a series of environmental fate models and a series of exposure models (Volume IV). These models are sets of mathematical equations which represent the Agency's understanding of the fate of environmental mercury. As a predictive tool employed in this risk assessment, environmental fate models provided critical findings from the standpoint of: 1) presenting a framework of understanding of how mercury cycles in the environment and the impacts of anthropogenic sources on the cycle, 2) estimating concentrations of environmental mercury including the sources of the predicted environmental concentrations, and 3) highlighting key areas of uncertainty. The implications of the uncertainties are critical to the interpretation and weight placed on the model predictions within the risk characterization. The results from these analyses are then applied in the exposure assessments presented in Volumes IV and VI to estimate the resulting exposures to hypothetical humans and animals that inhabit these sites.

Other models were considered during the development of this Report. The models utilized were selected because they best fit the Agency's understanding of this area and could be utilized within the project limits of both time and budget. Various factors precluded the use of other models: scientific data limitations associated with inputs needed for other models as well as other resources needed to develop/enhance/parameterize other quantitative models. The application of the models to hypothetical U.S. sites and to representative anthropogenic emissions sources was consistent with the goals of a national assessment as laid out by the Congressional mandate, the resource limitations of the project, and the variability of mercury fate as evidenced at specific sites.

4.1 The Modeling Analysis

4.1.1 Study Design of the Modeling Analysis

Given the scientific uncertainties associated with the fate of environmental mercury, U.S. EPA decided that it was most appropriate to examine the environmental fate of mercury at generalized, rather than specific, sites. Evidence indicated that spatial and temporal scales of atmospheric mercury transport differed for atmospheric mercury species as well as different atmospheric forms (i.e., gas and particulate). A single air model which was capable of modeling both the local as well as regional fate of mercury was not identified. This resulted in the use of two air models: Regional Lagrangian Model of Air Pollution (RELMAP) — for assessing regional scale atmospheric transport, and ISC3 — for local scale analyses. Evidence indicated that mercury exposures could occur through multiple exposure routes (see Figure 4-1). Two routes were modeled for humans — inhalation and ingestion — while for piscivores, only the ingestion route was modeled. Although other routes such as terrestrial exposures were considered, the most important exposure pathway appeared to be:

atmospheric deposition ⇨watershed ⇨water body⇨fish⇨piscivorous receptor.

To examine multiple pathways of exposure, U.S. EPA modified an existing generalized watershed and water body fate model to evaluate this pathway and other indirect pathways; the modified model is identified as IEM-2M (see Table 4-1).

Two generalized sites were developed for this risk assessment — a hypothetical western U.S. site and a hypothetical eastern U.S. site. 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 atmospheric modeling. The contributions of the RELMAP model to the eastern site were greater than to the western site due to the smaller number of anthropogenic sources per unit area in the west and less annual precipitation. The background concentrations in all environmental compartments, except for the atmosphere, were also assumed to be higher in the eastern United States than in the west.

In the first step of this risk assessment, RELMAP was used to simulate the regional-scale transport of anthropogenic mercury emissions over a one-year period. The predicted anthropogenic mercury emissions were added to a uniform elemental mercury background concentration of 1.6 ng/m^3 representing natural and recycled anthropogenic sources of mercury worldwide.

In the second step of this risk assessment, ISC3 was used to simulate the local-scale transport of anthropogenic mercury emissions. Rather than use specific mercury-emitting facilities for this assessment, a set of model plants was defined to represent typical rather than high-end source characteristics. The major anthropogenic combustion and manufacturing source categories evaluated were municipal waste combustors (MWCs), medical waste incinerators (MWIs), coal- and oil-fired utility boilers, and chlor-alkali plants. (The Report does not address all anthropogenic emission sources.) The hypothetical sites were placed at 2.5, 10, and 25 kilometers from the sources (model plants). Predicted mercury air concentrations and deposition rates that resulted from individual model plants were modeled using ISC3 at the specified distances.

To obtain the total atmospheric impact at a site, the 50th or 90th percentile predictions of the RELMAP model for the western or eastern sites were added to the predictions of the local atmospheric model (ISC3) for the individual model plants. These combined model predictions of average atmospheric concentrations and annual-average deposition fluxes were used as inputs to the IEM-2M aquatic and terrestrial fate models at the hypothetical western and eastern U.S. sites.

Table 4-1
Models Used in the Report to Congress

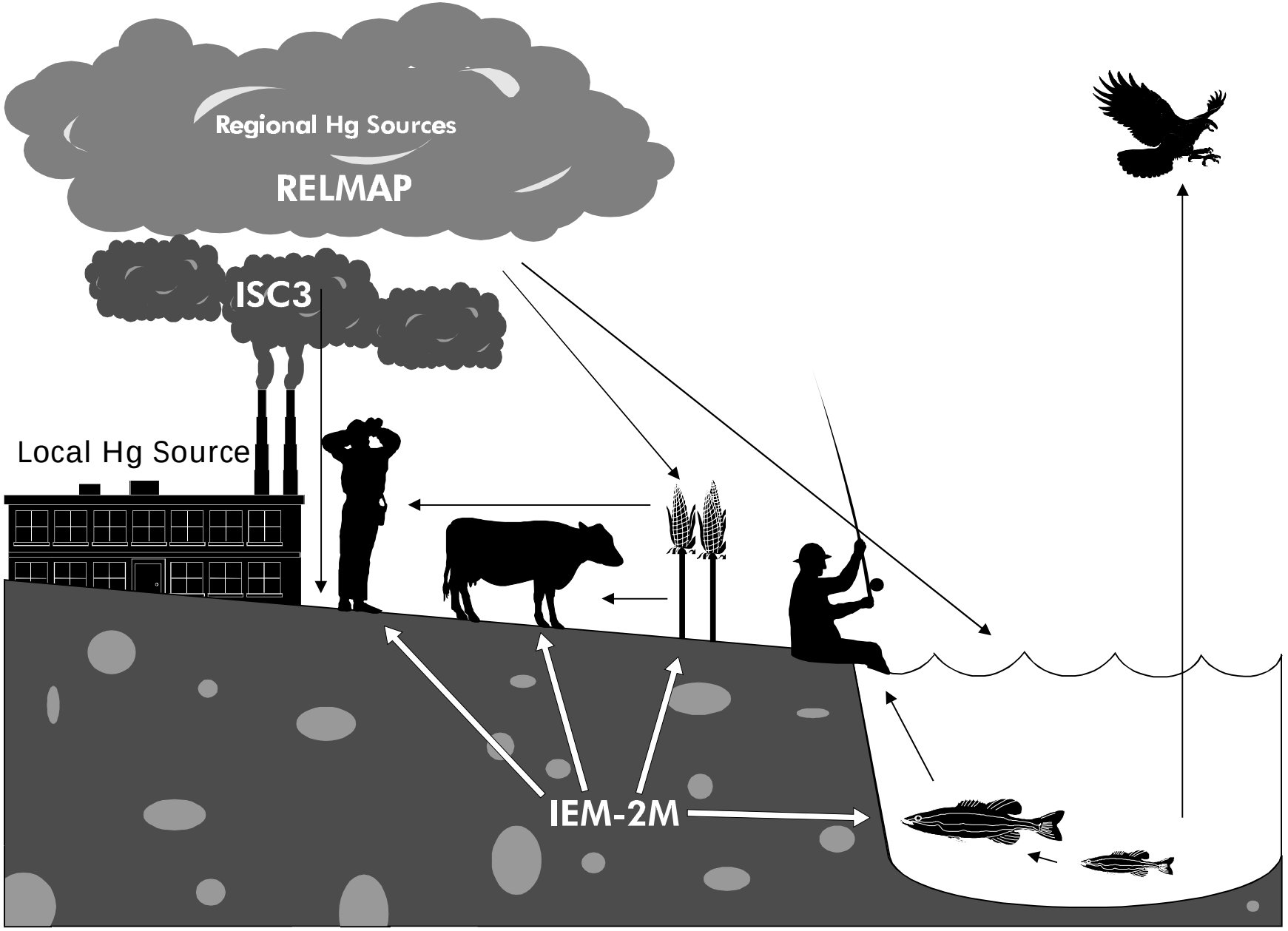
Model	Function
RELMAP	Predict average annual atmospheric mercury concentrations as well as wet and dry deposition flux for 40 km^2 grids across the continental United States. Model predictions were based on anthropogenic emissions from the sources described in Volume II, Inventory of Anthropogenic Mercury Emissions in the United States.
ISC3	Predict average annual atmospheric mercury concentrations as well as the wet and dry deposition fluxes that result from emissions within 50 km of a single source.
IEM-2M	Predict environmental media concentrations and the exposures that result from atmospheric mercury concentrations and deposition.

In the third step of this risk assessment, IEM-2M was utilized to predict mercury species concentrations in watershed soils, the water column and sediments of the hypothetical lake, and terrestrial and aquatic biota. A significant input to the IEM-2M model was the estimate of existing mercury concentrations in environmental media. To determine existing background concentrations in soil, water, and sediments, U.S. EPA estimated current "background" atmospheric concentrations and deposition rates to the hypothetical western and eastern sites. IEM-2M was then run until each site had achieved equilibrium with the specified atmospheric background conditions.

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 upper benthic sediment layer. The ratio for the watershed area to surface water area was 15 to 1, giving a watershed area of 33 km^2. Piscivorous wildlife species were also assumed to inhabit the lacustrine setting, including mink, otter, bald eagle, osprey and kingfisher; all were assumed to consume fish from the hypothetical lake in this setting.

The fourth step of this risk assessment, the predictions of mercury concentrations in soil, water, and biota were then used as inputs to the exposure assessment, as described in Volumes IV and V of this Report.

Figure 4-1
Fate, Transport and Expsoure Modeling Conducted in the Combined ISC3 and RELMAP Local Impact Analysis



4.1.2 Long-Range Atmospheric Transport Analysis

The long-range transport modeling was undertaken to estimate the regional and national impacts of mercury emissions to the atmosphere. It estimates the long-range atmospheric transport of mercury and the impact of mercury across the continental United States. The bases of this modeling were assumptions concerning the atmospheric chemistry of emitted elemental mercury (Petersen et al., 1995) and the numerous studies linking increased mercury levels in air, soil, sediments and biota at remote sites to distant anthropogenic mercury release followed by long range transport. Details of several studies which demonstrate the long-range transport of mercury are presented in this Volume III; these studies provide ample evidence to justify an assessment of long-range mercury transport.

The long-range transport of mercury was modeled using site-specific, anthropogenic emission source data (presented in Volume II of this Report) to generate mean, annual atmospheric mercury concentrations and deposition values across the continental United States. The Regional Lagrangian Model of Air Pollution (RELMAP) atmospheric model was utilized to model annual mercury emissions from multiple mercury emission sources. Assumptions were made concerning the form and species of mercury emitted from each source class. The results of the RELMAP modeling were utilized in these ways. First, the predicted atmospheric mercury concentrations and deposition rates were used to identify patterns across the United States. Secondly, the continental U.S. was divided into western and eastern halves along 90 degrees west longitude, and the 50th and 90th percentiles of the predicted atmospheric concentrations and deposition rates were then used as inputs in the indirect exposure models to examine the impacts of long range transport of emissions.

4.1.3 Analysis of Local-Scale Fate of Atmospheric Mercury

An analysis of the local atmospheric transport of mercury released from anthropogenic emission sources was undertaken to estimate annual average atmospheric concentrations and annual deposition rates of mercury that result from selected, individual sources. A publicly-available version of the ISC3 model was modified slightly and utilized to model these processes. Meteorologic data for one year were input into the model along with data from the model plants (hypothetical facilities). This approach was selected because some environmental monitoring studies described in Volume III suggest that measured mercury levels in environmental media and biota may be elevated in areas around stationary industrial and combustion sources known to emit mercury. The outputs of the model — air concentrations and deposition rates — were used in conjunction with the RELMAP predictions as inputs to the hypothetical watershed and water body.

The hypothetical sites were assumed to have flat terrain. This assumption simplified the analysis and site comparisons. Predicted impacts at locations with elevated terrain would generally have been higher than those with locations exhibiting flat terrain.

4.1.4 Assessment of Watershed and Water Body Fate

Atmospheric concentrations and deposition rates were used as inputs to a series of terrestrial and aquatic models originally described in U.S. EPA's (1990) *Methodology for Assessing Health Risks to Indirect Exposure from Combustor Emissions* and a 1994 Addendum (referred to as IEM2). These model algorithms were further refined in this assessment and now referred to as IEM-2M. This model was used to estimate mercury concentrations in soil, water and biota based on both regional and local-scale

estimates of atmospheric concentrations of mercury and mercury deposition. The two integrated modules that comprise IEM-2M simulate mercury fate using mass balance equations describing watershed soils and a shallow lake. IEM-2M simulates three chemical components — elemental mercury, Hg^0, divalent mercury, HgII, and methylmercury, MHg. Mass balances are performed for each mercury component, with internal transformation rates linking Hg^0, HgII, and MHg.

Mercury residues in fish were estimated by making the simplifying assumption that aquatic food chains can be adequately represented using four trophic levels: level 1 - phytoplankton (algal producers); level 2 - zooplankton (primary herbivorous consumers); level 3 - small forage fish (secondary consumers); and level 4 - larger, piscivorous fish (tertiary consumers). This type of food chain typifies the pelagic assemblages found in large freshwater lakes, and has been used extensively to model bioaccumulation of hydrophobic organic compounds. It is recognized, however, that food chain structure can vary considerably among aquatic systems resulting in large differences in bioaccumulation in a given species of fish. The second simplifying assumption used in this effort was that methylmercury concentrations in fish are directly proportional to dissolved methylmercury concentrations in the water column. It is recognized that this relationship can vary widely among both physically similar and dissimilar water bodies.

The results of these terrestrial and aquatic models were used to predict mercury exposure to hypothetical humans through inhalation, consumption of drinking water and ingestion of soil, farm products (e.g., beef product and vegetables) and fish (Volume IV). These models were also used to predict mercury exposure in hypothetical piscivorous (i.e., fish-eating) birds and mammals through their consumption of fish. The results of these models are utilized in the ecological assessment completed in Volume VI.

4.2 Important Uncertainties Identified in Environmental Fate Modeling

The 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.

Volume III and the appendices describe at length the justification for choices of values for model parameters, such as the amount of precipitation, various transformation rates, and the bioaccumulation factor. 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 uncertainty associated with the internal assumptions and equations that constitute the model structure itself.

4.2.1 Emissions Uncertainties

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: the combustion material or in the case of the chlor-alkali facility the process materials, pollution control equipment, and plant capacity factor (relative average operating hours per year).

The species and form (vapor or particulate) of mercury emitted from the stack are critically important to predictions of deposition by the air models. The data that have been collected to date are limited and the methods to determine the speciation of emitted mercury are still being developed. 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 range from nearly all elemental mercury to nearly all divalent mercury, contributing to the variability in atmospheric fate of mercury.

The chemical species released from anthropogenic sources are 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, for example, into 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 transport are uncertain and variable. The modeled mercury deposition rates depend on species and form of mercury emitted, stack height, stack diameter, exit gas velocity, stack gas temperature, plant capacity factor (relative average operating hours per year), stack mercury concentration, and combustion material. In the 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.

4.2.2 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. Modeled results depend on the assumptions used to represent these atmospheric processes. An important assumption utilized in the Report is that 25% of the emitted divalent mercury binds to existing atmospheric particles in the plume; this is based on a small number of measurements and scientific speculation on both the chemistry of atmospheric divalent mercury and the nature of particulates in the plume. Fluxes associated with vegetation also present a source of potential variability and uncertainty.

4.2.3 Deposition of Atmospheric Mercury

There is inadequate information on the atmospheric processes which affect wet and dry deposition of mercury to compare with model predictions. As a result, model results can not be completely verified. Atmospheric divalent species of mercury are thought to wet and dry deposit more rapidly than elemental mercury; however, the specific rates of deposition are uncertain.

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;
  — Particulate 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, emissions of mercury and particulates are 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).

The parameters exerting the most influence on the deposition rates are the following:

- 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.

4.2.3.1 Compensation Point

It is recognized that dry deposition of elemental mercury may not occur unless the air concentration is above a threshold value, which is termed the compensation point. Results of Hanson et al. (1995) suggest a threshold of approximately 10 ng/m^3. This may depend on factors such as the type of vegetation, season, and time of day. The sensitivity analysis showed that under certain circumstances the compensation point has substantial importance to deposition of elemental mercury; however, the elevated deposition of this fraction had very little bearing to overall deposition of total atmospheric mercury.

4.2.3.2 Pollutant Reactivity

A sensitivity analysis conducted on the pollutant reactivity parameter used in the calculation of dry deposition velocities for divalent mercury vapor showed that the value selected for the modeling, 800, resulted in nearly a maximum deposition rate for mercury. Pollutant reactivity evaluates the

resistance of the plant cuticle to vapor deposition in the ISC3 model. Increasing the value of this parameter could increase deposition of divalent mercury in plant tissues, as the result of decreasing the modeled resistance of the plant cuticle to vapor deposition. The value of 800 for this parameter was derived from evaluation of nitric acid which was used as a surrogate for divalent mercury vapor. Previous uses of the CalPuff model employed a parameter value of 18 for nitric acid. Increase of this parameter value from 800 to 800 million results in at most a 10% difference in deposition of divalent mercury. In contrast, an increase in this parameter from 18 to 800 often results in a several-fold to a many-fold increase in deposition.

If additional empirical data would show that the pollutant reactivity is less than 800 for divalent mercury vapor, then the present analysis has led to overestimation of mercury deposition by, at most, about a factor of five. An observation in strong support of the deposition results, obtained by setting this important parameter at the value of 800, is that the average predicted dry deposition velocity for divalent mercury vapor was about 2.9 cm/s, which is consistent with the table of values used by RELMAP for coniferous forests.

4.2.4 Mercury Concentrations in Water and Aquatic Biota

The ingestion of contaminated fish was indicated by the modeling to be the most important exposure pathway for methylmercury. In general, there is a lack of information characterizing the movement of mercury from watershed soils to water bodies, species transformation rates, and the uptake of abiotic mercury to biotic compartments. There appears to be a great deal of variability in these factors among watersheds; in the model, mercury concentrations in watershed soils are strongly influenced by atmospheric loading and soil loss processes, such as reduction of HgII in the upper soil layer and soil erosion. Influence of plant canopy and roots in mediating both the loading to the soil and the loss from the soil, although potentially important, is not well characterized at present.

In the model, total mercury concentrations in a water body are strongly influenced by atmospheric loading and, for drainage lakes, by watershed loading. Variations in watershed size and erosion rates can cause significant variability in lake mercury levels. Hydraulic residence time, the water body volume divided by total flow, affects the maximum possible level of total water column mercury for a given loading rate. Parameters controlling mercury loss through volatilization and net settling can also cause significant variations among lakes. Mercury loss through settling is affected by *in situ* productivity, by the supply of solids from the watershed, and by the solids-water partition coefficient. Dissolved oxygen concentrations (DOC) can significantly affect partitioning, and thus overall mercury levels. Mercury loss through volatilization is controlled by the reduction rate, which is a function of sunlight and water clarity. Reduction may also be controlled by pH, with lower values inhibiting this reaction and leading to higher total mercury levels.

In the model, fish mercury levels are strongly influenced by the same factors that control total mercury levels. In addition, fish concentrations are sensitive to methylation and demethylation in the water column and sediments. A set of water body characteristics appear to affect these reactions, including DOC, sediment total oxygen concentrations (TOC), sunlight, and water clarity. Variations in these properties can cause significant variations in fish concentrations among lakes. Other factors not examined in this analysis, such as anoxia and sulfate concentrations, can stimulate methylation and lead to elevated fish concentrations. Fish mercury levels are sensitive to factors that promote methyl mercury mobility from the sediments to the water column; these factors include sediment DOC and sediment-pore water partition coefficients.

Bioaccumulation factors (BAFs) were used to estimate fish methylmercury concentrations based on measured concentrations of dissolved methylmercury in the water column. The distribution of the BAFs (Appendix D, Vol. III) was designed to estimate an average concentration of methylmercury in fish of a given trophic level from an average concentration of dissolved methylmercury in the epilimnion for a (single) randomly-selected lake in the continental United States. The large amount of variability evidenced by the data and reflected in the output distributions arises from several sources, which were not quantified. Much of this variability depends on fish age, model uncertainty, and possibly the use of unrepresentative water column methylmercury measurements in the calculation of the BAFs.

The IEM-2M has not been validated with site-specific data. The model was benchmarked against the independently-derived R-MCM, which has itself been calibrated to several Wisconsin lakes. When driven by the same atmospheric loading and solids concentrations, IEM-2M predictions of mercury concentrations compare well with those calculated by R-MCM for a set of Wisconsin lakes.

4.3 Summary

The uncertainty inherent in the modeled estimates arises from many individual assumptions present within the three models. Quantitative estimates for hypothetical sites were developed; uncertainty in these estimates is acknowledged. As a result of these uncertainties, U.S. EPA looked to the model results for an indication of the comparative contribution of regionally transported mercury, current background mercury, and mercury emitted from a local source. Consequently, only a qualitative, rather than quantitative, description of conclusions is presented. The general framework of understanding of how mercury cycles in the environment presented in the Report supports the plausibility of mercury emissions from anthropogenic sources being linked to concentrations in environmental media and biota.

5. CHARACTERIZATION OF EXPOSURE

In the modeling analysis, 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 potential exposure situations likely to be found in the United States. 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.

The 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 meats 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, but consumed no locally-raised meat products.

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., non-inhalation) 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 six 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.

The predicted mercury concentrations and mercury exposures modeled for each site reflected inputs from (1) a single local anthropogenic source, (2) regional atmospheric transport, and (3) an estimate of the existing background concentrations. As noted in the previous chapter, many factors in the analysis affected the predicted concentrations and the resulting exposures. As a result of the uncertainty in the predicted concentrations, the conclusions developed from the exposure modeling were qualitative.

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 non-local fish and from occupational exposures were not added to the exposure estimates developed in Volume III. These sources of mercury exposure may be significant, and for a site-specific assessment, it may be appropriate to consider these sources for members of an exposed subpopulation. In fact, for the fraction of the human population that consumes marine fish, this is the primary exposure pathway for methylmercury.

5.1 Individual Human Results

5.1.1 Predicted Inhalation Exposures

Inhalation exposure are predicted to be primarily to elemental mercury. In the modeling analysis, local sources accounted for less than 50% of total mercury exposure due to inhalation; the only exception to this result was for humans located 2.5 km from the chlor-alkali plant. The primary source of inhalation exposure is based on predictions from the long-range atmospheric transport model. The results of the models indicate that, on an annual average basis, local atmospheric sources do not contribute significantly to atmospheric mercury concentrations at a distance of 2.5 km or greater. The inhalation route is rarely predicted to be the dominant pathway of total mercury exposure when compared to indirect exposure. The exception is the "urban average adult" exposure, in which the only non-inhalation exposure pathway is ingestion of average amounts of soil in the impacted area. The insignificance of exposure through the inhalation route when compared to ingestion routes was described previously by the WHO (WHO, 1990).

5.1.2 Predicted Terrestrial Food Chain Results

Local anthropogenic emission sources, in general, accounted for less than 10% of the total mercury exposure for the agricultural scenarios; contributions from regional sources (RELMAP) and estimated background were much greater. The dominant mercury exposure pathway within the terrestrial food chain is: atmospheric mercury ➜ green plants ➜ human consumption. The soil mercury ➜ green plant pathway is, on the whole, much less important. The contribution of a local source to the more important pathway is roughly equivalent to the impact of the local source on the air concentration. Only the chlor-alkali plant contributes more than 20% (at 2.5 km and 10 km). Divalent mercury accounts for approximately 90% of the total mercury intake for the agricultural scenarios, with the remainder being methylmercury. This partitioning reflects the predicted speciation of mercury in the ingested plant and animal products.

The differences between facilities are due to differences in parameters that affect effective stack height, and the total mercury emission rate. The speciation of mercury emissions is not an important factor because the speciation only affects the predicted deposition rates, not the total mercury air concentrations.

5.1.3. Predicted Soil Ingestion Results

The contributions of the local source on the soil concentrations are driven by the mercury deposition rates. The predicted mercury deposition rates are generally dependent on the speciation of mercury emissions. The contribution of the local source when pica behavior is exhibited (urban high end child) reflects the contribution of the local source to the soil concentration. The primary species of mercury from this pathway is divalent mercury. The highest predicted exposure from soil ingestion, 0.0002 mg/kg/day, occurs in the child at the eastern site and at 2.5 km from the chlor-alkali plant (90th Percentile RELMAP); approximately 80% of the mercury is the result of the chlor-alkali plant emissions. For most other sources, exposures are at least an order of magnitude lower and the percent contributions from the local sources are also lower, except at the western site.

5.1.4 Fish Ingestion Scenarios

Among the individual exposure pathways modeled, the pathway consisting of — atmospheric mercury deposition ➜ watershed soil ➜ dissolved methylmercury in water column ➜ methylmercury in fish through the bioaccumulation factor (BAF) ➜ human fish consumption — dominates all others on a total mercury exposure per kg body weight basis. This pathway is predicted to be the primary source of methylmercury to humans. This is primarily the result of the large values used for the bioaccumulation factor (See Appendix D of Volume III).

Predicted methylmercury exposures are largely dependent on the model plant parameters affecting total mercury deposition such as total mercury in emissions, percent divalent mercury, and effective stack height. The fish concentrations are driven by the predicted dissolved methylmercury concentrations in the surface water, which themselves are driven by the watershed soil concentrations and the waterbody atmospheric mercury deposition rate.

For several of the facilities at both the eastern and western sites, the majority of the exposure to mercury is predicted to be due to the local source for the waterbody located 2.5 km from the facility. This is also true for some facilities at both 10 km and 25 km. These results reflect the contribution of the local source to total mercury deposition onto the waterbody and the watershed soils.

The contribution of the local source is larger (on a percentage basis) at the western site because both the regional and pre-industrial deposition rates are lower than at the eastern site, while the results for the local source (using ISC) are more similar. However, the total mercury exposure is approximately twice as low at the drier western site compared to the eastern site due primarily to differences in meteorology.

It is important to note that the only source of fish in the diets of both the high-end fish consuming adult and children as well as the recreational angler is the local lake. These individuals may represent real humans with monotonous diets. Several surveys showed average daily fish consumption rates above this level for a small fraction (95th percentile and above) of the population or subpopulation studied.

Children's exposures, on a per kg body weight basis, are higher than those of adults. This is consistent with dietary evaluations presented in Volume IV. Since the methylmercury concentration in the fish consumed are the same at a given model site, exposure is the direct ratio of mass ingested per unit of body weight. On average, this ratio is higher for children than adults.

Although predicted fish concentrations around the sources fall within the range of those measured in the United States, U.S. EPA still interprets these modeling results qualitatively. While U.S. EPA considers the results to be reasonable for high-end consumers with monotonous diets, interpretations and conclusions from this effort are qualitative rather than quantitative. This effort indicates that high-end consumers of local fish are clearly a subpopulation of concern. Future efforts should be directed at evaluating local fish consumption rates and the resulting exposures at specific sites around some of these anthropogenic sources.

Table 5-1
Highest Predicted Ingestion Intakes of High-end Fisher Adult and Child (mg/kg/day)
for 90th Percentile RELMAP Results Only

Facility/Distance /%RELMAP	Eastern Site		Western Site	
	Child	Adult	Child	Adult
Chlor-alkali plant/ 2.5 km/90%	8.3E-3	6.1E-3	8.3E-3	6.1E-3
Large hospital HMI/2.5 km/90%	1.8E-3	1.3E-3	1.3E-3	9.5E-4
Chlor-alkali plant/ 10 km/90%	1.7E-3	1.3E-3	1.1E-3	8.2E-4
LargeMWC/ 2.5 km/90%	1.6E-3	1.2E-3	8.7E-4	6.4E-4
Large Coal Utility Boiler/90%	1.4E-3	1.0E-3	4.1E-4	3.0E-4

5.2 Other Sources of Human Mercury Exposure

In the modeling effort exposure for six different hypothetical adult humans was modeled. Atmospheric emissions of anthropogenic origin, local background and regional atmospheric mercury may not be the only sources of mercury exposure. Individuals can be exposed to mercury from other sources such as occupation and consumption of non-local (e.g., marine) fish. Quantitative estimates of these sources are presented in Volume IV. In the modeling effort, several hypothetical individuals were assumed to consume high levels of locally-caught fish. These individuals include: a high-end consumer, who is assumed to consume 60 grams of local fish/day; a child, who is assumed to consume 20 grams of local fish/day; and a recreational angler, who is assumed to consume 30 grams fish/day. Since these hypothetical individuals consume high levels of local fish, it is probably inappropriate to consider exposure through an additional fish consumption pathway. However, it is reasonable to assume that some individuals consume both local and other fish; for example, Fiore et al. (1989) documented the consumption of both self-caught and purchased fish in U.S. anglers. In this assessment, these data are not combined. It is important to note that exposure through consumption of marine species could result

in significant additional incremental exposures to high-end fish consumers.

In the modeling effort several hypothetical humans were assumed not to consume locally-caught fish. These hypothetical individuals include: a subsistence farmer and child, a rural home gardener, and the urban dwellers. For these hypothetical individuals, it is reasonable to assume that some fraction of the individuals they represent will consume marine fish. For this marine fish consuming subset, the ranges of methylmercury exposure from marine fish consumption that are estimated in Volume IV are applicable. Methylmercury from marine fish consumption, if considered, is an incremental increase over the estimated intakes.

Occupational mercury may be an important source of exposure. This source may apply to any hypothetical adult modeled here with the exception of the subsistence farmer. For a given area with a relevant industrial base, it may be appropriate to consider these exposures for appropriate members of the population. These exposures would be expected to be primarily to inorganic mercury species and would be incremental inhalation or ingestion exposures.

The initial conditions assumed before the facility is modeled (referred to here as "background") are potentially critical to the total mercury exposure. This is particularly important because the magnitude of the contribution of a local source to the total may be used to assess its impact. A delicate balance is required when including such a "background" in the analysis. This is because it is not just a matter of local source contributions to this background, but rather, the total impact of background plus the local source that is ultimately of primary concern. Overestimating the background will result in a concurrent decrease in the contribution of a given local source, but may result in exceeding thresholds that would not be exceeded if lower estimates of background are assumed. Resolution of this issue is not within the objectives of the current report; it is noted, however, that there is no available guidance on how to incorporate background in exposure assessment. For a local scale mercury exposure assessment it is important to measure mercury concentrations in various media.

The impact of the uncertainty in the predicted air concentrations and deposition rates for each facility is most important for the fish ingestion and pica child scenarios. This is because, in general, the local source does not contribute significantly to the mercury exposure for the agricultural and urban scenarios. Additionally, variability in watershed methylmercury "processing" may also result in vastly different impacts from sources emitting similar quantities and species of mercury to the atmosphere. The exception to this pattern is the chlor-alkali model plant. In this case, the low assumed mercury release height results in the facility having a substantial impact on the mercury air concentrations close to the facility.

5.3 Characterizing Wildlife Exposures

5.3.1 Modeled Wildlife Exposures

The only pathway of mercury exposure considered for the wildlife species consist of — atmospheric mercury deposition ⇨ watershed soil ⇨ dissolved methylmercury in water column ⇨ methylmercury in fish through the bioaccumuation factor (BAF) ⇨ wildlife fish consumption. Other pathways and perhaps other species of mercury should be evaluated as the data and models become available to assess them. These could include exposure assessments for predators of fish-eating species (e.g., fish ⇨ raccoon ⇨ panther), benthic-dwelling species as well as exposures to organisms that eat marine species and effects of mercury on microbial populations in soils or the water column.

Previous discussions of highest predicted fish concentrations and resulting highest human exposures could be reiterated here because fish consumption is the only pathway considered. Uncertainty and variability described in predictions of human exposures that result from fish consumption are also applicable to the wildlife. It is interesting to note that on a per kilogram body weight basis, predicted exposures to wildlife are much greater than to humans. Other factors such as range and migration may affect wildlife exposures that result from emissions of a local source.

5.3.2 Measured 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 more consistently fish eaters whose diet consists of at least 95% 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 in the diets of mink and otter.

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 exhibits the same progression of signs and symptoms observed in a laboratory setting. Under the experimental situation established by Wobeser (1973), the minks deteriorated, presenting with anorexia, to exhibiting 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 symptomology. 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 greater than 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 Georgia averaged 7.5 µg/g (Hallbrook et al., 1994); this is approximately 33% of the concentrations associated with severe intoxication and/or death in a closely related species, 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 otter tissues are 10-30% of the 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 sites of long-term mercury contamination. For example, Wren et al., (1986) found that wild mink trapped in the English River system, which was severely contaminated by mercury discharge from a chlor-alkali plant 15 to 22 years earlier than the dates of mink trapping, had a mercury concentrations in the 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).

5.3.3 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 sources remain. Between 1990 and 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).

Based on historical and recent information, mercury is a common contaminant of avian tissues from diverse geographic locations. Mercury concentrations 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).

The feeding habits of particular avian species are major predictors of risk of mercury toxicity in the 1990s. When seed grains were treated with organo-mercurial fungicides, herbivorous, omnivorous, and carnivorous species were all at risk of mercury toxicity. 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, that consume large fish as their prey, are predicted to be at greater risk of methylmercury poisoning than birds that consume smaller fish (Spalding et al., 1994; Sundlof et al., 1994). When the quantities of fish consumed on a body weight basis is also considered for smaller birds such as the kingfisher, there is an elevated risk of methylmercury poisoning.

Several estimates exist in the published literature on mercury concentrations in soft tissues (liver, kidney, brain) that are associated with mercury poisoning in avian species. Experimental studies of survival and reproductive success of black ducks (*Anas rubripes*) indicated that adult ducks would tolerate liver mercury concentrations of 23 ppm and appear in good health (Findley and Stendell, 1978). However, it was found that although the black ducks fed methylmercury in diet appeared in good health they had impaired reproductive success as 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) 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 incoordination that were associated with brain mercury concentrations of 15 µg/g (fresh weight), or liver or kidney mercury concentrations of 30 µg/g (fresh weight). Schuehammer (1991) observed that generally significant reproductive impairment due to methylmercury occured at about one-fifth the tissue concentrations required to produce overt neurotoxicity. 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 (Schuehammer, 1991). 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. The correlation coefficient between mercury and methylmercury is 0.98 in the brain, 0.84 in mucsle, and 0.23 in liver of adult loons. For liver versus brain, the correlation coefficeint is 0.58 for total mercury and 0.46 for methylmercury. 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 (≥30 µg mercury/g fresh weight). Furthermore, these investigators found between 30% and 80% 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 power lines 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 5-2). Using standard statistical procedures, it is estimated that 33.3% of the liver mercury concentrations for the respective species would be greater than the mean+one SD. 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 5-2
Liver Mercury Concentration (µg/g fresh weight) in Common Merganser, Red-Breasted Merganser and Herring Gulls from Northern Quebec (Langlois and Langis, 1995)

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 5-3. The concentration of total mercury residue in loon tissues decreased in the sequence---

Table 5-3
Mercury and Methylmercury Concentrations in Tissues (µg/g 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

liver > muscle >brain, but the percentage of methylmercury increased from liver < muscle < brain. Barr (1986) found that almost 100% 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 (Schuehammer, 1991). Schuehammer concluded that results suggest a reduction in egg laying and in nest and territorial fidelity at mercury concentrations 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.

5.4 Human Intake of Methylmercury Estimated through Dietary Surveys and Mercury Residue Data

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.

5.4.1 Estimates Based on Total Diet Studies

Overall, data from Total Diet Studies from multiple countries confirm the following:

- Fish and shellfishes are the predominant source of mercury in the diet;
- Methylmercury is the predominant form of mercury in fish and shellfish;
- Total exposure to mercury depends on the quantity of fish and shellfish consumed;
- Wide variability exists in the concentration of mercury in various species of fish/shellfish; and
- Mercury concentration within a fish species generally increases with the size of the individual fish.

In the United States, the Food and Drug Administration (FDA) has conducted a Total Dietary Survey including analyses for metals and elements since the early 1970s (Manske and Johnson, 1977). Most of the mercury reported in the total diet study is methylmercury because the mercury identified in Total Diet Study originates from seafood. In the early 1970s the meat, fish and poultry food group represented virtually the entire intake of mercury in the Total Diet Study (Mahaffey et al., 1975). Total Diet Study intake of mercury averaged about 2.8 µg/day for young adult males or approximately 0.04 µg/kg*bw*/day if a 70 kilogram body weight is assumed. Similar exposures to mercury from food were reported by Gunderson et al. (1995) using a revised approach to the FDA Total Diet Survey that presented µg/kg*bw*/day values for eight age-gender groupings. Persons aged 14 and older had a mean dietary intake between 0.03 and 0.04 µg/kg/day. Toddlers had approximately twice as high mercury exposure from food with an average of 0.07 µg/kgbw/day (Gunderson et al., 1995).

Results from total diet studies conducted in a number of different countries reconfirm that fish is the main contributor to the mercury intake. The magnitude of mercury exposures depends on the amount of fish and shellfish consumed. In Spain, the mean adult dietary intake for mercury was 12 µg/day (maximum, 18 µg/day) for adult men and women in 1990 and 1991 (Urieta et al., 1996). Japanese data on total dietary intake of mercury, conducted between 1979 and 1994, indicate average mercury intake of between 6.9 and 11.0 µg/man/day with the majority of mercury coming from fish (Ikarashi et al., 1996). Countries with lower total mercury intakes from diet consume smaller quantities of fish. For example, van Dokkum et al. (1989; as cited by Urieta et al., 1996) reported a fish consumption of 10 g/day and an mercury intake of 0.07 µg/kg/day as averages for the Dutch.

Within a particular species of fish (e.g., mackerel, croaker, flounder), larger members of the species contained higher concentrations of mercury and the increase was statistically significant (Ikarashi et al., 1996). Variability in mercury concentrations in fish was confirmed by an Italian study covering the period 1986 to 1995 (Haouet et al., 1996). Although mean values were within legal limits for Umbria and Marche regions, high levels of mercury were found in some species. Median values for various

species of mollusks and crustacea were in the range of 0.08 µg/gram with some concentrations averaging over 2 ppm for piscivorous species.

5.4.2 Estimates Based on Food Consumption Surveys

The development of the Total Diet Study in the United States relied on data from 1965 dietary survey conducted by the United States Department of Agriculture (USDA) (Mahaffey et al., 1975). Mean intakes for various food groups from the dietary survey were used to develop the quantities of food used in the Total Diet Studies. A major limitation of such data is that average intakes typically were used. Additional information on dietary intakes of fish and shellfish — ranging from long-term patterns of fish and shellfish intake by individuals to cross-sectional data for population groups — can be obtained from dietary surveys.

Available techniques to estimate fish consumption include long-term dietary histories and questionnaires to identify typical food intake or short-term dietary recall techniques. Day-to-day 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.

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 intakes of methylmercury. The survey and results are described in Volume IV.

Human methylmercury intake from fish for the general U.S. population was estimated in this *Mercury Study Report to Congress* 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 three of USDA's Continuing Surveys of Food Intake by Individuals (CSFII 89-91, CSFII 1994 and CSFII 1995) and in the third National Health and Nutrition Examination Survey (1988 through 1994). The CSFII 89-91 dietary survey methodology consisted of an assessment of three consecutive days of food intake and selection of interviewees from probability samples for non-institutionalized U.S. households. Use of these survey data provides a nationally based estimate of fish intake by the general population of the United States. Surveys conducted in CSFII 1994 and CSFII 1995 relied on two days of dietary recall for individuals. These days did not have to be consecutive. NHANES III relied on descriptions of food frequency (including responses to two questions specifically on patterns of consumption of fish and shellfish) collected from adult interviewees aged 12 years and older (approximately 19,000 individuals). A subset of NHANES respondents, which included both adults and children, provided 24-hour recall data.

These cross-sectional survey designs 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 epidemiologist (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 IV comparisons were made between quantities consumed and the upper quartile of the fish-consuming subpopulation of the general U.S. 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, to some extent, corroborated the daily consumption rates of the extreme end of the distribution of all three CSFII surveys and of NHANES III.

In CSFII 1989-1991, 31% of the people surveyed reported consumption of fish and/or combinations of fish, shellfish, or seafood with starches in a 3-day period. Of individuals reporting fish consumption, approximately 98% consumed fish only once, and about 2% 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. CSFII 1994 and CSFII 1995 reporting on individual days recall found 11 to 12% of individuals consuming fish/shellfish on any one day. A smaller percent of children less than 14 years-old reported eating fish/shellfish (approximately 8%). Among men and women of reproductive age (15 through 44 years) about 10 to 11% reported eating fish/shellfish on any one day. Adults 45 and older consumed fish and shellfish more frequently with about 15% of respondents consuming fish and shellfish based on individual day data.

One question raised in the process of review of data from the food consumption surveys was whether the estimates of fish/shellfish consumption too high. This issue can be partly addressed through comparison with the amount of fish available for consumption within the United States. The National Marine Fisheries Service provides data on fish and shellfish production. These data have been compiled since the early part of this century. Major increases in fish and shellfish consumption occurred post-1970. For example, in 1910 the U.S. population consumed an average of 11.0 pounds (edible meats) of commercial fish and shellfish. The consumption in 1970 was 11.8 pounds per capita, however, by 1990 fish and shellfish consumption had increased to 15.0 pounds per capita. Two major factors were associated with this trend. First, there was a major increase in population from 92.2 million in 1910, to 201.9 million individuals in the 1970s, and 247.8 million citizens in 1990. In 1995, (the latest year this source provided statistics on the civilian resident population) the U.S. population was estimated at 261.4 million persons. Combined with increased consumption on a per capita basis, the seafood market has dramatically increased throughout this century.

The second major factor was in availability of transportation and in food processing. Changes between 1910 and 1995 are shown in Table 5-4. Consumption of cured fish dramatically decreased from about 36% of per capita intake in 1910 to 2.0% in 1990. Fresh or frozen fish were about 40% of the per capita intake in 1910 and increased to about 67% (two-thirds) of fish and shellfish intake between 1990 and 1995. The consumption of canned fish and shellfish changed the least representing about one-fourth of all fish/shellfish intake in 1910 and about one-third of intake between 1990 and 1995.

Table 5-4
Percent of Fish/Shellfish by Processing Type between 1910 and 1995
(Source: National Marine Fisheries Service, 1997)

Year	Fresh/Frozen	Canned	Cured
1910	39.1	24.5	36.4
1970	58.5	38.1	4.0
1990	64.7	33.3	2.0
1995	66.7	31.3	2.0

Comparison of the amount of fish (grams per capita per day) reported in CSFII 1994, CSFII 1995 and NHANES III with the production of fish and shellfish is shown in Table 5-5. These data indicate that the amounts of fish/shellfish reported consumed in the surveys do not exceed production of fish and shellfish. The consumption data based on the dietary surveys provide reasonable estimates of intake particularly when it is recognized that some fish and shellfish entering the food supply is not consumed but is wasted either in distribution, in the home, or on the plate.

Table 5-5
Fish and Shellfish Production*

Year	U.S. Population (in millions)	Per Capita Per Year		Grams Per Capita Per Day
		Pounds	Grams	
1990	247.8	15.0	6810	18.7
1994	259.2	15.2	6901	18.9
1995	261.4	15.0	6810	18.7

**National Marine Fisheries Service Data*

Table 5-6
Fish and Shellfish Consumption

Survey	U.S. Population (in millions)	Number of Days of Dietary Records	Grams Per Capita Per Day
NHANES III (1988-1994)	241.6	29,989	17.6
CFSII 1994			
Day 1	258.9	5,296	11.1
Day 2	258.9	5,293	12.0
CFSII 1995			
Day 1	261.5	5,063	13.0
Day 2	261.5	5,062	14.3

An additional way to assess the reasonableness of the data provided in the consumption surveys is to compare the species of fish and shellfish reported to be consumed with the species of fish and shellfish that are produced, imported or exported into the United States. Analyses of the frequency of reporting fish/shellfish and menu items containing fish and shellfish were carried out using data from CSFII 1994 and CSFII 1995. The most commonly reported menu items were "seafood salads and seafood and vegetable dishes". Although other fishery products are possible in salads, this menu category typically describes dishes made with tuna, surimi (i.e., Alaskan pollock), crab, salmon, or other canned fish or shellfish. Overall, these dishes represented about 20% of overall seafood consumption. This major group was followed by shrimp, canned tuna, and the group "seafood cakes, fritters, and casseroles without vegetables." Identified finfish commonly consumed included salmon, cod, catfish, flounder, trout, seabass, ocean perch, haddock, and porgy. Although specific finfish were identified as among the top ten consumed sea foods, they represented less frequent selections than did processed fishery products; e.g., salads, fritters,"fast food" fillets, and shrimp.

Production, import and export data indicate that the predominant species of fish and shellfish in the United States are the various species of tuna, shrimp, and the Alaskan pollock. Superimposed on these broad national trends in fish/shellfish production are regional trends in fish/shellfish production and consumption. Table 5-7 provides an overview developed from business publications and interviews with leaders in the seafood industry of regional patterns in fish and shellfish consumption/production

Table 5-7
Regional Popularity of Fish and Shellfish Species

Region	Fish/shellfish Species
East Coast	Haddock, Cod*, Flounder, Lobster, Blue Crab, Shrimp
South	Shrimp, Catfish, Grouper, Red Snapper, Blue Crab
West Coast	Salmon, Dungeness Crab, Shrimp, Rock Fish
Mid-West	Perch, Walleye, Chubs, Multiple Varieties of Freshwater Fish

**In the mid-1990s cod has largely been replaced on menus by Alaskan pollock.*

Approximately 8 to 9% of children were reported fish/shellfish consumption in CSFII 1994, CSFII 1995, and NHANES III. The most common fish/shellfish product consumed was tuna salad and/or canned tuna, followed by fish sticks/patties, with shrimp and catfish distant third and fourth places in fish consumed by children. All other fish and shellfish made up 30 to 40% of children's fish and shellfish intake.

5.4.3 Mercury Concentrations in Fish and Shellfish

Selection of a data base for mercury residues in fish was based on the following characteristics:

- Data sets that were nationally based;
- Preferred data base that included as many individual fish to represent the species as possible; and
- Fish/shellfish species collected over a time period that approximated the years of the dietary survey.

Data describing methylmercury concentrations in marine fish came primarily from the National Marine Fisheries Service (NMFS) data base, the largest publicly available data base on mercury concentrations in marine fish. This NMFS data base has been compiled over the past two decades. Comparison of the values for central tendencies (e.g., 50th percentile) in mercury concentrations between the NMFS data base and FDA's compliance data on selected species (Carrington et al., 1995) indicated close agreement in mercury concentrations. The concentrations of methylmercury in marine fish and shellfish were derived from a data base that is national in scope and the data on freshwater 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.

A question raised in review of these data concerned the adequacy of the detection limits for chemical analyses of mercury used in obtaining these data. This issue has been addresses in detail in Volume IV (particularly see Appendix C). The judgment based on this statistical analysis was that the handling of zero values and trace values did not bias the mean value for mercury concentrations in species of fish in the National Marine Fisheries Service data base used for marine fish. The detection limits in the report by Bahnick et al. (1994) was sufficiently low that a very high percent of individual samples could be analyzed and quantitative values for mercury provided. Consequently, the analytical method, as well as handling of zero and trace values, is not an area of significant uncertainty in determining mean mercury concentration in these fish/shellfish species.

5.4.3.1 Estimates of Central Tendency for Mercury Concentration in Fish and Shellfish

Volume IV provides detailed tables describing the mercury concentration in fish and shellfish. The mean concentration of mercury for a specific species was used in calculating mercury exposures from marine seafood used in this assessment. Additional data (also provided in Volume IV) describe on mercury concentrations in particular fish/shellfish species reported by the FDA (1978) and by Stern et al. (1996).

Mean mercury concentrations for the mixture of fin fish and shellfish consumed by the general population average between 0.12 and 0.14 parts per million. Persons eating a variety of fish and shellfish that result in this mean mercury concentration will have dietary mercury intakes comparable to those estimated in this study. However, mercury exposure may be much higher or lower than those estimated

in the current Report. For example, if people select a few species of fish which are much higher in mercury concentrations (e.g., shark, swordfish, seabass, walleye, largemouth bass), their total mercury exposures would be far higher than the levels used in this Report. Likewise, if fish from a contaminated local supply are routinely consumed, mercury intake could be higher than those values calculated in this Report which relied on average mercury concentrations. If people either consume a very different mixture of fish/shellfish or consume fish/shellfish coming from a limited geographic area they may have either a much lower or a much higher dietary intake of methylmercury.

5.4.3.2 Ranges in Mercury Concentration in Fish and Shellfish

The issue of variability of mercury concentration within a particular species of fish and across species of fish/shellfish remains. In the estimates of dietary intakes of mercury from fish and shellfish the calculations were made using mean fish/shellfish mercury concentrations. This approach works well if the subpopulation of concern obtains their fish/shellfish from a variety of sources. However, if individuals or subpopulations obtain most of their fish/shellfish from one or a small number of geographic sources, their exposures could be either much lower or much higher than the mean value used in calculations in this volume. This source of variability can be seen in the mercury concentrations in freshwater fish compiled by U.S. EPA (1997). Data have been profiled describing the *mean* mercury concentration present in six species of freshwater fish collected from 1990 through 1995 (Table 5-8). These data are representative of major fish species throughout the United States and presents mean values for mercury concentrations in six species of freshwater fish in the United States.

Table 5-8
Range of Mean Mercury Concentrations (ppm) for Major Freshwater Fish Species*

Species	Mean Mercury Concentrations	Species	Mean Mercury Concentrations
Channel catfish	0.010-0.890	**Largemouth bass**	0.101-1.369
Smallmouth bass	0.094-0.766	**Walleye**	0.040-1.383
Brown trout	0.037-0.418	**Northern pike**	0.084-0.531

**Data source: The National Survey of Mercury Concentrations in Fish. Database Summary 1990-1995. September 29, 1997. Prepared for U.S. EPA under Contract No. 68-C4-0051.*

5.4.4 Subpopulations of Concern Based on Physiological Sensitivity to Adverse Developmental Effects of Methylmercury

In selection of sensitive subpopulations of humans, sensitivity may reflect an inherent responsiveness to the hazard (i.e., toxicity based sensitivity) or reflect elevated exposures to the agent of concern. With respect to risks posed by methylmercury from fish and shellfish, two subpopulations of humans are of particular interest in this risk characterization: women of childbearing age and children.

5.4.4.1 Mercury Intake by Women of Childbearing Age

Women of childbearing age are of concern because developmental effects following *in utero* exposures are the basis for the RfD and because the developing nervous system of the fetus would be

expected to be most sensitive to mercury toxicity. Because 9.5% 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 childbearing age is judged to be of concern.

Because the endpoint for the RfD is a developmental effect of methylmercury following *in utero* exposures, an uncertainty in the exposure analysis is the time period relevant to the developmental effects. Because methylmercury is stored in the body with a half-life averaging 70 days, mercury intake over time represents an important consideration in estimating exposures. U.S. EPA's Science Advisory Board (SAB) addressed this question at the request of U.S. EPA. SAB scientists advised the Agency that "there is sufficient data to conclude that the developing organism is vulnerable during the entire period of development and that *in utero* as well as early postnatal exposure to methylmercury is of concern. The SAB also indicated that intermittent or short-term exposure to methylmercury at a critical period in development should be considered. Exposures prior to pregnancy may also be of concern given the half-life of methylmercury" (SAB, 1997).

Mercury intakes from fish and shellfish among women of childbearing age (ages 15 through 44) can be estimated across the whole population whether or not they consume fish/shellfish during the survey period ("per capita" exposure), estimates for only those women who report consuming fish/shellfish during the survey period ("per user" exposure), and for typical patterns of exposure projected across time by using frequency of fish/shellfish intake data ("month-long per user estimates"). These different methods of presenting exposure information for women of childbearing age each offer information to the risk assessor.

As indicated by the SAB, the exact period of time of concern for adverse developmental effects is not known. Because methylmercury is bioaccumulated by the woman, high-dose short-term intakes may produce the same cumulative body burden as more frequent lower-exposures. Data on human biokinetics of methylmercury are not sufficiently abundant that these types of predictions can be made reliably. Consequently, all three types of exposure estimates (i.e., per capita, per user, and month-long per user) can contribute to the process of assessing risk.

Per Capita

CSFII 89-91 estimates of mercury intake are based on the average value for three-days of dietary recall and are shown below (Table 5-9). Estimated "per capita" mercury exposures (µg/kgbw/day) from all three CSFII data sets and from NHANES III indicate that the 95th percentile mercury exposure ranges between 0.03 and 0.20 µg/kg*bw*/day.

Table 5-9
Estimated Mercury Intake for Women of Childbearing Age
(CSFII 89-91)

Females Aged 15— 45 Years	25th	50th	75th	95th	Maximum Value
Fish/Shellfish Consumption (g/day)	Zero	Zero	19	73	461
Mercury Exposure (µg/kgbw/day)	Zero	Zero	0.03	0.20	2.76

Estimated mercury exposures "per capita" have also been made based on data in CSFII 1994, CSFII 1995, and NHANES III (Table 5-10). These are average values for individual 24-hour recalls.

Table 5-10
Fish and Shellfish Consumption (g/day) and Mercury Exposure (µg/kg*bw*/day)
by Women Ages 15 — 45 Years
United States *Per Capita*

Survey	Number of Women	Percentiles		
		50th	90th	95th
CSFII 94				
Day 1	842	Zero	26 0.03	80 0.12
Day 2	840	Zero	14 Zero	69 0.08
CSFII 95				
Day 1	635	Zero	30 0.03	87 0.13
Day 2	634	Zero	56 0.09	89 0.19
NHANES III	5,437	Zero	58 0.09	114 0.18

Per User

Estimated "per user" intake from CSFII 89-91, averages of three 24-hour recalls per individual subject, are shown below (Table 5-11).

Table 5-11
Per User Fish/Shellfish Consumption (g/day) and Mercury Exposures (µg/kg bw/day) Based on Average of Three 24-hour Dietary Recalls - CSFII 89-91

	Percentiles				
	25th	**50th**	**75th**	**95th**	**MaximumValue**
Fish/Shellfish Consumption	19	31	56	113	461
Mercury Exposure	0.04	0.08	0.16	0.33	2.76

Estimates from CSFII 1994 and CSFII 1995, as well as from NHANES III, are shown below (Table 5-12). These data are based on individual day 24-hour recalls. Predictably the data show higher values for individual days than were shown for the single day values calculated from averages of three days of dietary records.

Table 5-12
Fish and Shellfish Consumption (g/day) and Mercury Exposure (µg/kg*bw*/day) by Women Ages 15 — 45 Years, United States, *Per User on a Single DAy*

Survey	**Percentiles**			
	50th	**75th**	**90th**	**95th**
CSFII 1994				
Day 1	77 0.10	103 0.16	169 0.25	235 0.29
Day 2	62 0.08	106 0.18	156 0.34	184 0.45
CSFII 95				
Day 1	62 0.09	103 0.22	253 0.38	305 0.42
Day 2	77 0.14	113 0.23	217 0.47	325 0.97
NHANES III	66 0.10	131 0.21	228 0.39	287 0.53

Per User Month-Long Data

An area of concern express in review of this *Report to Congress* is the extent to which mercury

exposure "per user" based on single day 24-hour recall exposure estimates will be reflected in longer-term patterns of fish and shellfish consumption. Twenty-four hour recall dietary data provide a useful indication of variability in the species of fish/shellfish chosen for consumption and the portion size of the fish/shellfish consumed. The uncertainty is over how often the day's fish/shellfish consumption activity is repeated over a time period relevant to the toxicology endpoint of interest. As described above, the exact period of methylmercury intakes that is of concern for developmental effects is not known precisely and remains an uncertainty.

In NHANES III respondents were asked how often per day, per week, and per month they had consumed fish and shellfish over the past year. Details of the questions were provided in Volume IV. For women ages 15 through 44 years, the frequency of fish/shellfish consumption is shown below (Table 5-13).

Table 5-13
Percentage of Fish/Shellfish Consumers
(NHANES III, Food Frequency Questionnaire, Weighted Data)

Group	Number of Times Fish/Shellfish Eaten Per Month							
	Zero	1 or more	2 or more	4 or more	8 or more	12 or more	24 or more	30 or more
WomenAged 15 - 44 Years	14	86	78	56	25	12	3	2

Combining the distributions of "per user" consumption of fish and shellfish with the cumulative percentages of fish and shellfish consumption produces the pattern of fish and shellfish consumption over a one-month period described below (Table 5-14).

Table 5-14
Month-Long "Per User" Exposure Estimates for Women Ages 15-44 Years
NHANES III, All Ethnic Groups Combined
Combined Distributions of Fish/Shellfish Consumption Frequencies and "Per User" Dietary Data

Percentile	Grams/Day	µg Hg/kgbw/day
50th	9	0.01
75th	21	0.03
90th	46	0.08
95th	78	0.13

5.4.4.2 Subpopulations of Concern Based on Magnitude of Mercury Exposure Relative to Body Size

Ethnic/Racial Differences in Fish Consumption and Mercury Exposures

Data from the CSFII surveys and from NHANES III when appropriately weighted statistically provide estimates descriptive of the U.S. population as a whole. If these data are aggregated to provide estimates for particular age and sex subgroups, the estimates are representative for those subgroups in the United States. In addition to age and sex subgroups, survey respondents designate themselves as "white/NonHispanic", "black/NonHispanic", "Mexican American" and "Other". The category of "Other" includes persons who are of Asian/Pacific Islander ethnicity, NonMexican Hispanics (usually from Puerto Rica or other Caribbean Islands), Native American Tribal members and Alaskan Natives, as well as a remaining group of persons who designate themselves are "Other".

Published data files from NHANES III and CSFII 1994 and 1995 subdivide based on racial/ethnic categories. Patterns of fish and shellfish consumption vary by racial and ethnic group are given in Table 5-15 (See Volume IV for additional descriptions). Overall, persons who designate themselves as "Black/NonHispanic" and "Other" have higher fish and shellfish consumption and exposures to methylmercury compared with the population who categorize themselves as "White/NonHispanic". These data indicate that Black/NonHispanics and persons grouped as "Other" (Asians, Pacific Islanders, Native Americans, Alaskan Natives, persons of Caribbean ethnicity) consume fish and shellfish more frequently than do others in the U.S. population.

In contrast, persons of Asian/Pacific Islander ethnicity do not consume more fish on a "per user" basis, although they consume fish more often than do other population members. Black/NonHispanics have about twice as much fish consumption on a per capita basis and 12 to 14% greater fish and shellfish intake on a "per user" basis than do White/NonHispanics. Estimates for Native Americans and Alaskan Natives were not made because their numbers in the general population surveys were too small to provide reliable estimates. Data from surveys of subpopulations strongly support the observation that some Native American Tribes and many Alaskan Natives consume fish and shellfish frequently and in amounts greater than the general population.

Table 5-15
Consumption of Fish and Shellfish (g/day) and Mercury Exposure (µg Hg/kg bw/day) among Ethnically Diverse Groups on an Individual Day
(Source: CSFII 1994 and CSFII 1995)

Ethnic Group	Per Capita[1]		Per User[2]	
	Fish Consumption (g/day)	**Mercury Exposure (µg/kgbw/day)**	**Fish Consumption (g/day)**	**Mercury Exposure (µg/kgbw/day)**
White				
50th Percentile	Zero	Zero	72	0.12
90th Percentile	24	0.03	192	0.46
95th Percentile	80	0.14	243	0.67
Black				
50th Percentile	Zero	Zero	82	0.14
90th Percentile	48	0.05	228	0.54
95th Percentile	104	0.19	302	0.96
Asian and Pacific Islander				
50th Percentile	Zero	Zero	62	0.10
90th Percentile	80	0.15	189	0.39
95th Percentile	127	0.30	292	0.56
Native American and Alaska Native				
50th Percentile	Zero	Zero	*Estimate not made because of small numbers of respondents.*	*Exposures not made because of small numbers of respondents.*
90th Percentile	Zero	Zero		
95th Percentile	56	0.03		
Other				
50th Percentile	Zero	Zero	83	0.18
90th Percentile	Zero	Zero	294	0.64
95th Percentile	62	0.13	327	0.81

[1]*Total number of 24-hour food consumption recall reports: White (16,241); Black (2,580); Asian and Pacific Islander (532); Native American and Alaska Native (166): and Other (1,195).*
[2] *Number of 24-hour food consumption recall reports: White (1,821); Black (329); Asian and Pacific Islander (155); Native American and Alaska Native (12); and Other (98).*

Month-Long Per-User Projections

Estimates for month-long patterns of fish/shellfish consumption have been determined by using 1) fish/shellfish consumption frequency data to project consumption rates over a month-long period, and 2) NHANES III 24-hour recall data for users only. These data are shown for the total population by ethnic group (Table 5-16).

Table 5-16
Month-Long "Per User" Estimates of Fish Consumption (g/day)and Mercury Exposure (µg/kg*bw*/day)General Population by Ethnic/Racial Group; Combined Distribution Based on NHANES III Fish/Shellfish Frequency and "Per User" Data

White/NonHispanic			*Black/NonHispanic*			*Other*		
Percentile	**Fish/ Shellfish (g/day)**	**Mercury (µg/kgbw /day)**	**Percentile**	**Fish/ Shellfish (g/day)**	**Mercury (µg/kgbw /day)**	**Percentile**	**Fish Shellfish (g/day)**	**Mercury (µg/kgbw /day)**
50th	8	0.02	50th	10	0.02	50th	12	0.02
75th	19	0.04	75th	26	0.05	75th	29	0.06
90th	43	0.09	90th	60	0.13	90th	65	0.17
95th	69	0.15	95th	99	0.21	95th	105	0.31

Age-Related Differences in Fish/Shellfish Consumption and Mercury Exposure

A major uncertainty identified in this risk characterization are limitations in the data is the absence of data to assess health hazards of methylmercury for children. However, because brain development continues post-natally, mercury exposure among young children are of concern. Analyses of exposure to mercury among young children have identified children as the major subpopulation of concern. The basis for this concern is that intake of methylmercury from fish is estimated to be greater for children (on a per kilogram body weight basis) than for adults based on 24-hour recall data for fish consumption by children and the assumption that frequency of fish/shellfish consumption is comparable to that of adults. On a µg/kg*bw*/day basis, the exposure for children aged 14 years and younger is estimated to be up to two-to-three times that of the adult. These data are presented in Tables 5-17 and 5-18, respectively. The higher estimated exposure to methylmercury is the result of the higher intake of food on a per weight basis among children. exposed post-natally to methylmercury.

All of the dietary surveys evaluated for this Report indicate that children age 10 and younger have higher intakes of fish and shellfish on a body weight basis than do adults. This pattern occurs in the CSFII 89-91, CSFII 1994, and CSFII 1995 surveys, and in NHANES III. Detailed analyses for various age groups are found in Volume IV. As is the situation with adults, it is uncertain how often children consume the pattern of fish and shellfish that are shown in the 24-hour recall data. There are no specific fish/shellfish frequency of consumption data for children as there were for adults from the NHANES III data. Consequently, a simplifying assumption was made to utilize the fish/shellfish consumption frequency data from the corresponding adult group to represent children from that particular ethnic/racial group. The smaller portion size of fish/shellfish and the differences in species of fish selected by children were described with the 24-hour recall data specific for children. Only the data on frequency of consuming fish and shellfish represented by the 24-hour recall pattern come from the adult data.

Comparison of the 50th, 90th and 95th percentiles for fish/shellfish consumption for children aged 3 to 6 years on a "per user for individual days," and "month-long per user" estimates are shown in the following tables (Tables 5-17 and 5-18).

Table 5-17

Consumption of Fish and Shellfish (g/day) and Mercury Exposure (µg/kg*bw*/day)
For Children Aged 3—6 Years
Estimates "Per User" and "Month-Long Per User"
Dietary Survey Data from NHANES III

Percentile	*Per User Individual Day*		*Per User Month-Long Estimate*	
	Fish/Shellfish Consumption (g/day)	**Mercury Exposure (µg/kg*bw*/day)**	**Fish/Shellfish Consumption (g/day)**	**Mercury Exposure (µg/kg*bw*/day)**
50th	43	0.28	5	0.03
90th	113	0.77	25	0.17
95th	151	1.08	39	0.28

Table 5-18
Consumption of Fish and Shellfish (g/day) and Mercury Exposure (µg/kg*bw*/day)
For Children Aged 3 — 6 Years; Estimates "Month-Long Per User"
Individual Ethnic/Racial Groups
Dietary Survey Data from NHANES III

Percentile		**Ethnic/Racial Group**			
		All Groups	**White/Non-Hispanic**	**Black/Non-Hispanic**	**Other**
50th	Fish	5	5	6	7
	Mercury	0.04	0.04	0.03	0.04
75th	Fish	12	11	13	17
	Mercury	0.08	0.08	0.08	0.11
90th	Fish	25	24	27	27
	Mercury	0.18	0.16	0.19	0.25
95th	Fish	39	37	44	57
	Mercury	0.29	0.25	0.33	0.426

5.5 Comparison of Dietary Exposure Estimates with Hair Mercury Concentrations

As dietary intake of methylmercury from fish and shellfish increases, mercury concentrations in hair also increase. The association between dietary intake and hair mercury concentrations, and between

maternal hair mercury concentrations and changes the child's developmental profile have been discussed extensively in other Volumes and other Chapters within this Volume. U.S. EPA's Reference Dose (RfD) describes a dose within a range of methylmercury exposures judged to be without known adverse effects. The RfD for methylmercury is 0.1 µg/kg*bw*/day and is associated with a hair mercury concentration of 1.1 µg/kg hair or 1.1 ppm. The RfD is derived from a benchmark dose associated with hair mercury concentrations of 11 µg/g mercury in hair.

Normative data on hair mercury concentrations that are representative of the U.S. population do not exist. Such data were not included in NHANES III or previous NHANE Surveys. It is anticipated that hair mercury analyses will be included in the biological samples and chemical analyses that are conducted in the fourth National Health and Nutrition Examination Survey. In 1997, however, there are available data from two diverse groups of subjects. The first group is general populations living in the United States that are anticipated to have no unusual exposures to methylmercury. The second group are populations that are thought to consume higher than typical amounts of fish/shellfish and methylmercury.

5.5.1 General Population

General population data on hair mercury concentrations in the United States are described by Crispin-Smith et al. (1997), Creason et al. (1978 a,b,c), and Airey (1983). The data described by Crispin-Smith et al. were published in 1997 and indicate that the mean mercury concentration in hair was 0.48 ppm based on 1,431 individuals. Within this group 1,009 individuals who reported consuming some seafood had hair mercury concentrations of 0.52 ppm. The highest hair mercury concentration described by these data suggest a maximum value of 6.3 ppm.

Creason et al. (1978 a,b,c) described hair mercury concentrations in three geographic regions: New York Metropolitan Area (1978a); New Jersey (1978b); Birmingham, Alabama (1978c); and Charlotte, North Carolina (1978c). Although these data are unpublished, reports describing the data are available as these studies were conducted by U.S. EPA. The data fit a log-normal distribution in which the arithmetic mean of the data is higher than the geometric mean in the data. A major uncertainty in these data is that, although the data are log-normally distributed, the data were truncated with individual values outside ± 3 standard deviations from the mean of the logs of the sample excluded from calculations. Consequently, values that are high or low are excluded from these data. The detection limit based on the analytical method is not provided and it is unclear from the written reports how "zeros" and "trace concentrations" were handled in calculation of the means upon which these exclusion criteria (i.e., ± 3 S.D.) were applied. As a result, major uncertainties exist regarding these data.

Airey (1983) reported on hair mercury levels in 13 countries including data from the United States. Arithmetic means ranged between 1.8 and 3.3 ppm from geographic locations including La Jolla/San Diego, Maryland, and Seattle. The number of U.S. subjects totaled 196 adult men and women. The maximum value for hair mercury concentration reported was 7.9 ppm. The arithmetic mean was 2.4 and the geometric mean was 1.9 ppm — consistent with a log normal distribution. Information on the detection limit and how "zero" and trace values were incorporated into calculations of the mean was not described. As with the work described by Crispin-Smith (1997) and Creason et al. (1978a,b,c), uncertainties exist making these data difficult to interpret fully.

Overall, the data from Crispin-Smith (1997) and Creason et al. (1978a,b,c) suggest that the geometric mean for hair mercury content for the general population is less than 1 ppm. Considering data described by Airey (1983), the mean for the United States is between 1.9 ppm (geometric mean) and

2.4 ppm (arithmetic mean). Because the data reported by Creason et al. (1978 a,b,c) were censored to exclude values outside ± 3 S.D. from the geometric mean, estimates of typical hair mercury concentrations carry substantial uncertainty. Data by Crispin-Smith (1997) have not been adequately assessed as to the level of uncertainty that should be associated with their findings.

5.5.2 Subpopulations with Higher Exposures to Fish/ Shellfish and Mercury

During the period 1995 through 1997 reports of hair mercury concentrations among people likely to have higher than typical levels of fish consumption have appeared either in the unpublished or published literature (Knobeloch et al., 1995; Gerstenberger et al., 1997; Harnly et al., 1997). In 1991, Lasora et al. (1991) reported on hair mercury concentration in 80 women of childbearing age from Alaska. Data describing more highly exposed individuals are very limited in number of subjects and show diverse results. Maximum values from Gerstenberger et al. (1997) and Harnly et al. (1997) were between 2 and 3 ppm. Values reported by Knobeloch et al. (1995), Fleming et al. (1995) and Lasora et al. (1991) were between 10 and 16 ppm. The highest values reported in these surveys are in the range of the benchmark dose for methylmercury: 11 µg Hg/g hair.

5.5.3 Comparison with Dietary Intake of Mercury

The comparisons that follow are only for women aged 15 through 44 years. A summary of the results from the "per capita" data on the dietary surveys at the 50th percentile indicate there is no consumption of fish/shellfish and methylmercury. At the 95th percentile fish/shellfish intake is slightly over 100 grams per day and mercury exposures are about 0.16 µg/kg*bw*/day. On a per user basis, when only one 24-hour recall is used to estimate mercury exposure, a distribution of daily exposures is calculated (Table 5-19). If typical hair mercury concentrations are less than 1 ppm, the "per capita" 95th percentile data, the 50th percentile of the "per user" based on a single day of recall, and all of the month-long projections of the per user data are consistent with hair mercury concentrations of less than 1 ppm. If the value reported by Airey (1983) of 2-3 ppm is the appropriate estimate for hair mercury concentrations in the general population, then all estimates of mercury intake from the dietary surveys (except the 90th and 95th percentile estimates from the "per user"method of calculation based on single days recall information) are consistent with hair mercury data.

The upper range of mercury exposures in the United States is associated with hair mercury concentrations estimated to be approximately 5 to 16 ppm. There are no data indicating how commonly hair mercury concentrations at these levels occur. The highest values are associated with dietary mercury intakes greater than any projected using concentrations for mercury in fish and shellfish (e.g., approximately 0.12 to 0.15 ppm). Persons or subpopulations with these elevated exposures may be eating fish/shellfish coming from a more contaminated source (see Table 5-8) for ranges of mean mercury concentrations reported in the United States). Alternately these individuals may have an additional source of mercury exposure.

Table 5-19
Fish Consumption (g/day) and Mercury Exposure (µg/kg*bw*/day) Among Women Aged 15-44, Based on Per Capita, Short-term Per User, and Month-long Projections

Basis for Comparison	Fish Consumption (g/day)	Mercury Exposure (µg/kg bw/day)
Per Capita from Dietary Surveys		
50th Percentile	Zero	Zero
95th Percentile	102	0.16
Per User - Single Day Data		
50th Percentile	68	0.10
75th Percentile	122	0.20
90th Percentile	210	0.38
95th Percentile	278	0.53
Per User - Month-Long Projections		
50th Percentile	9	0.01
75th Percentile	21	0.03
90th Percentile	46	0.08
95th Percentile	78	0.13

5.6 Estimates of Sizes of At-Risk Populations

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

The number of human subjects who constitute the at-risk subpopulation depends on the health-based endpoint(s) used in the risk assessment. If paresthesias are the health-based endpoints of concern, then any adult male or female can be considered potentially at-risk depending on the quantity of fish consumed. The total population of the United States aged 15 years or older is approximately 194,858,000 million based on 1990 U.S. Census data. The male population in this age group numbers approximately 93,669,000. The female population in these ages numbers approximately 101,187,000.

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 was to methylmercury contaminated fish, indicated that the highest frequency of disease was observed among subjects aged 20-59 years. Fish consumption among subjects in the age category birth to 10 years of age was lower than for older subjects (Tsubaki and Irukayama, 1977). Cases of fatal Minamata disease, however, included six children (aged 2.5, 4.5, 5.0, 6.4, 7 and 8 years) among 38 cases (Tsubaki and Irukayama, 1977). Because the methylmercury contamination in the Minamata area existed for a number of years, it is not possible to clearly separate prenatal from postnatal exposure. Harada (1977; as cited 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% incidence of paresthesia. Occurrence of paresthesia among congenital cases and children was considered to be unclear, but Harada noted that all patients had a sensation of pain.

Children were also affected by methylmercury poisoning in an 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" (Rustam and Hamdi, 1974).

Exposure patterns for children (see Volume IV and Chapters 4 and 5 of this Volume) suggest that they may be an at risk group because of their exposure to methylmercury on a "per kilogram body weight" basis is much higher compared with adults. Neuronal migration, a process specifically affected by methylmercury, begins at about six weeks *in utero*, and the 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 until approximately age 20 (Rodier, 1994), children may be at greater risk of 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 of chilren is approximately 53,853,000 based on 1990 census data (Table 5-20).

Table 5-20
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
% 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 childbearing 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 are shown in Table 5-21.

Women aged 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 5-22). 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 also have fish consumption patterns that differ from those of the contiguous United States.

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 5-22. 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% 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 ages. 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.

It was estimated that within the contiguous United States 9.5% 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 5-22).

Table 5-21
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 U.S.	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
% Female	51.3	48.8	49.9	55.1

Table 5-22
Pregnancies by Outcome for Resident Females by Divisions and States, U.S. 1990, by Age*

United States	Outcome	**Total****	**<15 Years**	**15-44 Years**	**≥45 Years*****
	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
	% 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
	% Pregnant	--	--	9.5	--

* 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.
** 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% of all legal abortions.
*** 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.

6. INTEGRATIVE ANALYSIS FOR METHYLMERCURY

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

6.1.1 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. (These are defined in Volumes V and VI).

The purpose of Section 6.2 was to determine which of the species (humans and other animals) considered to consume fish from the hypothetical water body (developed in Volumes III and IV) 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 V and VI) and the health endpoint data (developed in Volumes V and VI) for the species considered are presented. Assumptions employed to estimate the transport of mercury through the aquatic food chain model (developed in Volumes III) 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 the methylmercury levels which correspond to exceedences of health criteria.

The aim of Section 6.3 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.

6.1.2 Description of Critical Terminology for this Section

Definitions and descriptions of several terms used in this section are reviewed for the reader in this section.

6.1.2.1 Human Health Based Levels

No-Observed-Adverse-Effect Level (NOAEL)

An exposure level at which there are no statistically or biologically significant increases in the frequency or severity of adverse effects between the exposed population and its appropriate control; *some effects may be produced at this level, but they are not considered adverse or precursors to specific adverse effects.* In an experiment with several NOAELs, the regulatory focus is primarily on the NOAEL seen at the highest dose. This leads to the common use of the term NOAEL to mean the highest exposure without adverse effect.

Lowest-Observed-Adverse-Effect Level (LOAEL)

The lowest exposure level at which there are statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group.

Uncertainty Factor (UF)

One of several, generally 10-fold, factors used in operationally deriving the reference dose (RfD) from experimental data.

Reference Dose (RfD)

An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

$$RfD = NOAEL \text{ or } LOAEL \div UF \times MF$$

6.1.2.2 High-End Fish/Shellfish Consumers

Within each of the three general groups of fish consumers described in the Report, the general population, recreational anglers, and subsistence fish-consumers, there are high end fish consumers. The proportion of high-end consumers within these groups is thought to increase from the general population, to recreational anglers, and finally to subsistence fish-consumers. The term "subsistence fish-consumers" has been used to describe various persons who rely on fish as a major source of protein. "Subsistence fish-consumers" 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.

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

This section presents an integrated risk characterization for the humans and wildlife that were assumed to reside in the hypothetical lacustrine (fresh water waterbody) setting developed in Volumes 3 and 4 of this Report. The approach selected includes both avian and mammalian wildlife species. It

utilizes a common exposure medium and the foodchain relationships developed in the IEM-2M model. This approach also draws upon the reference dose (Volume 5) and wildlife criterion (Volume 6) developed in the Report.

The approach attempts to answer three questions for the hypothetical site:

1) Which species is the most exposed (daily) to methylmercury on a per kg bw basis?,

2) Using the health criteria developed, which species is most sensitive to methylmercury on a per kg bw basis?, and finally

3) In this hypothetical ecosystem, at what methylmercury concentration in fish are the health criteria exceeded?

Answering these questions would indicate which species are most susceptible to methylmercury contamination of fish. Clearly, many uncertainties and simplifying assumptions are employed in the analysis to address the questions. See Figure 6-1.

6.2.1 Methylmercury Intake by Humans and Wildlife Based on the IEM-2M Modeling

A comparison of pollutant exposure levels across the species in an ecosystem requires, among other things, a knowledge of :

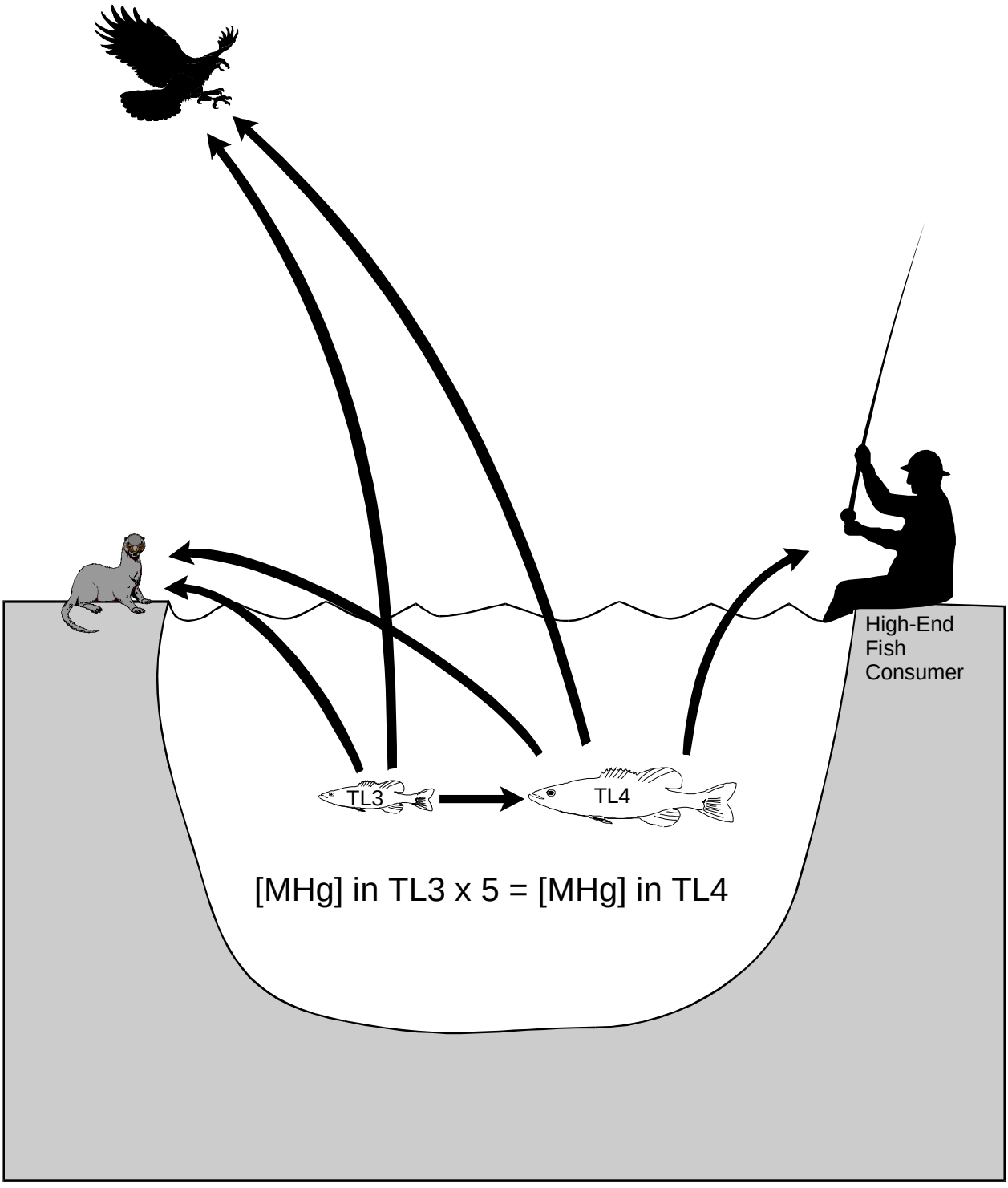
- the environmental fate of the pollutant (including chemical transformation of the pollutant in the environment);
- significant contact medium (or media); and
- contact rates and body weights of the wildlife species and the human subpopulations in the ecosystem.

The source of much of this data was the results of and inputs to the IEM-2M model (Volume III of this Report).

Although methylmercury is found in other media and biota, it accumulates to the highest concentrations in fish, particularly piscivorous fish. This conclusion is based upon both the measurement data and the results of the modeling presented in Volume III of this Report. Methylmercury remains essentially unchanged in fish tissue, when subjected to human preparation methods (e.g., cooking). Although methylmercury exposure may occur through other routes, 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. Since they are not known to accumulate in commonly eaten foods, and since they are not as bioavailable as methylmercury in most media, they do not dominate human exposure to mercury and 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 relationship between the methylmercury concentrations in both planktivorous and piscivorous fishes.

Figure 6-1
Overview of Integration of Modeled Exposure Estimates



The piscivores selected for analysis were these: human high-end local fish consumer (or subsistence fisher), bald eagle, osprey, loon, 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 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.

In the Report mercury residues in fish were estimated by making the simplifying assumption that aquatic food chains could be adequately represented using four trophic levels. Respectively, these trophic levels are the following: level 1 - phytoplankton (algal producers); level 2 - zooplankton (primary herbivorous consumers); level 3 - small forage fish (secondary consumers); and level 4 - larger, piscivorous fish (tertiary consumers). While the exact quantity of methylmercury in fish in this analysis of fish consumers is not critical, the relationship between the methylmercury concentration of trophic level 3 fish and the methylmercury concentration in trophic level 4 fish is critical. This relationship is defined by the predator-prey factor for trophic level 4 fish (The symbol is PPF_4 in Appendix D of Volume III). PPF_4 is defined as the (unitless) factor by which methylmercury concentrations in trophic level 4 organisms exceed those in the trophic level 3 organisms upon which they prey. Appendix D concluded that the value was distributed lognormally (GM = 4.95; GSD = 1.464), through rounding a geometric mean of 5 is estimated. As a result, trophic level 4 fish are predicted by the model employed to have levels of methylmercury in their tissues that are 5 times those of trophic level 3 fish in the same water body. Appendix D of Volume III details the distribution of this relationship between the trophic levels.

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 (Table 6-1) would be predicted to receive approximately 5 times less (20 percent of) methylmercury per gram of fish eaten than those eating trophic level 4 fish from the same water body. 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 levels 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 (Table 6-2) 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% of body weight and that of mink is 20%. Trophic level 4 fish are assumed to make-up roughly 20% of the otter's total fish consumption with the other 80% 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 concentrations described by PPF_4, the estimates of exposure based on 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 have residue levels of 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 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 at this lake:

Ospreys: 0.1 µg/g x 300g/day/1.5 kg bw = 20 µg/kg bw/day;

Kingfishers: 0.1 µg/g x 75g/day/0.15kg bw = 50 µg/kg bw/day;

Loons: 0.1 µg/g x 800g/day/4 kg bw = 20 µg/kg bw/day;

Otters 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: 0.1 µg/g x 160.2 g/day/0.8 = 20 µg/kg bw/day; and

High-end fish-consuming humans at this lake: 0.5 x 60 g/day/70 = 0.4 µg/kg bw/day.

For the purposes of this analysis, the methylmercury level in the fish is irrelevant to the rank; only the relationship between the aquatic trophic levels and the amount a piscivore consumes from each level are critical. Using this model and the assumptions in Tables 6-1 and 6-2, question 1, which asks which species is the most exposed (daily) to methylmercury on a per kg bw basis, can be addressed. The predicted piscivore exposure ranking from highest to lowest is: kingfisher > otter > osprey, mink, loon > bald eagle > human high-end fish consumer.

Table 6-1
Assumed Fish Consumption Rates by Trophic Level for
Piscivorous Birds, Mammals, and Human High-end Fish Consumer

Animal	Trophic Level 3 Fish Ingestion Rate ($g_{wet\ weight}$/day)	Trophic Level 4 Fish Ingestion Rate ($g_{wet\ weight}$/day)
Bald Eagle	370	90
Osprey	300	0.00
Loon	800	0.00
Kingfisher	75	0.00
River Otter	976	244
Mink	160.2	0.00
Human High-End Fish Consumer	0	60.00

Table 6-2
Exposure Parameters for Mink, Otter, Kingfisher, Loon, Osprey, and Eagle

Species	Body Wt. (Wt_A) kg	Ingestion Rate (F_A) kg/d	Trophic Level of Wildlife Food Source	% Diet at Each Trophic Level (3,4)	% of Non-Aquatic Foods in Diet
Mink	0.80	0.178	3	90	10
Otter	7.40	1.220	3,4	80,20	0
Kingfisher	0.15	0.075	3	100	0
Loon	4.0	0.8	3	100	0
Osprey	1.50	0.300	3	100	0
Eagle	4.60	0.500	3,4	74,18	8
Human High End Fish Consumer	70	0.06	4	100	NA

NA- Not Addressed

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 exposure rate based on fish consumption is much lower than that of these piscivorous wildlife.

6.2.2 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 criteria and endpoints 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 species and humans. 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 V and VI 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 susceptible 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 V and VI.

6.2.2.1 Human Health Endpoints and the 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 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 populations around the U.S. Great Lakes. In addition, there are new evaluations of published work described in Volume V, 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. The U.S. EPA's Science Advisory Board (1997) concurred with this decision.

The neurotoxicity of methylmercury in children exposed *in utero* has been determined to be the critical effect for the human RfD. The current 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 incidences 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 6-3. The NOAEL of 10 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 V of this Report.

A composite Uncertainty Factor (UF) of 10 was developed in the derivation of the oral RfD. This composite UF accounted for a several UFs which potentially had values of between 1 and 10. These UFs included a human population variability, specifically, variations in the biological half-life of methylmercury, variation in human hair:blood mercury ratios, the lack of a two generation reproductive study, and the lack of data on sequelae that result from longer durations of exposure.

Table 6-3
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	5	3	6	8	14
N (sample size)	27	14	13	12	15

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

6.2.2.2. Wildlife Health Endpoints and the RfD

The RfDs for avian and mammalian wildlife are derived in Volume VI 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:

$RfD = TD \div (UF_A \times UF_S \times UF_L)]$,

where:

RfD = 64 µg/kg bw/day ÷ (1 x 1 x 3)

= 21 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 1 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 (i.e., LOAEL to NOAEL). A factor of 3 was applied; there was a separate analysis of LOAEL to NOAEL data and the analysis 3 was most appropriate data.

The mammalian RfD was based on the data from a series of studies by Wobesser and collaborators (Wobesser, 1973; Wobesser et al., 1976a,b). Wobesser 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 uncertainty factors.

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

$RfD = TD \div (UF_A \times UF_S \times UF_L)$

RfD = 55 µg/kg bw/day ÷ (1 x 3 x 1)

= 18 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 3 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 RfD is about 200 times lower than the corresponding RfDs of the other animals (Table 6-4). On a per kilogram of body weight basis, humans exceed this health criterion at lower rates of exposure to methylmercury. 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 human RfD is based on less severe (or more subtle) effects than the wildlife RfDs; the RfD for mammals is based on neurologic damage in the mink and the avian RfD is based upon behavioral and reproductive effects in mallards. There is also an inconsistency between the approaches used to derive RfDs for humans and wildlife; the assessment of RfD for wildlife is based on health endpoints that relate to population effects rather than effects to a subpopulation.

Table 6-4
Animal and Human Health Endpoints for Methylmercury in µg/kg bw/day

Animal	RfD	Health Effect Related to RfD
Human	0.1	Neuro-developmental effects in children
Mammalian Quadrupeds	18	Frank neurological damage
Avian	21	Severe reproductive effects

6.2.3 Integration of Modeled Methylmercury Exposure Through Fish Consumption with Health Criteria

In this section the dose-response and exposure estimates are integrated to predict concentrations of methylmercury in fish tissue which correspond to the health criteria of the piscivore. The methylmercury body burdens in fish which correspond to piscivore health criteria are estimated by dividing the product of the piscivore body weight (kg) and the human or wildlife RfD (µg/kg bw/day) by the daily rate of fish consumption (g/day). The units that result are expressed on the basis of fish muscle methylmercury concentration (µg methylmercury/g fish muscle tissue). The corresponding fish muscle concentrations also account for the differences in methylmercury bioaccumulation between trophic level 3 and 4 fish (PPF_4). 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. Based on the predator-prey factor, the$_3$difference in BAF and BAF_4 is approximately a factor of 5 . This conversion provided a standard medium (i.e., methylmercury concentrations in trophic level 3 fish tissues) for comparison among all of the piscivorous species.

Table 6-5
Concentrations of Methylmercury in Trophic Level 3 Fish Which, if Consumed at the Assumed Rates on a Daily Basis, Result in Exposure at the RfD

Population	Body Weight (kg)	TL3 Fish Consumption (g/day)	TL 4 Fish Consumption (g/day)	RfD (µg/kg/day)	Methylmercury Conc. in Trophic Level 3 Fish at RfD (µg/g)
Kingfisher	0.15	75	0	21	0.04
Loon	4	800	0	21	0.11
Osprey	1.5	300	0	21	0.11
Eagle	4.6	370	90	21	0.12
Otter	7.4	976	244	18	0.06
Mink	0.8	160.2	0	18	0.08
High-End Human	70	0	60	0.1	0.02

The results presented in Table 6-5 show the methylmercury levels in trophic level 3 fish which correspond to the health criteria. From these results the species considered can be ranked based on the fish concentration which corresponds to the RfD; from lowest to highest these are: Human ➡ Kingfisher ➡ Otter ➡ Mink ➡ Loon, Osprey, Eagle. Using the common medium of trophic level 3 fish, high-end fish-consuming humans are predicted to exceed the health criteria at the lowest levels of methylmercury in fish. The range of concentrations in the fish muscle tissue corresponding to the respective RfDs extends less than an order of magnitude. The analysis shows that 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 the wildlife species considered.

Some of the reported measured mercury concentrations in trophic level 3 fish would be predicted to result in exceedence of the RfD. For example, in Volume VI a national mean of 0.08 µg methylmercury/g fish was developed for trophic level 3 fish from the data of Bahnick et al., (1994). The mean exceeds the fish tissue levels that correspond to RfD of both the human and kingfisher given the assumptions of daily consumption rates and body weights. The trophic level 3 fish mean methylmercury concentration of 0.08 µg/g is roughly equal to fish tissue levels that correspond to the RfD of the mammalian wildlife given the assumptions of daily consumption rates and body weights . The estimate of mean trophic level 3 fish methylmercury concentration is below that corresponding to the RfD of the other avian species (other than kingfisher). In Volumes III and VI the representativeness of the fish collected for the Bahnick study was questioned. Much of the Bahnick et al. data was collected from contaminated or industrial sites. The mean trophic level 3 fish methylmercury concentration may be higher than a true national average. Many of the trophic level 3 fish concentrations predicted by the model particularly in the eastern site would exceed concentrations listed in the last column of Table 6-5. (See Volume III for measured and predicted concentrations in fish).

There is a great deal of uncertainty in this comparison. The uncertainty relates to the variability in relationship between methylmercury concentrations in trophic level 3 and 4 fish, sources of fish, fish consumption rates, differences in approach to developing RfDs for human and wildlife, and other factors that could affect the wildlife RfD that were developed.

Across natural water bodies a fairly large variability was shown for the trophic level 4 predator-prey factor (PPF_4). For a specific water body, the factor of 5 utilized here could be quite different from the actual relationships of methylmercury concentrations among the species of fish that comprise these trophic levels. The distribution of PPF_4 is presented in Appendix D of Volume III.

Fish consumption rates among wildlife and humans are variable. For example, freshwater fish consumption by some persons in the U.S. reportedly exceeds 60 grams/day. These individuals are clearly at the upper end of the distribution.

6.3 Comparison with Other Recommendations

Because of the adverse effects of methylmercury on human health, a number of recommendations have been made regarding tolerable limits for mercury exposure and for acceptable levels in biological materials. These have been expressed in a variety of units including: 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).

6.3.1 Reference Values for Biological Monitoring

Mercury concentrations in biological materials depend on mercury exposures. Background levels for persons with low level exposures to mercury have been published by various organizations. Reference values for mercury concentrations in biological materials commonly used to indicate human exposures to mercury were published by the WHO/IPCS (1990): in whole blood, ~ 8 μg/L; in hair, ~ 2 μg/g; and in urine ~ 4 μg/L. Wide variation occurs about these values (WHO/IPCS, 1990). The International Union of Pure and Applied Chemistry (1996) revised reference values for blood and urine to reflect decreased contamination secondary to improvements in contamination control during sample handling and chemical analysis. IUPAC (1996) indicated that for healthy people the mercury levels in serum should be less than 0.5 µg/L, packed cells less than 5 µg/kg; and < 2.5 µg/L in whole blood.

6.3.1.1 Blood Mercury Concentrations

Blood mercury concentrations allow back calculation of the amount of methylmercury ingested. Because methylmercury in the diet comes almost exclusively from consumption of fish and shellfish, methylmercury concentration in blood are very strong predictors of methylmercury ingestion from fish and shellfish. Studies are found that provide data on chemically speciated blood mercury concentrations (see Chapter 6 of Volume IV), however, the majority of data on human blood mercury concentrations report on total blood mercury. The information summarized below represent reports of blood mercury levels among persons living in the United States between 1990 and 1997.

6.3.1.2 United States

Normative data to predict blood mercury concentrations for the United States population are not available. With a very few exceptions all of the data that have been identified are for adult subjects. The largest single study appears to be that of former United States Air Force pilots. Kingman et al. (Kingman et al., in press; Nixon et al., 1996) analyzed urine and blood levels among 1127 Vietnam-era United States Air Force pilots (all men, average age 53 years at the time of blood collection). Mean total blood mercury concentration was 3.1 ug/L with a range of “zero” (i.e., detection limit of 0.2) to 44 ug/L. Overall, 75% of total blood mercury was present as organic/methylmercury.

Additional North American studies have been reported by various individual states in the United States. These are described below and summarized in Table 6-6.

Table 6-6
Blood Mercury Concentrations Values Reported for the United States

Study	Community	Measure of Central Tendency	Maximum	Additional Information on Study
Burge and Evans, 1994	236 participants from Arkansas	Mean: 10.5 µg/L among men: 12.8 µg/L; among women, 6.9 µg/L. Median: All subjects 7.1 µg/L Men: 9 µg/L Women: 4.8 µg/L	All subjects: 75 µg/L Males: 75 µg/L Females: 27 µg/L.	139 participants exceeded 5 µg/L. 30 participants in the range of 20 to 75 µg/L or 15% >20 µg/L. 5% of men had >30 µg/L. No women had values > 30 µg/L.
Centers for Disease Control 1993	Micousukee Indian Tribe of South Florida. 50 blood samples from subjects with mean age=34 years (Range 8 to 86 years).	Mean: 2.5 µg/L Median: 1.6 µg/L	13.8 µg/L	
Gerstenberger et al. (1997)	68 Ojibwa Tribal members from the Great Lakes Region	57 participants < 16 µg/L. Remaining 11 subjects averaged 37 µg/L.	53 µg/L	11 individuals had blood mercury in the range 20 to 53 µg/L.

Table 6-6 (continued)
Blood Mercury Concentrations Values Reported for the United States

Study	Community	Measure of Central Tendency	Maximum	Additional Information on Study
Harnly et al. (1997)	Native Americans living near Clear Lake, California. Group studied include 44 Tribal members, and 4 nontribal members.	Mean for 44 Tribal members: 18.5 µg/L (2.9 µg/L inorganic Hg + 15.6 µg/L for organic Hg). Mean for 4 nontribal members: 11.5 µg/L (2.7 µg/L inorganic + 8.8 µg/L organic Hg).	Among Tribal members: Total Hg was 43.5 µg/L (4.7 µg/L inorganic + 38.8 µg/L organic). For nontribal members: Total Hg 15.6 µg/L (3.4 µg/L inorganic + 12.2 µg/L organic).	20% of all participants (9 persons including four women of childbearing age) had blood mercury concentrations ≥ 20 µg/L.
Humphrey and Budd (1996)	Lake Michigan residents studied in 1971.	Algonac, Lake St. Clair: fisheaters (n=42) mean 36.4 µg/L compared with 65 low fish consumers having mean of 5.7 µg/L. South Haven, Lake Michigan with lower Hg contamination. Fisheaters (n=54) had mean 11.8 µg/L and the comparison group of low fish consumers mean (n=42) of 5.2 µg/L	Algonac, Lake St. Clair fisheaters: 3.0-95.6 µg/L Comparison: 1.1 - 20.6 µg/L South Haven, Lake Michigan fisheaters: 3.7-44.6 µg/L Comparison: 1.6-11.5 µg/L	Mercury contamination less intense in South Haven compared with Algonac.
Knobeloch et al. (1995)	Family consuming commercially obtained seafood.	Initial blood values for wife (37 µg/L) and husband (58 µg/L) following regular consumption of imported seabass having mercury concentrations estimated at 0.5 to 0.7 ppm Hg.	Six months after family stopped consuming seabass, blood mercury concentrations for the wife (3 µg/L) and husband (5 µg/L) had returned to “background” concentrations.	

Study	Community	Measure of Central Tendency	Maximum	Additional Information on Study
Schantz et al., 1996	Adult men and women aged 50 to 90 years. Michigan residents.	104 fisheaters: mean=2.3 µg Hg/L 84 nonfisheaters: mean=1.1 µg Hg/L.	Maximum for fisheaters: 20.5 µg Hg/L Maximum for nonfisheaters: 5.0 µg Hg/L.	Questionnaire on fish-eating patterns included sport-caught Great Lakes fish and purchased fish, as well as questions on patterns of wild game consumption.

6.3.1.3 Blood Mercury Among More Highly Exposed Subpopulations

As indicated above normative data for the United States population are not currently available. There are, however, some data indicating blood mercury concentrations among persons likely to be more highly exposed to methylmercury because of their higher levels of fish consumption. During the 1990s seven surveys of angler and Native American Tribal groups have been conducted in which blood mercury concentrations were measured and reported. Table 6-6 shows these data. The highest blood mercury concentrations were in the 50 to 90 µg/L range (Humphrey and Budd, 1996 - Lake Michigan; Burge and Evans, 1996 - Arkansas; Knobeloch et al., 1995 - Wisconsin urban family). Mean blood mercury concentrations between 10 to 20 µg/L occurred in a population of anglers from Arkansas (Burge and Evans, 1996) , among Native American Tribal group members from California (Harnly et al., 1995); and among Ojibwa Tribal members in the Great Lakes Region (Gerstenberger et al., 1997).

6.3.1.4 Hair Mercury

Methylmercury exposures for general populations are reflected by hair mercury levels. Higher hair mercury concentrations are associated with increases in fish consumption (among other see: Abe et al., 1995; Akagi et al., 1995; Aks et al., (1995); Airey et al., 1983; Barbosa et al., 1995; Chai et al., 1994; Girard and Dumont, 1995; Grandjean et al. (1992); Hansen et al. (1990 and 1996); Oskarsson et al., 1990; Wheatley and Paradis, 1995). 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).

Data on hair mercury concentrations that can be extrapolated to represent the general population of the United States do not exist. There are some data available on hair mercury concentrations from persons living in the United States including reports shown in Table 6-7. 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 less than 1 ppm. However, for a number of the surveys the detection limit was sufficiently high that a substantial number of zero or trace values were reported. Many reports did not indicate how "zero" and trace values were handled statistically creating uncertainties in the reported mean values. In other reports "outliers" were removed if they were outside a defined range (e.g., ± 3 standard deviations). Some statistical "outliers" may represent the upper ranges of hair mercury among persons with higher exposures to mercury.

The maximum values reported in these individual surveys range from 2.1 to 15.6 ppm. Hair mercury concentrations greater than 5 ppm have been reported by Airey (1983), Crispin-Smith et al. (1997), Lasora et al. (1991), Fleming et al. (1995), and by Knobeloch et al. (1995). 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. Lasora et al. (1991) whose subjects were women of childbearing age identified a subject with a hair mercury concentration > 15 ppm. Knobeloch et al. (1995) identified a family whose hair mercury concentrations exceeded 10 ppm with the mercury exposure directly attributable to mercury from commercially obtained fish. It is uncertain how common hair mercury concentrations more than 5 ppm (as well as greater than 10 to 15 ppm) are among the general United States population. Until appropriate survey data for the general United States population exist, the overall pattern of hair mercury concentrations for the United States remains unclear.

Hair mercury concentrations of groups consuming high levels of fish and marine mammals have a much higher frequency of hair mercury concentrations > 5 ppm. An example is found in data from Canadian Aboriginal subpopulations. Girard and Dumont (1995) summarized data on hair mercury concentrations among the Cree Indians of Quebec and found 18% had hair mercury concentrations > 2.5 ppm. 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.

Table 6-7
Hair Mercury Concentrations (µg Hg/gram hair or pm) from Residents of Various Communities in the United States

Study	Community	Mean Concentration ppm	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-117) 0.78	Children - 5.4; Adults - 7.5	Survey conducted in 1972 and 1973

Table 6-7 (continued)
Hair Mercury Concentrations (µg Hg/gram hair or pm) from Residents of Various Communities in the United States

Study	Community	Mean Concentration ppm	Maximum Concentration ppm	Additional Information on Study
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 924 subjects) 2.9 ppm. 6) Males and Females (79 subjects), 2.4 ppm.	1. 6.2 pm 2. 5.5 ppm 3. 5.6 ppm 4. 6.6 ppm 5. 7.9 ppm 6. 7.9 ppm	
Airey, 1983	U.S. data cited by Airey, 1983 Community identified: LaJolla-San Diego	1) 2.4 ppm (13 men). 2) 2.7 ppm (13 women); 3) 2.3 ppm (8 subjects including men and women); 4) 2.9 ppm (17 subjects including men and women). 5) 2.6 ppm (5 subjects including men and women); 6) 2.8 (30 subjects including men and women).	1) 6.2 ppm 2) 5.5 ppm 3) 4.5 ppm 5) 6.2 ppm 6) 6.6 ppm	
Airey, 1983	U.S. data cited by Airey, 1983. Area identified: Maryland	1) 1.8 (11 subjects, men and women); 2) 1.5 (11 subjects, men and women); 3. 2.3 (11 subjects, men and women); 4. 1.9 (33 subjects, men and women).	1) 3.8 ppm 2) 3.9 ppm 3) 4.5 ppm 4) 4.4 ppm	

Table 6-7 (continued)
Hair Mercury Concentrations (µg Hg/gram hair or pm) from Residents of Various Communities in the United States

Study	Community	Mean Concentration ppm	Maximum Concentration ppm	Additional Information on Study
Airey, 1983	U.S. data cited by Airey, 1983 Community identified: Seattle.	1) 3.3 ppm (9 men); 2) 2.2 (3 women); 3) 2.6 (5 subjects men and women); 4) 1.5 (3 subjects, men and women); 5) 3.8 (8 subjects, men and women); 6) 3.0 (16 subjects, men and women).	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., 1997	U.S., communities and distribution not identified	0.48 (1,431 individuals); 0.52 (1009 individuals reporting some seafood consumption)	6.3 ppm	The 1009 individuals are a subset of the 1431 subjects.
Lasora et al., 1991	Nome, Alaska	1.36 (80 women of childbearing age)	15.2	
Lasora et al., 1991	Sequim, Washington	0.70 (7 women of childbearing age)	1.5	
Fleming et al., 1995	Florida Everglades	1.3 (330 subjects, men and women)	15.6	To be included in the survey the subjects had to have consumed fish or wildlife from the Everglades.
Knobeloch et al., 1995	Wisconsin, urban	2 adult subjects (1 man, 1 woman); 11 and 12 ppm		
Gerstenberger et al., 1997	Ojibwa Tribal members from the Great Lakes Region	47% > 0.28 ppm. Among individuals with values above the level of detection, the mean was 0.83 ppm based on 78 subjects	2.6	

Study	Community	Mean Concentration ppm	Maximum Concentration ppm	Additional Information on Study
Harnly et al., 1997	Native Americans living near Clear Lake, California.	68 Tribal members. Mean value: 0.64 ppm. 4 non-Tribal members. Mean value: 1.6 ppm	Maximum value for Tribal members: 1.8 ppm Maximum value for non-Tribal members: 2.3 ppm	

Cross-comparisons methylmercury exposure in various populations are facilitated by the work of Airey (1983) (Table 6-8) who analyzed mercury concentrations in 559 samples of human hair from 32 locations in 13 countries. The results summarized by Airey (1983) showed the United States averaged 2.4 µg mercury/gram hair compared with Germany at 0.5 µg mercury/gram (the lowest mean reported and Japan at 3.9 µg mercury/gram hair (the highest mean reported). Comparisons across a number of countries show that as the frequency of fish/shellfish intake increases the mean hair mercury concentrations increase. This is, however, only part of the comparison. Review of the ranges around the mean indicated that the upper limit for the category "once a month or less" is 6.2 ppm which overlaps with the lower range of hair mercury associated with consuming fish/shellfish every day - i.e., 3.6 ppm. Consequently to interpret data associating hair mercury concentrations with the frequency of fish consumption it is necessary to consider the concentration of mercury in the fish and shellfish consumed.

Table 6-8
Association 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

6.3.1.5 Hair Mercury Concentrations in Children

Hair mercury concentrations reported by Creason et al. (1978a, 1978b and 1978c) included data on hair mercury levels of children (defined as persons age 15 and younger). The age distribution for children were not included in their published studies. In contrast to these limited data on hair mercury concentrations, data on fish consumption by children aged 10 years and younger indicate that children are exposed to about three times more mercury from fish and shellfish as are adults.

Because children's mercury exposures are higher than are those of adults the question arises on why children's hair mercury concentrations are not higher than those of adults. The number of young children (if any) included in the data reported by Creason et al. (1978 a,b,c) is undocumented and this remains an important area of uncertainty. An additional, and far more important, area of uncertainty is the tissue distribution of mercury (i.e., the biokinetics of mercury in the human body). Young children may be diluting their mercury body burden by tissue growth and the distribution of mercury into body compartments by young children may differ from that of adults. Pharmacokinetics of mercury (e.g., rate of demethylation of methylmercury in neural tissue and macromolecular binding of mercury to proteins in the central nervous system) may impact the redistribution of mercury within tissues. The concentration of mercury in critical nervous system tissue is of much greater relevance to developmental deficits than is the concentration of mercury in hair. .

6.3.1.6 Dose Analysis and Health Effects in Relation to Hair Mercury Concentrations

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 pregnancy are more sensitive to the effects of methylmercury with fetuses at particularly increased risk. The World Health Organization/ International Programme for Chemical Safety (WHO/IPCS, 1990) indicated, based on analysis of the Iraqi data, a 30% or greater 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% 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.

The conclusions of WHO/IPCS (1990) reflect an evaluation given the available data at the time. The U.S. EPA's "benchmark" dose of 11 ppm mercury in hair is associated with the lower bound of the 95% confidence limit on a 10% effect level. The type of effects that were the basis the U.S. EPA "benchmark" dose estimate are clinically evident neurological/developmental changes. Using these endpoints as the basis for effect, a low likelihood of these endpoints occurring has been interpreted as establishing NOAEL. Theis NOAEL was associated with hair mercury concentrations of approximately 10 ppm. Recent epidemiological studies of chronic mercury exposures from seafood indicated that developmental delays and broad-based cognitive differences occur in children whose mother's hair mercury concentrations were less than 10 ppm mercury (Grandjean et al., 1997). Investigations of children chronically exposed to methylmercury from fish/shellfish in the Seychelle Islands have been interpreted as indicating no adverse developmental effects based on testing paradigms used in this study (Myers et al., 1996). These differ from those used in the study in the Faroe Islands (Grandjean et al., 1997). Results of these, and additional studies appearing in the scientific literature in the latter part of 1997, as well as those *in press* for 1998, will require reevaluation to assess doses of methylmercury associated with onset of subtle neurobehavioral effects.

6.3.2 Recommendations Based on Grams of Fish Consumed Per Day

The WHO/IPCS recommended that special attention be paid to populations consuming large amounts of fish (1990). Dietary intakes of 100 grams of fish and shellfish were used as a measure that additional attention was warranted for women of childbearing age because of risk to the developing fetus (WHO/IPCS, 1990). 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 estimated from the general U.S. population dietary surveys. Analyses of contemporary food consumption surveys (NHANES III, 1988 to 1994; CSFII 89/91, CSFII 94, and CSFII 95) have provided the estimates of fish and shellfish consumption shown in Tables 6-9 and 6-10. Depending on the survey used to make these estimate, between 52,000 people (based on data from the NPD, Inc., 1973) and 166,000 people (based on month-ling estimates from NHANES III, 1988 to 1994) routinely consume fish in the amounts of 100 grams per day or more. Higher estimates are based on short-term dietary recall data (single or three-day averages) which are useful only when combined with estimates of how often such levels of intake occur.

Table 6-9
Fish and Shellfish Consumption (grams per day) and Mercury Exposure (µg/kg*bw*/day) by Women Ages 15 through 45 Years United States *Per Capita*

Survey	Number of Women	Percentiles		
		50th	90th	95th
CSFII 94				
Day 1	842	Zero	26 0.03	80 0.12
Day 2	840	Zero	14 Zero	69 0.08
CSFII 95				
Day 1	635	Zero	43 0.04	87 0.13
Day 2	634	Zero	56 0.09	89 0.19
NHANES III	5,437	Zero	56 0.09	114 0.18

Table 6-10
Fish and Shellfish Consumption (grams per day) and Mercury Exposure (µg/kg*bw*/day) by Women Ages 15 through 45 Years United States *Per User on an Individual Day*

Survey	Percentiles			
	50th	75th	90th	95th
CSFII 94				
Day 1	77 0.10	103 0.16	169 0.25	235 0.29
Day 2	62 0.08	106 0.18	156 0.34	184 0.45
CSFII 95				
Day 1	62 0.09	103 0.22	253 0.38	305 0.42
Day 2	77 0.14	113 0.23	217 0.47	325 0.97
NHANES III	66 0.10	131 0.21	228 0.39	2878 0.53

These two tables provide essentially different descriptions of the frequency of fish/shellfish consumption. The "per capita" consumption presentation describes the distribution of fish/shellfish intake and mercury exposure over the United States population based on a "snap shot" on any one day. These results indicate that the 95th percentile of fish/shellfish consumption for adult women is approximately 100 grams of fish and shellfish. The "per user on an individual day" consumption patterns show the distribution of fish and shellfish consumptions among persons who reported eating these foods on the day of the survey. Consequently, these "per user" data present the distribution of portion sizes and fish/shellfish species for the fish/shellfish consuming population. Combining these with mercury concentrations in the fish provides an indication of the distribution of mercury exposure from fish/shellfish on the day surveyed. A highly relevant question is that of how often during a month does the population of concern repeat the consumption patterns shown on the day surveyed. These are addressed Section 6.3.2.

6.3.2 Population-Based Projections of the Number of Women Consuming Fish/Shellfish in Excess of 100 Grams per Day

6.3.2.1 General Population

The estimated number of women of child-bearing age (ages 15 through 44 years) in the contiguous 48 states is approximately 58,222,000 based on data from the 1990 United States Census (Table 5-22). It is estimated that in a given year 9.5% of women in this age group are pregnant (Appendix C, Exposure Volume). 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 whose fish/shellfish intake is at or above 100 grams/day.

- Based on the number of women consuming 100 grams of fish/day or more from the CSFII 89/91 survey the estimated number of pregnant women consuming fish in amount > 100 grams/day was 84,000 (Table 6-11).

- The number of women of child-bearing age consuming fish and/or shellfish in excess of 100 grams per day was 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. The estimated number of women consuming > 100 grams of fish/shellfish was approximately 52,000 (Table 6-12).

- Results from the contemporary 1990s food consumption surveys using single day dietary data show that the 95th percentile of fish/shellfish consumption for adult women exceeds 100 grams of fish/shellfish per day (Table 6-13). The number of pregnant women with this level of consumption is 277,000.

- Extrapolation of the single day's dietary data to a month-long pattern of fish and shellfish intake shows that the 95th percentile of fish/shellfish consumption for adult women is between 73 grams of fish/shellfish per day (Table 6-14). Based on the month-long per user projection 3% of women consume fish and shellfish in amounts of 100 grams/day or more. The number of pregnant women consuming 100 grams or more per day (projected to month-long exposure patterns) is approximately 166,000.

Table 6-11
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	~ 84,000

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

Table 6-12
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	
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	~ 52,000

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

Table 6-13
Estimated Population in the United States, excluding Alaska and Hawaii, Consuming 100 Grams or more of Fish and Shellfish on an Individual Day

Population Group	Estimated Number of Persons
Total U.S. Population	247,052,000
Total Female Population Aged 15 to 45 Years	58,222,000
Total Population of Children Aged < 15 years	53,462,000
Percent of Adult Female Population Ages 15 through 45 Consuming 100 grams of Fish & Shellfish/Day	
5%	2,911,100
Estimated Number of Adult Pregnant Women in Fraction of Adult Female Population Ages 15 to 45 Consuming 100 grams of Fish and Shellfish/Day	
Number of Adult Females x Percentage of Women Pregnant in a Given Year (9.5%)	~ 276,000

Table 6-14
Estimated Population in the United States, excluding Alaska and Hawaii, Routinely Consuming 100 Grams or more of Fish and Shellfish Per Day Based on Month-Long Projections of "Per User" Data from NHANES III

Population Group	Estimated Number of Persons
Total U.S. Population	247,052,000
Total Female Population Aged 15 to 45 Years	58,222,000
Total Population of Children Aged < 15 years	53,462,000
Percent of Adult Female Population Ages 15 through 45 Routinely Consuming 100 grams of Fish & Shellfish/Day	
3%	1,747,000
Estimated Number of Adult Pregnant Women in Fraction of Adult Female Population Ages 15 to 45 Consuming 100 grams of Fish and Shellfish/Day	
Number of Adult Females x Percentage of Women Pregnant in a Given Year (9.5%)	~ 166,000

6.3.3 Subpopulations of Anglers, Subsistence Fishers

The rate of fish and shellfish consumption for the general population may be low compared with special subpopulations. These subpopulations can have substantially higher mercury exposures than does the general population consuming a diet containing a mixture of fish species from diverse geographic locations. By contrast subpopulations and/or subsistence fishers may obtain most of their fish from one source.

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 estuarine 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. Volume IV 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.

6.4. Recommendations Based on Micrograms of Methylmercury Per Day

6.4.1 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 on lthe 95% confidence interval 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. 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.

6.4.1.1 Comparison with the General Population

Cross-Sectional Data

Estimates based on cross-sectional data provide a description of mercury intake for individuals in the surveyed population. This provides information on the species of fish/shellfish selected and on the portion size of the fish/shellfish consumed. Summed this information describes a distribution of total mercury intakes or if divided by body weight estimates dose of mercury on a µg/kg*bw*/day basis.

Based on data from contemporary food consumption surveys (NHANES III, CSFII 94, and CSFII 95) the RfD is exceeded at approximately the 93th percentile of all women. At the 95th percentile the estimated mercury exposure from fish and shellfish is 0.16 µg/kg*bw*/day based on per capita data. Among women who reported consuming fish and shellfish in the survey (per user data on an individual day), the 50th percentile consumer has exposures at the RfD. The 75th, 90th, and 95th percentile consumers are twice, approximately four-times, and about five-times the RfD respectively.

Two issues need to be noted regarding these comparisons. Estimated dietary intakes at the 95th or 99th percentiles are at the extremes of the distribution. Short-term dietary intakes based on short-term food consumption records (i.e., individual day's data) are known to be subject to substantial variability at the extremes of the distribution. Consequently, interpretation of these data must be made with recognition that these extreme values can vary greatly.

Month-Long Estimates of Mercury Exposure

To reflect the sub-acute nature of developmental toxicity of methylmercury exposures over a period of at least one month were considered to be relevant to the health endpoint used to establish US EPA's RfD. Estimates of month-long exposures to methylmercury were calculated by use of NHANES III data. Specifically the NHANES III "per user" data supplied the distribution of mercury exposures on a µg/kg*bw*/day basis on an individual day. The frequency of fish/shellfish consumption data for survey respondents 14 years of age and older provided a distribution of how often fish and shellfish were consumed on a monthly basis. This distribution included in the frequency distribution the individuals who reported they did not consume fish/shellfish during the past month. Consequently the overall distribution is considered to be representative of the United States population.

Analysis of frequency of fish and shellfish consumption (see Exposure Volume) showed that consumption patterns were consistent among men and women and among persons ages 15 to 45 and persons older than 45. Review of the "per capita" and "per user" data for ethnically and racially defined subpopulations indicated that major subpopulations consumed fish and shellfish with different frequency and in different quantities. This pattern persisted when mercury exposures were expressed as month-long estimates (µg/kg*bw*/month). Consequently, the major subpopulations have differences in the frequency with which they consume fish and shellfish.

Month-long projections of mercury exposure from ingestion of fish and shellfish were made using NHANES III data for both 24-hour recalls and fish consumption frequencies. Subpopulations considered were: "White/NonHispanic", "Black/NonHispanic" and "Other". The "Other" category consists predominantly of persons of Asian/Pacific Island ethnicity, Native American Tribal members, NonMexican Hispanics (e.g., persons from Puerto Rica and other Caribbean islands), and additional persons). These month-long projected mercury exposures (µg/kg*bw*/month) are shown in Table 6-15. The percentile in the distribution at which the exposure exceeds the RfD is also shown in Table 6-16.

Table 6-15
Month-Long Exposures to Mercury (µg/kg*bw*/day)
National Estimates Based on NHANES III Data
All Age Groups

Percentile	Subpopulation		
	White/NonHispanic	Black/NonHispanic	Other*
50th	0.01	0.02	0.02
75th	0.04	0.05	0.06
90th	0.09	0.12	0.18
95th	0.15	0.21	0.34

* NHANES III category that includes persons of Asian/Pacific Islander ethnicity, Native American Tribal members, Non-Mexican Hispanics (e.g., persons from Puerto Rica and other Caribbean Islands), and others.

Table 6-16
Month-Long Mercury Exposures (µg/kg*bw*/day)
Percentiles at Which Exposures Exceed 0.1 µg/kg*bw*/day or the R*f*D
National Estimates Based on NHANES III Data
All Age Groups

	Subpopulation		
	White/NonHispanic	Black/NonHispanic	Other*
Percentile	91.0	87.3	83.4
% of Subpopulation Exceeding RfD	9.0%	12.7%	16.6%

* NHANES III category that includes persons of Asian/Pacific Islander ethnicity, Native American Tribal members, Non-Mexican Hispanics (e.g., persons from Puerto Rica and other Caribbean Islands), and others.

Women of childbearing age are the subpopulation of major concern with regard to methylmercury exposures. Exposure to methylmercury on a body weight basis when projected to month-long exposures has been estimated. These are shown in Table 6-17.

Table 6-17
Month-Long Mercury Exposures (µg/kg*bw*/day) for Women Ages 15 through 44 Years
National Estimates Based on NHANES III Data
All Subpopulations Combined

Percentiles	µg/kgbw/day
50th	0.01
75th	0.03
90th	0.08
95th	0.13
99th	0.34
Exposures Exceed RfD at the 93rd Percentile	

6.4.2 Children's Exposures to Methylmercury

Children are estimated to have higher mercury exposures (µg/kg*bw*/day) than do adults because of children's higher consumption of food on a body weight basis. NHANES III did not include questions on frequency of fish consumption in the survey. Consequently the authors of this Report to Congress have made the simplifying assumption that the fish consumption frequency of the children was the same as the adults. This particular assumption is an uncertainty in this analysis. Differences in the species and quantity of fish and shellfish consumed by children is not an uncertainty in this analysis because the 24-hour recall data in NHANES III were determined in this survey.

Table 6-18
Month-Long Estimates of Mercury from Fish and Shellfish for Children Ages 3 through 6 Years
National Estimates Based on NHANES III Data

Percentile	All Groups	White/ NonHispanic	Black/ NonHispanic	Other
50th	0.03	0.03	0.04	0.04
75th	0.08	0.08	0.08	0.11
90th	0.17	0.17	0.19	0.27
95th	0.289	0.28	0.30	0.46

The RfD of 0.1 µg/kg*bw*/day is based on a "benchmark" dose of 1.1 µg/kg*bw*/day. This "benchmark dose" reflects the lower bound of a 95% confidence interval for a 10% prevalence of effects. The effects on which the "benchmark" dose for methylmercury are based were clinically evident developmental deficits in children following *in utero* exposure to methylmercury. The RfD was derived

from the "benchmark" dose of 1.1µg methylmercury/kg*bw*/day through application of a composite uncertainty factor of 10.

It is recognized that development of the nervous system does not cease at birth but continues throughout early life. The magnitude of an uncertainty factor that should be applied to a benchmark dose to provide an appropriate RfD for children is an issue that, in itself, carries additional uncertainty. Because the nervous system continues to develop during childhood (in particular duringthe first six years of life), it is judged that an RfD for children is probably higher than that protective of the fetus but lower than the former RfD which was protective of sensitive adults. For these reasons U.S. EPA acknowledges that application to young children of the RfD based on developmental deficits produced by fetal exposures to methylmercury carries additional uncertainty beyond that applied to the "benchmark" dose. Nonetheless, because of concern that young children have higher exposures to methylmercury on a per kg*bw* basis than do adults, U.S. EPA believes that it is appropriate to apply the fetal protective RfD to young children to be protective of public health.

Applying the fetal-protective RfD to mercury exposures arising from month-long patterns of fish and shellfish exposures (Table 6-18), it is estimated that as many as 20% of U.S. children ages 3 through 6 years have exposures to methylmercury greater than the RfD. An uncertainty in this estimate is whether or not children consume fish/shellfish at frequencies comparable to adults. The total population of children in the United States aged 3 thought 6 is 14,965,000 based on 1990 Census statistics.

6.4.3 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 from Volume IV. More precise estimates of mercury intake for these subpopulations will require site-specific determinations of mercury in the fish consumed.

6.4.4 Freshwater Fish Consumption

U.S. EPA (1997) compiled meassured fish methylmercury concentration data for eight species of fish for each U.S. State where such data had been collected. The locations within each state from which individual fish were collected were reported as were the type of fish, the methylmercury concentration, and the tissue(s) from which the sample was collected (e.g., fillet). The reported methylmercury concentrations

were showed a great deal of variability both within a particular species of fish and across species of fish. Table 6-19 summarizes the range of U.S. State mean methylmercury concentrations present in six species of freshwater fish collected from 1990 through 1995 (U.S. EPA, 1997). Note the broad range in the State means. The concentrations listed in Table 6-19 show the range of average (mean) fish mercury concentrations. These do not fully describe the range of individual data that were used to calculate the mean.

When estimating the dietary intakes of methylmercury from fish and shellfish the calculations were made using mean U.S. fish/shellfish mercury concentrations. The freshwater fish methylmercury concnetrations were derived from a national survey presented in Bahnick et al., (1994). This approach works well if the subpopulation of concern obtains their fish/shellfish from a variety of sources. However, if individuals or subpopulations obtain most of their fish/shellfish from one or a small number of geographic sources, the resulting exposures could be substantially lower or higher than the mean value used in calculations in this volume.

For individuals or subpopulations consuming freshwater fish from a geographically limited area, only a local survey of the types and quantities of fish consumed as well as the measured methylmercury concentrations in the fish tissues actually consumed can accurately predict exposure. The aim of this Report is not to estimate exposure at specific sites. The figures that follow show the range of specific fish tissue methylmercury concentrations on the horizontal axis and a range of fish consumption estimates that correspond to exposure at the RfD on the vertical axis. Figures 6-2 through 6-8 use the oral RfD for methylmercury of 0.1 µg/kg bw/day and assume that the body weight of the hypothetical female is 60 kg [U.S. EPA (1997)] Exposure Factors Handbook).

Figure 6-2
Exposure at the Oral RfD for a Range of Fish Methylmercury Concentrations

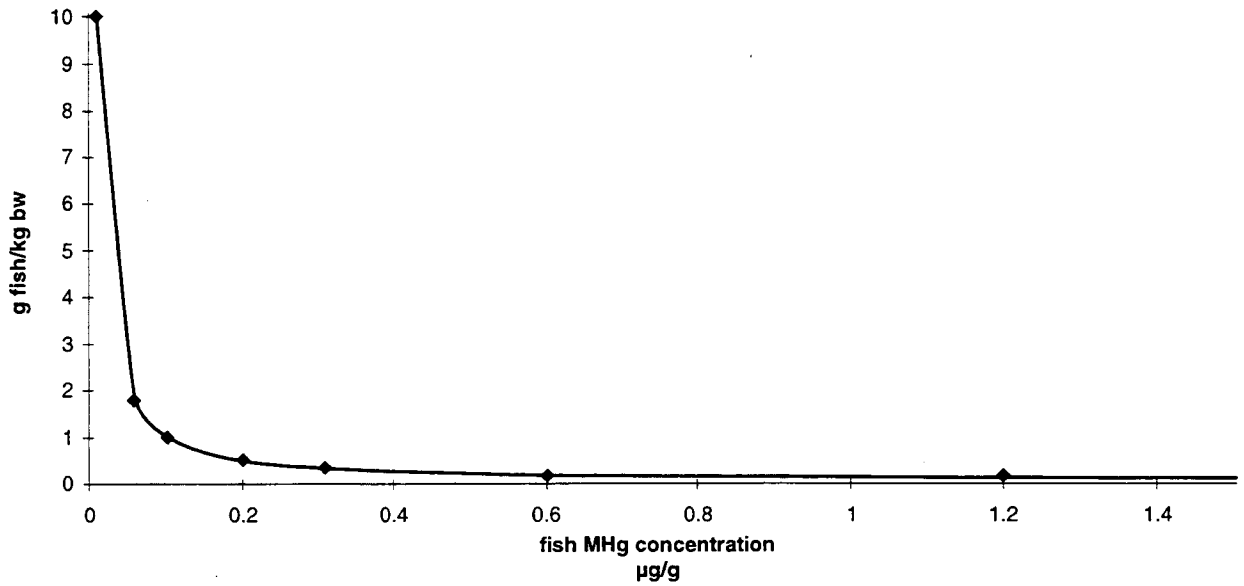


Figure 6-3
Exposure at the Oral RfD for a Range of Channel Catfish Methylmercury Concentrations

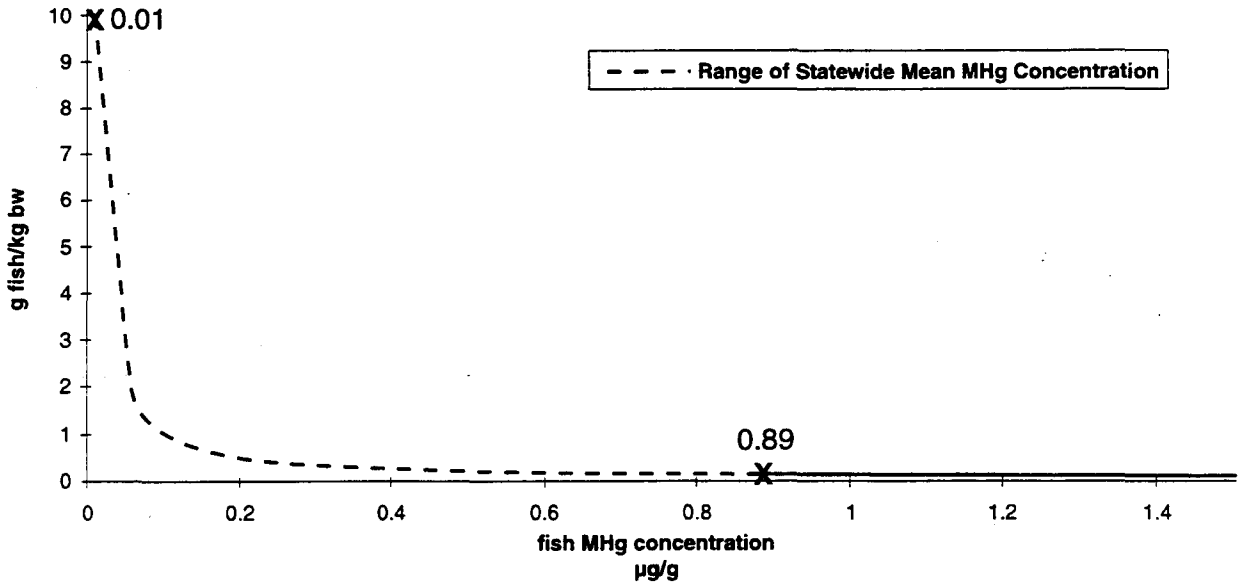


Figure 6-4
Exposure at the Oral RfD for a Range of Brown Trout Methylmercury Concentrations

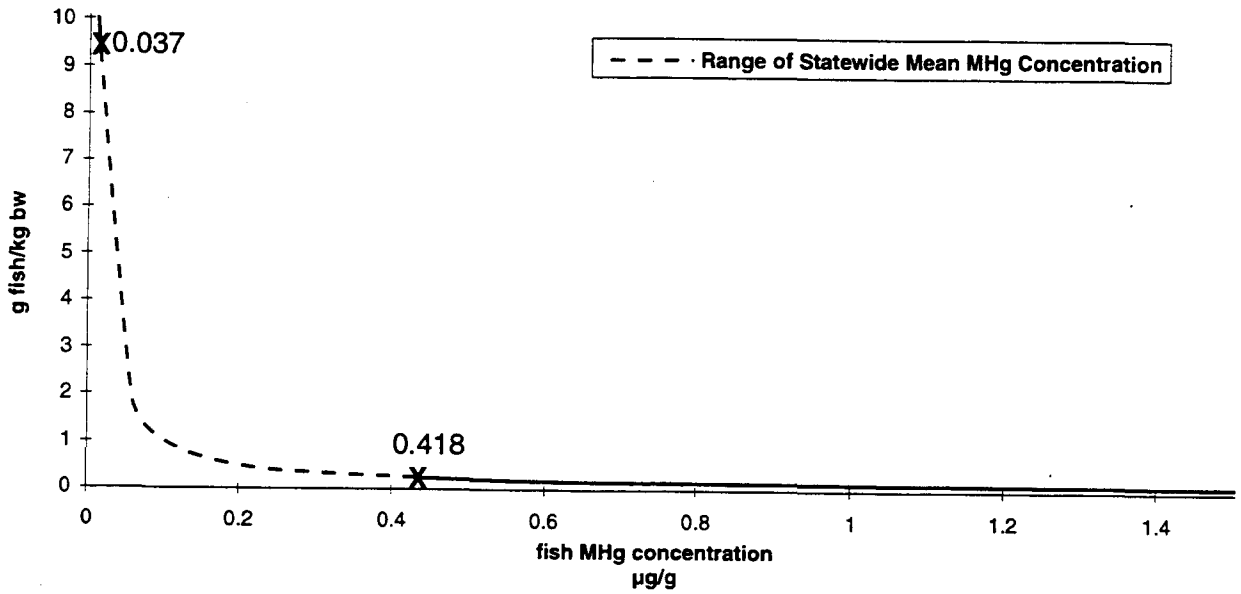


Figure 6-5
Exposure at the Oral RfD for a Range of Smallmouth Bass Methylmercury Concentrations

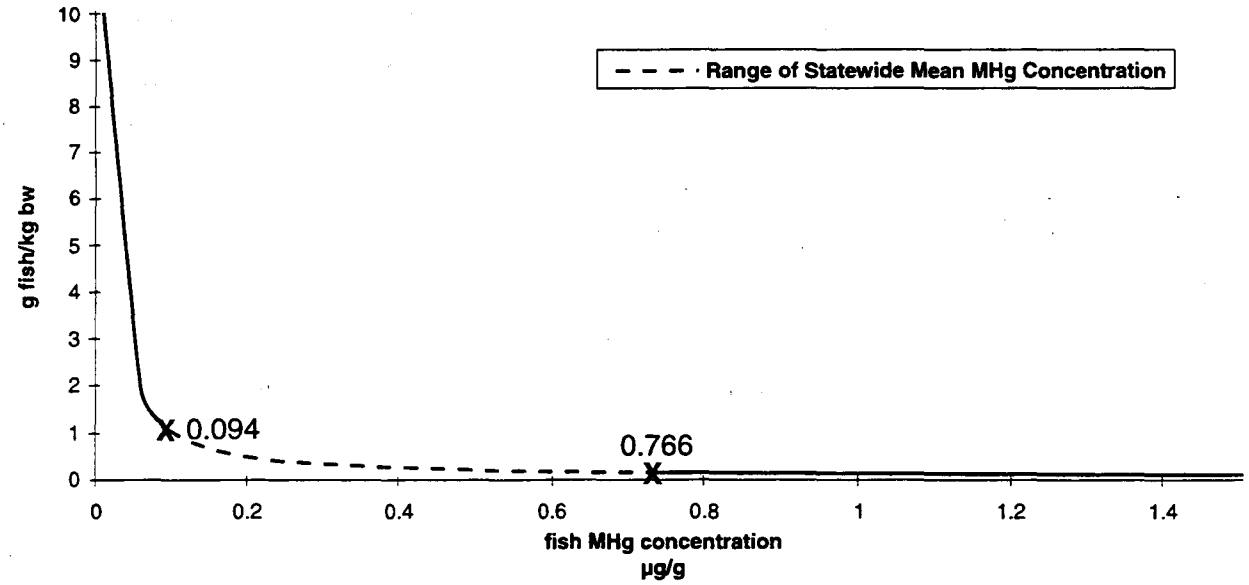


Figure 6-6
Exposure at the Oral RfD for a Range of Largemouth Bass Methylmercury Concentrations

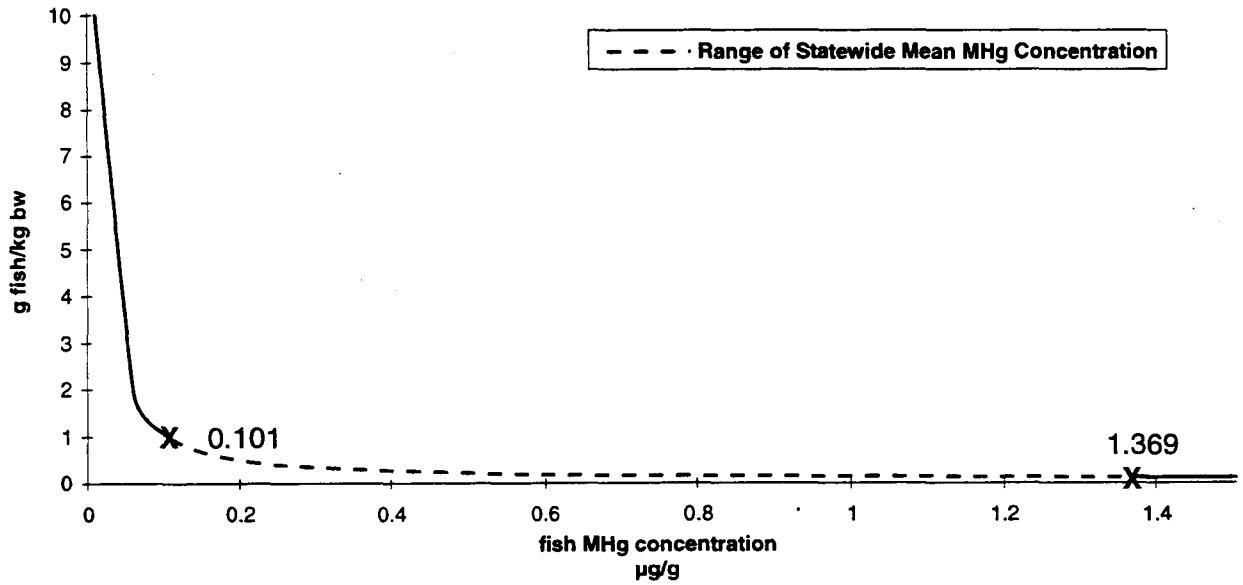


Figure 6-7
Exposure at the Oral RfD for a Range of Walleye Methylmercury Concentrations

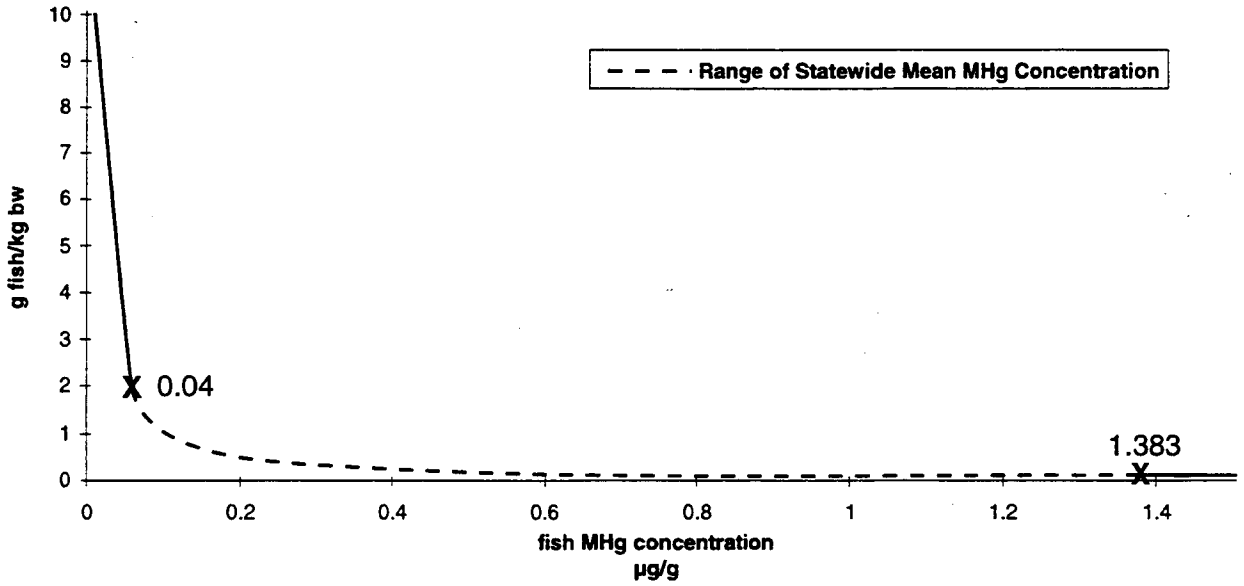


Figure 6-8
Exposure at the Oral RfD for a Range of Northern Pike Methylmercury Concentrations

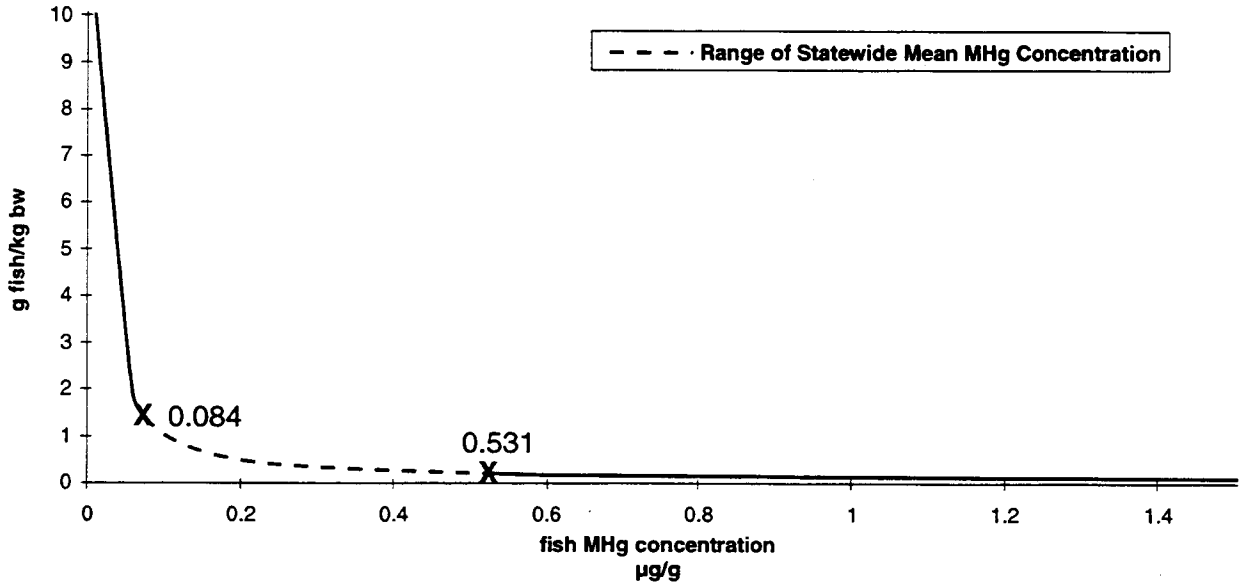


Figure 6-2 presents the curve corresponding to exposure at the oral RfD for a range of fish methylmercury concentrations (see Table 6-19). The curve shows that individuals who eat small quantities of fish per day are not predicted to exceed the RfD unless the fish are highly contaminated. Individuals who consume large quantities of fish per day would be expected to excede the RfD unless the fish consumed contains a small quantity of methylmercury. Table 6-20 shows specific point estimates for the curve and the corresponding consumption rates. In contrast, with low methylmercury in fish/shellfish, individuals must consume large quantities of fish (e.g., hundreds of grams/day) to exceed the RfD.

Table 6-19
Range of Mean Mercury Concentrations (µg/g) for Major Freshwater Sport Fish among U.S. States

Species	Mean Mercury Concentrations	Species	Mean Mercury Concentrations
Channel catfish	0.010-0.890	**Largemouth bass**	0.101-1.369
Smallmouth bass	0.094-0.766	**Walleye**	0.040-1.383
Brown trout	0.037-0.418	**Northern pike**	0.084-0.531

*Reference: U.S. EPA (1997). The National Survey of Mercury Concentrations in Fish. Database Summary 1990-1995. September 29, 1997.

Table 6-20
Fish Consumption Rates and Methylmercury Concentrations Which Correspond to Human Exposures at the Oral Reference Dose (0.1 µg/kg bw/day)*

Human Fish Consumption Rates (g/day)	g fish consumed/ kg bw/day	Fish MHg Concentration Corresponding to the Oral RfD (µg/g) or ppm
1	0.017	6
2	0.033	3
3	0.05	2
5	0.083	1.2
10	0.17	0.6
20	0.33	0.3
30	0.5	0.2
60	1	0.1
100	1.7	0.06
200	2.3	0.01

* Assumes that the individual weighs 60 kg.

6.4.2 Children's Exposures to Methylmercury

The figures that follow show the curve of human consumption rates for measured mean methylmercury concentrations in specific species that corresponds to the human oral RfD. These are mean values for individual U.S. States; some more geographically limited fish sources may result in exposures which excede the RfD. These data highlight the importance of public awareness of fish consumption advisories. It should be noted that exceding the RfD does not indicate that an adverse health effect will result. Exposures below the RfD should be without an appreciable risk of deleterious effects during a lifetime.

6.5 Wildlife Species

6.5.1 Comparison with Great Lakes Water Quality Initiative Criteria

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 6-21).

Table 6-21
Comparison of Wildlife Criteria Calculated by
Great LakesWater Quality Initiative and by the Mercury Study

Species	Wildlife Criterion (pg/L)	
	GLWQI	MSRC
Mink	2880	415
Otter	1930	278
Kingfisher	1040	193
Loon		
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 V.

6.5.2 Estimates for the Size of the Piscivorous Wildlife Population

Six wildlife species were considered in the exposure and ecological risk Volumes of this assessment. The six species were selected because they consumed fish. The selected species consisted of four avian species (the bald eagle, the loon, 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.

6.5.2.1 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).

6.5.2.2 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).

6.5.2.3 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.

6.5.2.4 Loon

Evers (1997) estimated the population of adult loons in the contiguous U.S.and Alaska to number approximately 28,800, including 10,600 territorial pairs (David Evers, of BioDiversity, Inc. personal communication to G. Rice U.S. EPA,10/30/97). The estimates are based on the author's experience and surveys conducted by State and Federal Agencies and Organizations. (See Table 6-22).

6.5.2.5 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.

6.5.2.6 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.

Table 6-22
Breeding Loon Population Estimates by State (Source: Evers, 1997)

State	Number of Adults	Number of Territorial Pairs
Alaska	8,886	3110
Idaho	10	4
Maine	3,500	1,400
Massechusettes	24	10
Michigan	882	315
Minnesota	11,630	4,070
Montana	150	60
New Hampshire	502	209
New York	804	301
North Dakota	12	5
Vermont	60	25
Washington	38	16
Wisconsin	3,017	1,056
Wyoming	92	37
Total	**28,803**	**10,618**

Table 6-23
Summary of Contiguous U.S. Population Estimates for Piscivorous Wildlife Evaluated in the Report

Species	Estimated Population Size
Bald Eagle	10,000-12,000
Osprey	10,000-20,000
Belted Kingfisher	170,000
Loon	19,900 (Adults)
Mink	10,000,000
River Otter	300,000

Reference: Evers, D. 1997. Personnal communication between D. Evers of Biodiversity, Inc., 195 Main St. Freeport, Maine and G. Rice, U.S. EPA, October 30, 1997.

7. 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 and animals via the food chain.

- The human RfD for methylmercury is estimated 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.

- Subtle, adverse developmental deficits have been observed among children from a seafood-consuming population (Grandjean et al., 1997). These deficits have been associated with maternal hair mercury concentrations less than 10 ppm. Hair mercury concentrations of less than 10 ppm are associated with ingestion of less than 1 µg mercury/kg body weight/day. Because these are recently published reports, these findings, as well as, those from studies of fish-consuming populations that did not show adverse effects (but were based on different neurobehavioral endpoints) require additional evaluation.

- The probability of adverse effects increase as exposures increase above the RfD,however, quantitative risk projections cannot be made for ingestion of methylmercury above the RfD given currently available human data.

- 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.

- Within the general U.S. population, 85% of people consume fish and shellfish over the course of a month, with 40% consuming fish weekly. An additional 1-2% of people eat fish and shellfish almost daily. Among this group of fish consumers roughly 50% 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 year-long dietary 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 5 percent of women of child-bearing age regularly consume fish and shellfish at average intakes of 100 grams per day or greater. National estimates based on projectsion made using NHANES III data indicate that 3% of women of childbearing age consume 100 grams or more of fish per day and 7% exceed the RfD. Whether or not methylmercury intakes are elevated above the estimated NOAEL depends on the concentration of methylmercury in the fish and shellfish consumed.

- Children are more highly exposed to mercury on a body weight basis than are adults. National estimates of month-long fish/shellfish consumption using NHANES III data indicate that 5% of 3-to-6 year olds are exposed to approximately 0.3 µg Hg/kg bw/day.

- 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 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 methylmercury 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 gathered. 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.

- Inproved information on biochemistry, physiology, and toxicology of mercury in children.

- 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.

8. 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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