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AN SAB REPORT: REVIEW OF THE EPA DRAFT MERCURY STUDY REPORT TO CONGRESS

REVIEW OF THE EPA'S MERCURY REPORT TO CONGRESS BY THE MERCURY REVIEW SUBCOM-MITTEE

October 10, 1997

EPA-SAB-EC-98-001

Honorable Carol M. Browner
Administrator
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, DC 20460

Subject: Science Advisory Board's review of the EPA Draft Mercury Study Report to Congress

Dear Ms. Browner:

The 1990 Clean Air Act Amendments directed the EPA to perform a study on the impacts of mercury as an air pollutant and to provide a report to the Congress. The Act required EPA to address several specific topics, including mercury emissions from electric utility steam generating units, municipal waste combustion units, and “area” sources; the rate and mass of these emissions; the associated health and environmental effects; technologies for controlling these emissions; and the costs of such control technologies.

In response, the EPA developed a seven volume draft report (EPA-452/R-96-001a-h, June, 1996) which was stated by the Agency to provide data on types, sources, and trends in mercury emissions; evaluated the atmospheric transport of mercury; assessed the impacts of mercury emissions on organisms/ecosystems close to the emitting source; identified major exposure pathways to humans and non-human biota; identified mercury exposure levels likely to produce adverse effects in humans, and the nature of those effects; evaluated mercury exposure effects for ecosystems and non-human organisms; identified populations especially at risk from mercury exposure due to special sensitivity or high exposure; and made estimates of the effectiveness of control technologies and their costs.

After completing the draft report, the Agency stopped short of issuing a formal final mercury report to Congress because of a growing consensus that such an analysis should wait for a full assessment of several relevant studies now underway. These

studies address the effects of methylmercury on neurological development of children in fish-consuming populations in the Seychelles and Faeroe Islands, and were expected to be completed and published in the next year or two. Their results should be considered before making a new assessment of health risks. In terms of currently available data, however, the Agency decided to proceed with finalizing the existing report by having the Science Advisory Board (SAB) review it (as is customary with major scientific documents) before transmitting it to the Congress. The Agency's goal was "... to receive SAB's view of the overall report as well as to seek SAB assistance in prioritizing research needs and identifying any important weaknesses in the current evaluation -- other than those which are addressed by the on-going studies -- with an eye on improving the assessment" (memorandum from Dr. Robert Huggett, then Assistant Administrator for Research and Development (ORD) and Ms. Mary Nichols, then Assistant Administrator for the Office of Air and Radiation (OAR), June 23, 1996).

Following receipt of the above referenced memorandum from the ORD and the OAR, the SAB created a special Subcommittee (the Mercury Review Subcommittee (MRS)) of its Executive Committee. Composed of 34 scientists from the United States and Canada, and reflecting a wide range of disciplines and expertise, the MRS convened in public meeting on February 13/14, 1997 in Washington, DC. The Subcommittee was organized into three Workgroups (Sources; Exposure, Doses, and Body Burdens; and Human Health Effects), and addressed a Charge of 46 enumerated questions developed via discussions between EPA, the Food and Drug Administration, and SAB staff. This report, developed via mail in the several months following the public meeting, reflects the discussions at that meeting.

The following discussion presents the Subcommittee's conclusions regarding the major topic areas of the Charge; because of the unusual length and complexity of the Charge (which is provided in its entirety in Enclosure A), this letter will not attempt to address every specific enumerated issue.

First, and perhaps most importantly, the Subcommittee believes that the major findings of the draft report are well supported by the scientific evidence, and that the Agency has done a very creditable job in amassing, analyzing, and drawing conclusions from a truly vast amount of data. Naturally, as with any such project of this scope and depth, there are areas where improvement in the use of available scientific information is possible, as well as in the organization and presentation of information. Detailed suggestions for such improvements are noted in our report, and are noted below.

Addressing specific findings, the MRS concluded that:

a) The majority of the human population is not experiencing methylmercury exposures that are of concern from the standpoint of human health. It is

not now possible to establish a quantitative relationship between sources and actual exposures in humans or wildlife. The draft EPA report is seen by the Subcommittee as a document which, in general, reflects the current state of the art with regard to human health and atmospheric mercury transport issues. However, the Subcommittee feels that the report does not adequately present or model Hg fate and transport in ecosystems, Hg bioaccumulation or wildlife exposure. It is also noted that the high end of the distribution of methylmercury exposures is very uncertain with respect to exposures, total number of people (and percent of the population) who may be experiencing exposures high enough to cause adverse health effects, and the actual sub-groups who are highly exposed. Consequently, total population risk is not, and cannot be, fully characterized at this time.

b) In general, from the standpoint of looking at human health effects and the uncertainties in general, the draft report is a very good document and an important step forward in terms of bringing the relevant information together into one place for the first time. The current Reference Dose (RfD), based on the Iraqi and New Zealand data, should be retained at least until the on-going Faeroe and Seychelles Islands studies have progressed much further and been subjected to the same scrutiny as has the Iraqi data.

c) The Subcommittee identified some problems *vis-a-vis* human health issues as discussed in the draft document -- a lack of recognition and emphasis on consistency of the data across multiple studies, and, most seriously, a failure to link animal studies to the human risk assessment process. Major problems also exist in interpreting the biology of the outcome in children versus adults; interpreting potential susceptibility differences between populations; and identifying factors which may modify response, such as diet. Note however, that the Subcommittee believes 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.

d) With respect to modeling the linkage between emissions from anthropogenic sources and human exposures, the Subcommittee agrees that it is plausible that current anthropogenic emissions are contributing to human exposures. However, the relative contributions of current anthropogenic emission sources, global backgrounds, recycling of old emissions and natural background to human exposures of methylmercury are highly uncertain and difficult to determine. Furthermore, the time constants for intermedia transport are not known. Since mercury does not degrade in the global environment, current anthropogenic emissions will add to the

fraction of global mercury that is actively circulating in the biosphere, surface water, and soils. In addition, emissions from both the U.S. and from other countries can impact the U.S. environment and exposures of humans and wildlife. The Subcommittee also notes, however, that this section of Volume III of EPA's draft report is not clearly written and confuses environmental transport and fate modeling with exposure analysis.

e) The Subcommittee concurs with the conclusion that fish are the major source of methylmercury exposures for the human population. The exposure analysis based on fish consumption must be regarded as a "snapshot" in time, however. In addition, there are two potential biases affecting the exposure analysis based on fish consumption. First, the consumption data from the Department of Agriculture's Continuing Surveys of Individual Food Consumption (CSFII) should be checked against production data. These will not agree exactly but should be reasonably consistent. Second, the average concentrations of methylmercury in fish used for the exposure assessment were provided by the National Marine Fisheries Service. The Subcommittee recommends that EPA determine how measurements of methylmercury in fish which were below the analytical limits of detection (BDL) were statistically treated in arriving at the mean concentrations.

f) The Subcommittee strongly recommends that EPA edit and shorten Volume III on Exposure to eliminate redundancies and clarify the logical sequence of the exposure analysis.

g) The Subcommittee notes that in the process of assessing control costs, the draft mercury report devotes most of the cost analysis to end-of-pipe controls and gives little attention to other types of controls. The Subcommittee recommends that the cost analysis also give consideration to other approaches for controlling mercury emissions that might prove to be more flexible and more cost-effective.

h) The Subcommittee generally agreed that the mercury wildlife criterion (as currently presented) is overly conservative and is lower than appears necessary to protect wildlife species. The criterion was derived from a bioaccumulation factor (BAF) based on total Hg rather than methylmercury (MeHg), which is the mercury species that bioaccumulates. As a result, the magnitude of the error in the BAF is associated with, and reflects, the wide variability in MeHg concentrations among ecosystems. The Subcommittee suggests that EPA, using the best techniques now available to recalculate BAF and wildlife risk criteria based on dissolved

MeHg in water, and that BAF calculations be specific to ecosystem or water body type.

The problems noted above notwithstanding, the Subcommittee believes that piscivorous wildlife are at risk from elevated mercury exposures and exhibit toxic effects in the areas of concern identified by the U.S. EPA. In addition, there is good evidence showing effects of mercury on wildlife; a summary of the population that appear to be affected; and a statement that wildlife exposure can be a harbinger of hard-to-detect human effects should be added to the final report

I) The Subcommittee finds that Volume V, in total, is not based on the best available and sound science. To a large degree this chapter follows EPA guidelines for ecological risk assessment. However, it deviated in terms of quantifying the risk. This is a critical component of risk assessment.

j) The final document should emphasize the fact that there are significant information gaps in the understanding of the biogeochemistry of mercury species and that the absence of this information limits the reliability with which any mercury control program can be evaluated.

k) The modeling of atmospheric mercury transport and deposition is largely sound, but the modeling of the post-deposition fate of mercury in ecosystems is oversimplified, neglects available information on speciation, and does not reflect recent advances in the science. This deficiency is one of the most serious problems in the draft report. This modeling should be revised, with the goal of having the report reflect current scientific understanding. Also, the modeling, as used, contributed to sizeable errors in the estimated wildlife criterion. It is important to bring out the importance of MeHg production in ecosystems in the report. Because MeHg is the species that bioaccumulates in human and wildlife food supplies, understanding the methylation process is critical to modeling Hg fate and exposure. Mercury methylation and the variability in MeHg among ecosystems were neglected in the report, because of the perceived difficulties in modeling methylation. The report assumes that MeHg constitutes the same fraction of total Hg in sediments, soils and waters across ecosystems. This is not the case. Rather, the variability in MeHg production and bioaccumulation among ecosystem types is many orders of magnitude, and may be as large as the influence of Hg contamination. Without consideration of this variability, the report's fate and transport models, and the resultant exposure models and wildlife criteria models cannot predict Wildlife Criteria with less than two to three orders of magnitude associated error.

The final EPA report should detail the state of our understanding of Hg methylation process within Volume III; address MeHg production along with fate and transport models in Volume III (which models should be specific for a suite of ecosystem types); and the resultant information be used to model and discuss wildlife exposure in Volume V. Because the models for estimating the distributions of human exposure were based on measured values for Hg in fish and other food, rather than modeled values, these suggested changes will not affect the human exposure analysis in the report.

We appreciate the opportunity to review this document, and look forward to your response to the issues we have raised.

/signed/
Dr. Genevieve Matanoski, Chair
Science Advisory Board, and
Co-chair, Mercury Review Subcommittee

/signed/
Dr. Joan Daisey, Co-chair
Mercury Review Subcommittee

ENCLOSURE

ENCLOSURE A
DETAILED CHARGE FOR THE MERCURY REVIEW SUBCOMMITTEE

GENERAL

1. The EPA has decided to defer evaluation of the dose-response relationship between methylmercury and fetal and developmental effects until additional scientific data have been evaluated. These issues will be addressed in Phase Two of the SAB review. **Putting these matters aside, are the overall assessment and conclusions based on sound and appropriate evaluation of the relevant science?**

SOURCES

2. In order to approximate future mercury emissions, the sources are simplified to model plants placed to approximate current U.S. emission patterns. **Is this approach consistent with the best available scientific practice? Are the implications of this simplifying assumption adequately presented?**

3. US EPA limited the scope of its assessment to anthropogenic sources of mercury emissions. **Are these reasonable and defensible assumptions?** The emissions inventory estimates these emissions in the United States. There is a short discussion of natural emissions and re-emitted emissions as well. The discussion of these emissions was based on language suggested by the scientific peer review panel. The modeling of local point sources did not include natural emissions, while the long-range transport modeling did incorporate a background level of mercury (to account for natural and re-emitted Hg) which has been measured over the open ocean. **Are the reasons for this approach adequately stated? Are the uncertainties and implications of this approach consistently and appropriately described?**

4. For the atmospheric fate and transport modeling conducted using both the Regional Lagrangian Model of Air Pollution (RELMAP) and the Complex Terrain and Deposition Air Dispersion Model (COMDEP), best estimates from the peer-reviewed literature of the species of mercury emitted from each source were utilized. **Were these speciation profiles appropriate?**

5. **Can the Committee comment on the evidence concerning the role of human activity, and if possible, the role of U.S. sources to methylmercury in ocean seafood?**

ENVIRONMENTAL FATE/TRANSPORT

6. US EPA relied on modeling to describe mercury fate and transport. In the report, the inventory served as the building block and was linked to the models (which were themselves linked). Both local and regional impacts were assessed together (additive) and separately for both humans and wildlife. Model plants were used as surrogates for actual facilities as well as hypothetical locations and populations. **Would a case study approach using actual facilities be more appropriate? Are the rationales for the selected approach appropriately presented? Please comment on the usefulness of measured data for estimating mercury exposures.**

7. In its assessment, US EPA assumed that available data on the deposition of nitric acid could be used to approximate the likely wet deposition of divalent mercury. **Is the rationale for this assumption adequate (see Volume 3, Section Chapter 6, Section 6.1.3, and Volume 3, Appendix D, Section D.1.3.2)?** Classical Gaussian and Lagrangian puff models were adapted to reflect mercury chemistry. **Were these modifications appropriate?**

8. Further, the assessment neglects the potential conversion of elemental mercury to divalent forms in cloud droplets in both the local scale and the regional analysis. The Agency has assumed that any such conversions would happen on such a small scale that they could have only a very nominal impact on the ultimate exposure characterization. **Is this rationale fully explained and adequate? Are the uncertainties of this assessment explained?**

9. The Agency recognizes that mercury fate and transport is an immature field; capabilities to describe phenomena such as the temporal distribution of mercury concentrations in soil continue to evolve. In its assessment, US EPA attempted to modify existing approaches (the 1990 Methodology of Assessing Health Risks associated with Indirect Exposure to Combustor Emissions and the 1993 Addendum) to reflect the more recent science. **Were the assumptions regarding equilibrium among mercury species present in soil appropriate?**

10. **Was the selection of the model input parameters (such as the soil-to-water partition coefficients) appropriately justified and the uncertainties explained? Is the estimation of the watershed and water body fluxes adequate and appropriate? Should fluxes in large lakes, rivers and other large water bodies also have been estimated? Is the rationale for not doing so adequate? Does the Agency appropriately justify and explain the uncertainty surrounding assumptions about plant uptake of mercury directly from the atmosphere? Is the likely contribution of mercury from plants to soil contributions sufficient that such sources should be added to future modeling efforts?**

11. A number of qualitative conclusions are drawn from the results of the atmospheric modeling; given the uncertainty in the modeling and in the state of the science, evaluate the scientific quality of these conclusions. **Were the uncertainties adequately described?**

12. A key variable in estimating ultimate potential human exposure is the bioaccumulation factor (BAF) for methylmercury through the aquatic chain. **Was the BAF developed by the Agency appropriate and its utilization in the models scientifically sound? Was the uncertainty analysis adequate?**

13. **Were the models and modeling conducted for the terrestrial food chain adequate and appropriate?**

EXPOSURE

14. The exposure assessment is contained in Volume III. **Please comment on the scientific basis of this assessment, alternative approaches, and research priorities. In particular, please advise the Agency on how Appendix H should be used, improved, or expanded.**

15. Because of uncertainties inherent in the emissions inventory and the model, the exposure assessment was characterized as being a "qualitative assessment based on quantitative modeling." **Is this a reasonable characterization? Were the uncertainties of and conclusions drawn from linking the models together appropriately described?**

16. US EPA has estimated methylmercury and fish consumption using both cross-sectional and longitudinal data for the general US population. In these studies, EPA consistently finds that a portion (albeit a small one) of the population consumes very large quantities of fish. It is these individuals who face the largest risks from methylmercury exposure and who pose the greatest concern to the Agency. **Has EPA adequately assessed the number and types of individuals who consume fish in these relatively large quantities?** The group at issue includes 5% of the fish-consuming population. **Are the uncertainties associated with characterization of such small portions at the extreme end of the population distribution appropriately considered and presented? Could the estimate of 5% of the fish-consuming population be a methodologic artifact?**

17. US EPA has relied on three nationally-based sources of data for mercury concentrations in marine and fresh-water fish and shellfish. Some of these data were obtained within the past three years, whereas other data were obtained as long ago as 20 years.

Is the use of these older data appropriate? Does the document appropriately note the limitations of this methodology?

18. The USDA has published data indicating that fish and shellfish consumption have risen approximately 25% since the early 1970s . These consumption data were employed without adjustment in this report to estimate current fish consumption (Volume III, Appendix H; and Volume VI, Section 4.2.3.1). **Should these data be adjusted to reflect the overall trends in fish consumption? If so, how would the estimates of very high consumption (above the 90th percentile) be adjusted?**

19. In Volume III, Appendix H, calculations of methylmercury intake from crab were grouped without specific consideration of the particular species. These data are then linked to dietary survey data which typically do not list the individual species of many fish and shellfish consumed. **How might this approach bias the final assessment? Are the limitations of this approach adequately characterized in the report? Are these limitations going to materially alter the assessment of health risk associated with methylmercury exposures?**

20. In early versions of the draft report (and in Volume III, Appendix H), US EPA characterized total risk by considering methylmercury exposure from marine fish and shellfish together with consumption of methylmercury from fresh-water or estuarine fish and shellfish. It has been recommended that the report focus exclusively on fish from inland sources. **Does the current version adequately characterize total risk? Are the uncertainties resulting from this methodology appropriately presented?**

21. Some data exist on hair mercury concentrations in U.S. residents. **Is this data base adequate to predict the distribution of hair mercury in the general U.S. population?**

22. The draft report identifies hair mercury concentration as the most appropriate available index of methylmercury exposure. **Is this assumption consistent with the available data? Are the exposure estimate approaches used relevant and appropriate? Are the predicted exposure ranges consistent with other published exposure analyses? Are the uncertainties of this assumption appropriately presented?**

23. Although the modeling exposure assessment focused on anthropogenic emissions, the fish consumption analysis considered measured mercury concentrations in fish tissue regardless of the mercury's origin. Thus, there is considerable difficulty in assessing or describing how much of the mercury in fish is attributable to current anthropogenic emissions. **Is the approach taken by the Agency in this assessment appropriate given the available data? What is the advice of the SAB regarding**

the differentiation between current emissions and their impacts relative to the "body burden" approach of the fish consumption analysis?

DOSES/BODY BURDENS

24. In its assessment, U.S. EPA assumes that the biokinetics of methylmercury from contaminated grain approximate those resulting from methylmercury from fish. **Is this assumption consistent with the available science?**

25. **Are the uncertainties in the fish and grain consumption analyses adequately and consistently presented in the draft report?**

26. Similarly, US EPA assumes the biokinetic parameters for children are identical to those of adults. **Does such an assumption introduce bias into the assessment? Are the uncertainties adequately and consistently presented in the draft report? Is the conclusion that children's lower body weight results in higher exposure than to adults? Could this be an artifact of exposure modeling using 3-day consumption survey data?**

27. **What methodologies other than hair concentrations could be used to estimate body burdens of mercury?**

HEALTH ENDPOINTS and SUSCEPTIBLE SUBPOPULATIONS

28. Volume 4, Section 6.3, and Volume 6, Chapter 2, Sections 2.1 and 2.2.21 present US EPA's interpretation of the data demonstrating increasing severity and frequency of nervous system effects (particularly impairment in visual-motor integration) among pediatric subjects with increasing levels of maternal hair mercury. These sections present US EPA's interpretation of the data demonstrating increasing severity and frequency of nervous system effects (particularly impairment in visual-motor integration) among pediatric subjects with increasing levels of maternal hair mercury. **Recognizing that additional data may shortly be available, is EPA's assessment methodology based on the best scientific practice? Are the uncertainties in the characterization of potential effects accurately described in the draft text?**

29. Data from experimental animals (including primates with long-term exposures to methylmercury) show methylmercury-induced nervous system damage, particularly on the visual system, although the animals appear clinically normal. The traditional RfD methodology neglects such impairment. **Are these data important endpoints? Are they appropriately characterized in the draft report? How could such data be better evaluated by the Agency?**

30. The available data present information on fish consumption drawn over relatively short time periods (e.g., days) and are used to extrapolate consumption patterns over longer periods (e.g.. a month). Although the exact developmental window affected by methylmercury in humans is not precisely defined, it is thought to be less than three months. **Is such extrapolation appropriate in this case? Does the document appropriately present the limitations of this methodology**?

31. Volume 4, Section 6.3, and Volume 6, Chapter 2, Sections 2.1 and 2.2.21 present US EPA's interpretation of the data demonstrating increasing severity and frequency of nervous system effects (particularly impairment in visual-motor integration) among pediatric subjects with increasing levels of maternal hair mercury. **What biases are introduced into the assessment by focusing on subtle endpoints of neurobehavioral function in contrast with traditional metrics of child development? Should these indicators be dismissed if traditional metrics (such as age of first walking) are within normal ranges? Do the available data indicate whether children are more sensitive than adults to the effects of methylmercury?**

32. **Are the uncertainties in the characterization of potential effects accurately described in the draft text?**

33. Traditional methods for estimating potential human health risks from environmental hazards do not distinguish risks among subpopulations (e.g. racial or ethnic) groups. **If methylmercury exposures are comparable and some groups, but not all, show impairment in traditional and/or specialized neurophysiological/neurobehavioral tests, how should US EPA reflect these differences in its analyses? Do factors such as nutritional status, life-styles (e.g., substance abuse), or economic status play a role is mediating these differences?**

34. Similarly, many assessments of methylmercury risk clump risk to fetuses and children together with risk to adults. **Is this approach scientifically valid for methylmercury?** Methods for estimating potential human health risks from environmental hazards do not distinguish risks among subpopulations (e.g. racial or ethnic) groups. **If methylmercury exposures are comparable and some groups, but not all, show impairment in traditional and/or specialized neurophysiological/neurobehavioral tests, how should US EPA reflect these differences in its analyses?**

35a. **What wildlife effects (based on what metric) can be interpreted as harbingers of likely human health effects?**

35b. **Could the Committee provide any short-term advice on human health issues not addressed in the coming epidemiologic studies such as toxicokinetics?**

ISSUES ON WILDLIFE ASSESSMENT

35c. Chapter VI presents the Agency's current mercury risk characterization. **Please advise the Agency on the appropriateness and environmental significance of the characterization of wildlife effects.**

36. Volume V describes fairly significant wildlife effects which are attributed to elevated mercury concentrations in some ecosystems. **Is this evaluation based on the best available and sound science, and are they consistent with EPA eco risk guidelines? How could this evaluation be improved?**

37. This report makes the inference that mercury emissions are related to reproductive effects and neurobehavioral changes in fish consuming birds and mammals. These effects have been documented in the Great Lakes and in the Southeastern United States. EPA's models predict that regional hot spots (relatively high concentrations of methylmercury) would occur in these same areas. **Is the analysis of the evidence linking emissions and effects scientifically sound?**

38. **Have any "hot spots" not shown evidence of wildlife effects? Do these predicted "hot spots" correlate with methylmercury levels in fishery products?**

39. **Which mercury-related effects in wildlife should be identified as warning signs that analogous effects may occur in humans? Could "wildlife epidemiology" be used as a surrogate for controlled lab studies?**

RESEARCH NEEDS

40. **Based on the research needs identified in the draft report, areas identified through discussion of the report, or on other information, has EPA identified the highest priority areas for research? If not, could the Committee suggest what areas need to be addressed?**

QUESTIONS RELATED TO SOCIAL COST

41. Chapter VII previously contained a section on the "Social Costs" of mercury contamination (this section is attached to comments by the Council of Economic Advisors in the supplementary information). This section described the value of the fisheries in the U.S. as well as other values such as maintaining a healthy ecosystem. The intent was to balance the discussion of mercury control costs. Some reviewers objected to the inclusion of the Social Costs section partly because the impact of anthropogenic sources could not be directly and quantitatively related to these impacts (e.g., the declining Florida panther population). The section was consequently deleted.

Is such a discussion appropriate for this study? How would the SAB advise the EPA to describe benefits of mercury reductions if a) the impacts of such reductions are not directly quantifiable, and b) the monetary value of such benefits are not easily quantified?

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NOTICE

This report has been written as a part of the activities of the Science Advisory Board, a public advisory group providing extramural scientific information and advice to the Administrator and other officials of the Environmental Protection Agency. The Board is structured to provide balanced, expert assessment of scientific matters relating to problems facing the Agency. This report has not been reviewed for approval by the Agency and, therefore, the contents of this report do not necessarily represent the views and policies of the Environmental Protection Agency, nor of other agencies in the Executive Branch of the Federal government, nor does mention of trade names or commercial products constitute a recommendation for use.

ABSTRACT

In response to the 1990 Clean Air Act Amendment's directive, the EPA developed a draft report on mercury, and asked the Science Advisory Board to review it. The Mercury Review Subcommittee convened on February 13/14, 1997 in Washington, DC.

The Subcommittee believes that the major findings of the draft report are well supported by the scientific evidence. There are areas where improvement in the use of available scientific information is possible. Detailed suggestions for such improvements are noted below:

a) The majority of the human population is not experiencing methylmercury exposures that are of concern from the standpoint of human health. The current Reference Dose, based on the Iraqi and New Zealand data, should be retained at least until the on-going Faeroe and Seychelles Islands studies have progressed much further and been subjected to the same scrutiny as has the Iraqi data.

b) The Subcommittee identified some problems *vis-a-vis* human health issues - a lack of recognition and emphasis on consistency of the animal data across multiple studies.

c) It is plausible that current anthropogenic emissions are contributing to human exposures, and that fish are the major source of methylmercury exposures for the human population.

d) The Subcommittee recommends that the cost analysis also give consideration to other approaches for controlling mercury emissions that might prove to be more flexible and more cost-effective.

e) The mercury wildlife criterion is overly conservative and is lower than appears necessary to protect wildlife species. However, piscivorous wildlife are at risk from elevated mercury exposures.

f) Volume V, in total, is not based on the best available and sound science.

g) The final document should emphasize the fact that there are significant information gaps in the understanding of the biogeochemistry of mercury species.

h) The modeling of atmospheric mercury transport and deposition is largely sound, but the modeling of the post-deposition fate of mercury in ecosystems does not reflect recent advances in the science.

KEYWORDS: mercury; methylmercury; RfD; piscivorous wildlife; fish; seafood; mercury biogeochemistry.

U.S. Environmental Protection Agency
Science Advisory Board
Mercury Review Subcommittee

February 26-27, 1997

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TABLE OF CONTENTS

1. EXECUTIVE SUMMARY

The EPA undertook a “Herculean” effort developing its draft report on mercury. Members of the Mercury Review Subcommittee were impressed by the robust and extensive data amassed for the report, and by its generally correct analysis and interpretation. As with any such large and complex task, however, modifications and clarifications can be identified. The Subcommittee’s major conclusions, based on the existing data as presented in the EPA's draft report and the analysis of these data (based on the scientific background of the Subcommittee's Members) are outlined below. Such a listing tends to highlight problem areas rather than areas of strength, and readers of this summary should keep this fact in mind. Specific findings of the Subcommittee are:

a) **That the majority of the human population is not experiencing methylmercury exposures that are of concern from the standpoint of human health.** The current state of the science, however, doesn't allow the establishment of a quantitative relationship between the sources and actual exposures in humans or wildlife. The draft report is seen by the Subcommittee as a document which, in general, reflects the current state of the art with regard to human health and atmospheric mercury transport issues. However, the Subcommittee feels that the report does not adequately present or model Hg fate and transport in ecosystems, Hg bioaccumulation or wildlife exposure. **It is also noted, however, that the high end of the distribution of methylmercury exposures is very uncertain with respect to exposures, total number of people (and percent of the population) who may be experiencing exposures high enough to cause adverse health effects, and the actual sub-groups who are highly exposed. Consequently, total population risk is not, and cannot be, fully characterized at this time.**

b) **In general, from the standpoint of looking at human health effects and the uncertainties in general, the draft report is a very good document and an important step forward in terms of bringing the relevant information together into one place for the first time. The current Reference Dose, based on the Iraqi and New Zealand data, should be retained at least until the on-going Faeroe and Seychelles Islands studies have progressed much further and been subjected to the same scrutiny as has the Iraqi data.**

c) **The Subcommittee identified some problems *vis-a-vis* human health issues as discussed in the draft document -- a lack of recognition and emphasis on consistency of the data across multiple studies,**

and, most seriously, a failure to link animal studies to the human risk assessment process. As pointed out at the public meeting, the animal studies are poorly integrated into the general document In addition, major problems exist in interpreting the biology of the outcome in children versus adults; interpreting potential susceptibility differences between populations; and identifying factors which may modify response, such as diet. Note however, that the Subcommittee believes that there is sufficient data to conclude that the developing organism is vulnerable during the entire period of development and that i*n utero* as well as early postnatal exposure to methylmercury is of concern. Also, very little is known about long-term chronic exposure in adults, because of the issue of possible heightened sensitivity to mercury in older people, and whether long-term exposure causes some different neurological responses.

d) With respect to the modeling linkage between emissions from anthropogenic sources and human exposures**, the Subcommittee agrees that it is plausible that current anthropogenic emissions are contributing to human exposures. However, the relative contributions of current anthropogenic emission sources, global backgrounds, recycling of old emissions and natural background to human exposures of methylmercury are highly uncertain and difficult to determine.** Furthermore, the time constants for intermedia transport are not known. **Since mercury does not degrade in the global environment, current anthropogenic emissions will add to the fraction of global mercury that is actively circulating in the biosphere, surface water, and soils. In addition, emissions from both the U.S. and from other countries can impact the U.S. environment and exposures of humans and wildlife.** However, this section of Volume III of EPA's draft report is not clearly written and confuses environmental transport and fate modeling with exposure analysis.

e) **The Subcommittee concurs with the conclusion that fish are the major source of methylmercury exposures for the human population.** The exposure analysis based on fish consumption must be regarded as a "snapshot" in time. The species of fish that are being consumed and their sources are both changing rapidly due to over fishing of some species, changes in the global market in marine fish and more domestic fish supplied by fish farms. The impact of local anthropogenic sources of mercury is likely to be greatest on freshwater and estuarine fish. There are, however, two potential biases affecting the exposure analysis based on fish consumption which should be checked in order to provide greater confidence in the analysis. First, the consumption data from the

Department of Agriculture's Continuing Surveys of Individual Food Consumption (CSFII) should be checked against production data. These will not agree exactly but should be reasonably consistent. Second, the average concentrations of methylmercury in fish used for the exposure assessment were provided by the National Marine Fisheries Service. The Subcommittee recommends that EPA determine how measurements of methylmercury in fish which were below the analytical limits of detection (BDL) were statistically treated in arriving at the mean concentrations. If the BDL values were excluded, then the means are biased high. If BDL values were included in the estimation of the mean using one of the standard methods for this, then the means can be considered good estimators. However, if a very large percentage of the measurements for any fish species were BDL, then the estimates of the means are much less reliable.

f) The Subcommittee strongly recommends that EPA edit and shorten Volume III on Exposure to eliminate redundancies and clarify the logical sequence of the exposure analysis. In particular, the definitions of dose and exposure presented in this volume should be used correctly and consistently throughout the Volume, and transport and fate modeling be clearly distinguished from exposure analysis. In general, the earlier EPA Dioxin Risk Assessment provides a good model for the organization and analysis of information on mercury for the entire draft report.

g) The Subcommittee notes that in the process of assessing control costs, the draft mercury report devotes most of the cost analysis to end-of-pipe controls and gives little attention to other types of controls. The Subcommittee recommends that the cost analysis also give consideration to other approaches for controlling mercury emissions that might prove to be more flexible and more cost-effective. For example, new FDA regulations (FDA 21 CFR Parts 123 and 1240-12/18/95) could have an impact on exposures of the U.S. population to methylmercury. Some analysis of their potential impact would be useful to EPA in evaluating possible approaches for control.

h) The Subcommittee generally agreed that the mercury wildlife criterion as currently presented) is overly conservative and is lower than appears necessary to protect wildlife species. **The criterion was derived from a bioaccumulation factor (BAF) based on total Hg rather than methylmercury (MeHg), which is the mercury species that bioaccumulates**. As a result, the magnitude of the error in the BAF is associated with, and reflects, the wide variability in MeHg concentrations among ecosystems. Further, statements in the report (page ES-5) infer

risk to various species without presenting risk calculations, a serious shortcoming.

The Subcommittee suggests that EPA, using the best techniques available in 1997, calculate BAF and wildlife risk criteria based on dissolved
MeHg in water, and that BAF calculations be specific to ecosystem or water body type.

The problems noted above notwithstanding, the Subcommittee believes that piscivorous wildlife are at risk from elevated mercury exposures and exhibit toxic effects in the areas of concern identified by the U.S. EPA. In addition, there is good evidence showing effects of mercury on wildlife; a summary of the population that appear to be affected; and a statement that wildlife exposure can be a harbinger of hard-to-detect human effects should be added to the final report

l) **The Subcommittee finds that Volume V, in total, is not based on the best available and sound science. To a large degree this chapter follows EPA guidelines for ecological risk assessment. However, it deviated in terms of quantifying the risk. This is a critical component of risk assessment.**

j) The final document should emphasize the fact that there are significant information gaps in the understanding of the biogeochemistry of mercury species and that the absence of this information limits the reliability with which any mercury control program can be evaluated.

k) **The modeling of atmospheric mercury transport and deposition is largely sound, but the modeling of the post-deposition fate of mercury in ecosystems is oversimplified, neglects available information on speciation, and does not reflect recent advances in the science. This deficiency is one of the most serious problems in the draft report. This modeling should be revised, with the goal of having the report reflect current scientific understanding**. Also, the modeling, as used, contributed to sizeable errors in the estimated wildlife criterion. It is important to bring out the importance of MeHg production in ecosystems in the report. Because MeHg is the species that bioaccumulates in human and wildlife food supplies, understanding the methylation process is critical to modeling Hg fate and exposure. Mercury methylation and the variability in MeHg among ecosystems were neglected in the report, because of the perceived difficulties in modeling methylation. The report assumes that MeHg constitutes the same fraction

of total Hg in sediments, soils and waters across ecosystems. This is not the case. Rather, the variability in MeHg production and bioaccumulation among ecosystem types is many orders of magnitude, and may be as large as the influence of Hg contamination. Without consideration of this variability, the report's fate and transport models, and the resultant exposure models and wildlife criteria models cannot predict Wildlife Criteria with less than two to three orders of magnitude associated error.

In addition, the proposed use of nitric acid as a surrogate for the wet deposition of mercury may not be justified, given the differences in the chemical and physical properties of the two species.

The final EPA report should detail the state of our understanding of Hg methylation process within Volume III; address MeHg production along with fate and transport models in Volume III (which models should be specific for a suite of ecosystem types); and the resultant information be used to model and discuss wildlife exposure in Volume V. **Because the models for estimating the distributions of human exposure were based on measured values for Hg in fish and other food, rather than modeled values, these suggested changes will not affect the human exposure analysis in the report.**

2. BACKGROUND AND CHARGE

2.1 Background

The 1990 Clean Air Act (CAA) Amendments (section 112(n)(1)(B)) directed the EPA to perform a study on the impacts of mercury as an air pollutant and provide a report to the Congress. The subject section required EPA to address several specific topics, including mercury emissions from electric utility steam generating units, municipal waste combustion units, and "area" sources; the rate and mass of these emissions; the associated health and environmental effects; technologies for controlling these emissions; and the costs of such control technologies.

In response, the EPA developed a seven volume (draft) report which:

a) provides data on types, sources, and trends in mercury emissions

b) evaluates the atmospheric transport of mercury

c) assesses the impacts of mercury emissions on organisms/ecosystems close to the emitting source

d) identifies major exposure pathways to humans and non-human biota

e) identifies mercury exposure levels likely to produce adverse effects in humans, and the nature of those effects.

g) evaluates mercury exposure effects for ecosystems and non-human organisms

h) identifies populations especially at risk from mercury exposure due to special sensitivity or high exposure

I) estimates effectiveness of control technologies and their costs

As noted above, the EPA report is still in draft. The Agency initially stopped short of issuing a formal final mercury report to Congress because of a growing consensus that such an analysis should wait for a full assessment of several relevant studies now underway. These studies address the effects of methylmercury on neurological development of children in fish-consuming populations in the Seychelles and Faeroe Islands, and were expected to be completed and published in the next year or two. Their results should be considered before making a new assessment of health risks. In terms of current data, however, the Agency decided to proceed with finalizing

the existing report by having the Science Advisory Board (SAB) review it (as is customary with major scientific documents) before transmitting it to the Congress.

Following a request from the Office of Air Programs and the Office of Research and Development, the SAB created a special Subcommittee (the Mercury Review Subcommittee (MRS)) of its Executive Committee. Composed of 34 experts on mercury from the United States and Canada, the MRS convened in public meeting on February 26/27, 1997 in Washington, DC. The Subcommittee was organized into three Workgroups, and addressed a Charge of 43 enumerated questions (see section 2.2) developed via discussions between EPA and SAB staff. This report, developed via mail in the several months following the public meeting, reflects the discussions at that meeting.

2.2 Detailed Charge

The detailed Charge follows. Specific questions are set in boldface type to differentiate them from background/expository material.

GENERAL

1. The EPA has decided to defer evaluation of the dose-response relationship between methylmercury and fetal and developmental effects until additional scientific data have been evaluated. These issues will be addressed in Phase Two of the SAB review. **Putting these matters aside, are the overall assessment and conclusions based on sound and appropriate evaluation of the relevant science?**

SOURCES

2. In order to approximate future mercury emissions, the sources are simplified to model plants placed to approximate current U.S. emission patterns. **Is this approach consistent with the best available scientific practice? Are the implications of this simplifying assumption adequately presented?**

3. U.S. EPA limited the scope of its assessment to anthropogenic sources of mercury emissions. **Are these reasonable and defensible assumptions?** The emissions inventory estimates these emissions in the United States. There is a short discussion of natural emissions and re-emitted emissions as well. The discussion of these emissions was based on language suggested by the scientific peer review panel. The modeling of local point sources did not include natural emissions, while the long-range transport modeling did incorporate a background level of mercury (to account for natural and re-emitted Hg) which has been measured over the open ocean. **Are the reasons**

for this approach adequately stated? Are the uncertainties and implications of this approach consistently and appropriately described?

4. For the atmospheric fate and transport modeling conducted using both the Regional Lagrangian Model of Air Pollution (RELMAP) and the Complex Terrain and Deposition Air Dispersion Model (COMDEP), best estimates from the peer-reviewed literature of the species of mercury emitted from each source were utilized. **Were these speciation profiles appropriate?**

5. **Can the Committee comment on the evidence concerning the role of human activity, and if possible, the role of U.S. sources to methylmercury in ocean seafood?**

ENVIRONMENTAL FATE/TRANSPORT

6. U.S. EPA relied on modeling to describe mercury fate and transport. In the report, the inventory served as the building block and was linked to the models (which were themselves linked). Both local and regional impacts were assessed together (additive) and separately for both humans and wildlife. Model plants were used as surrogates for actual facilities as well as hypothetical locations and populations. **Would a case study approach using actual facilities be more appropriate? Are the rationales for the selected approach appropriately presented? Please comment on the usefulness of measured data for estimating mercury exposures.**

7. In its assessment, U.S. EPA assumed that available data on the deposition of nitric acid could be used to approximate the likely wet deposition of divalent mercury. **Is the rationale for this assumption adequate (see Volume 3, Section Chapter 6, Section 6.1.3, and Volume 3, Appendix D, Section D.1.3.2)?** Classical Gaussian and Lagrangian puff models were adapted to reflect mercury chemistry. **Were these modifications appropriate?**

8. Further, the assessment neglects the potential conversion of elemental mercury to divalent forms in cloud droplets in both the local scale and the regional analysis. The Agency has assumed that any such conversions would happen on such a small scale that they could have only a very nominal impact on the ultimate exposure characterization. **Is this rationale fully explained and adequate? Are the uncertainties of this assessment explained?**

9. The Agency recognizes that mercury fate and transport is an immature field; capabilities to describe phenomena such as the temporal distribution of mercury concentrations in soil continue to evolve. In its assessment, U.S. EPA attempted to modify existing approaches (the 1990 Methodology of Assessing Health Risks

associated with Indirect Exposure to Combustor Emissions and the 1993 Addendum) to reflect the more recent science. **Were the assumptions regarding equilibrium among mercury species present in soil appropriate?**

10. **Was the selection of the model input parameters (such as the soil-to-water partition coefficients) appropriately justified and the uncertainties explained? Is the estimation of the watershed and water body fluxes adequate and appropriate? Should fluxes in large lakes, rivers and other large water bodies also have been estimated? Is the rationale for not doing so adequate? Does the Agency appropriately justify and explain the uncertainty surrounding assumptions about plant uptake of mercury directly from the atmosphere? Is the likely contribution of mercury from plants to soil contributions sufficient that such sources should be added to future modeling efforts?**

11. A number of qualitative conclusions are drawn from the results of the atmospheric modeling; given the uncertainty in the modeling and in the state of the science, evaluate the scientific quality of these conclusions. **Were the uncertainties adequately described?**

12. A key variable in estimating ultimate potential human exposure is the bioaccumulation factor (BAF) for methylmercury through the aquatic chain. **Was the BAF developed by the Agency appropriate and its utilization in the models scientifically sound? Was the uncertainty analysis adequate?**

13. **Were the models and modeling conducted for the terrestrial food chain adequate and appropriate?**

EXPOSURE

14. The exposure assessment is contained in Volume III. **Please comment on the scientific basis of this assessment, alternative approaches, and research priorities. In particular, please advise the Agency on how Appendix H should be used, improved, or expanded.**

15. Because of uncertainties inherent in the emissions inventory and the model, the exposure assessment was characterized as being a "qualitative assessment based on quantitative modeling." **Is this a reasonable characterization? Were the uncertainties of and conclusions drawn from linking the models together appropriately described?**

16. U.S. EPA has estimated methylmercury and fish consumption using both cross-sectional and longitudinal data for the general U.S. population. In these studies, EPA

consistently finds that a portion (albeit a small one) of the population consumes very large quantities of fish. It is these individuals who face the largest risks from methylmercury exposure and who pose the greatest concern to the Agency. **Has EPA adequately assessed the number and types of individuals who consume fish in these relatively large quantities?** The group at issue includes 5% of the fish-consuming population. **Are the uncertainties associated with characterization of such small portions at the extreme end of the population distribution appropriately considered and presented? Could the estimate of 5% of the fish-consuming population be a methodologic artifact?**

17. U.S. EPA has relied on three nationally-based sources of data for mercury concentrations in marine and fresh-water fish and shellfish. Some of these data were obtained within the past three years, whereas other data were obtained as long ago as 20 years. **Is the use of these older data appropriate? Does the document appropriately note the limitations of this methodology?**

18. The USDA has published data indicating that fish and shellfish consumption have risen approximately 25% since the early 1970s . These consumption data were employed without adjustment in this report to estimate current fish consumption (Volume III, Appendix H; and Volume VI, Section 4.2.3.1). **Should these data be adjusted to reflect the overall trends in fish consumption? If so, how would the estimates of very high consumption (above the 90th percentile) be adjusted?**

19. In Volume III, Appendix H, calculations of methylmercury intake from crab were grouped without specific consideration of the particular species. These data are then linked to dietary survey data which typically do not list the individual species of many fish and shellfish consumed. **How might this approach bias the final assessment? Are the limitations of this approach adequately characterized in the report? Are these limitations going to materially alter the assessment of health risk associated with methylmercury exposures?**

20. In early versions of the draft report (and in Volume III, Appendix H), U.S. EPA characterized total risk by considering methylmercury exposure from marine fish and shellfish together with consumption of methylmercury from fresh-water or estuarine fish and shellfish. It has been recommended that the report focus exclusively on fish from inland sources. **Does the current version adequately characterize total risk? Are the uncertainties resulting from this methodology appropriately presented?**

21. Some data exist on hair mercury concentrations in U.S. residents. **Is this data base adequate to predict the distribution of hair mercury in the general U.S. population?**

22. The draft report identifies hair mercury concentration as the most appropriate

available index of methylmercury exposure. **Is this assumption consistent with the available data? Are the exposure estimate approaches used relevant and appropriate? Are the predicted exposure ranges consistent with other published exposure analyses? Are the uncertainties of this assumption appropriately presented?**

23. Although the modeling exposure assessment focused on anthropogenic emissions, the fish consumption analysis considered measured mercury concentrations in fish tissue regardless of the mercury's origin. Thus, there is considerable difficulty in assessing or describing how much of the mercury in fish is attributable to current anthropogenic emissions. **Is the approach taken by the Agency in this assessment appropriate given the available data? What is the advice of the SAB regarding the differentiation between current emissions and their impacts relative to the "body burden" approach of the fish consumption analysis?**

DOSES/BODY BURDENS

24. In its assessment, U.S. EPA assumes that the biokinetics of methylmercury from contaminated grain approximate those resulting from methylmercury from fish. **Is this assumption consistent with the available science?**

25. **Are the uncertainties in the fish and grain consumption analyses adequately and consistently presented in the draft report?**

26. Similarly, U.S. EPA assumes the biokinetic parameters for children are identical to those of adults. **Does such an assumption introduce bias into the assessment? Are the uncertainties adequately and consistently presented in the draft report? Is the conclusion that children's lower body weight results in higher exposure than to adults? Could this be an artifact of exposure modeling using 3-day consumption survey data?**

27. **What methodologies other than hair concentrations could be used to estimate body burdens of mercury?**

HEALTH ENDPOINTS and SUSCEPTIBLE SUBPOPULATIONS

28. Volume 4, Section 6.3, and Volume 6, Chapter 2, Sections 2.1 and 2.2.21 present U.S. EPA's interpretation of the data demonstrating increasing severity and frequency of nervous system effects (particularly impairment in visual-motor integration) among pediatric subjects with increasing levels of maternal hair mercury. These sections present U.S. EPA's interpretation of the data demonstrating increasing severity and frequency of nervous system effects (particularly impairment in visual-motor

integration) among pediatric subjects with increasing levels of maternal hair mercury. **Recognizing that additional data may shortly be available, is EPA's assessment methodology based on the best scientific practice? Are the uncertainties in the characterization of potential effects accurately described in the draft text?**

29. Data from experimental animals (including primates with long-term exposures to methylmercury) show methylmercury-induced nervous system damage, particularly on the visual system, although the animals appear clinically normal. The traditional RfD methodology neglects such impairment. **Are these data important endpoints? Are they appropriately characterized in the draft report? How could such data be better evaluated by the Agency?**

30. The available data present information on fish consumption drawn over relatively short time periods (e.g., days) and are used to extrapolate consumption patterns over longer periods (e.g.. a month). Although the exact developmental window affected by methylmercury in humans is not precisely defined, it is thought to be less than three months. **Is such extrapolation appropriate in this case? Does the document appropriately present the limitations of this methodology**?

31. Volume 4, Section 6.3, and Volume 6, Chapter 2, Sections 2.1 and 2.2.21 present U.S. EPA's interpretation of the data demonstrating increasing severity and frequency of nervous system effects (particularly impairment in visual-motor integration) among pediatric subjects with increasing levels of maternal hair mercury. **What biases are introduced into the assessment by focusing on subtle endpoints of neurobehavioral function in contrast with traditional metrics of child development? Should these indicators be dismissed if traditional metrics (such as age of first walking) are within normal ranges? Do the available data indicate whether children are more sensitive than adults to the effects of methylmercury?**

32. **Are the uncertainties in the characterization of potential effects accurately described in the draft text?**

33. Traditional methods for estimating potential human health risks from environmental hazards do not distinguish risks among subpopulations (e.g. racial or ethnic) groups. **If methylmercury exposures are comparable and some groups, but not all, show impairment in traditional and/or specialized neurophysiological/neurobehavioral tests, how should U.S. EPA reflect these differences in its analyses? Do factors such as nutritional status, life-styles (e.g., substance abuse), or economic status play a role is mediating these differences?**

34. Similarly, many assessments of methylmercury risk clump risk to fetuses and children together with risk to adults. **Is this approach scientifically valid for**

methylmercury? Methods for estimating potential human health risks from environmental hazards do not distinguish risks among subpopulations (e.g. racial or ethnic) groups. **If methylmercury exposures are comparable and some groups, but not all, show impairment in traditional and/or specialized neurophysiological/neurobehavioral tests, how should U.S. EPA reflect these differences in its analyses?**

35a. **What wildlife effects (based on what metric) can be interpreted as harbingers of likely human health effects?**

35b. **Could the Committee provide any short-term advice on human health issues not addressed in the coming epidemiologic studies such as toxicokinetics?**

ISSUES ON WILDLIFE ASSESSMENT

35c. Chapter VI presents the Agency's current mercury risk characterization. **Please advise the Agency on the appropriateness and environmental significance of the characterization of wildlife effects.**

36. Volume V describes fairly significant wildlife effects which are attributed to elevated mercury concentrations in some ecosystems. **Is this evaluation based on the best available and sound science, and are they consistent with EPA eco risk guidelines? How could this evaluation be improved?**

37. This report makes the inference that mercury emissions are related to reproductive effects and neurobehavioral changes in fish consuming birds and mammals. These effects have been documented in the Great Lakes and in the Southeastern United States. EPA's models predict that regional hot spots (relatively high concentrations of methylmercury) would occur in these same areas. **Is the analysis of the evidence linking emissions and effects scientifically sound?**

38. **Have any "hot spots" not shown evidence of wildlife effects? Do these predicted "hot spots" correlate with methylmercury levels in fishery products?**

39. **Which mercury-related effects in wildlife should be identified as warning signs that analogous effects may occur in humans? Could "wildlife epidemiology" be used as a surrogate for controlled lab studies?**

RESEARCH NEEDS

40. **Based on the research needs identified in the draft report, areas identified through discussion of the report, or on other information, has EPA identified the**

highest priority areas for research? If not, could the Committee suggest what areas need to be addressed?

QUESTIONS RELATED TO SOCIAL COST

41. Chapter VII previously contained a section on the “Social Costs” of mercury contamination (this section is attached to comments by the Council of Economic Advisors in the supplementary information). This section described the value of the fisheries in the U.S. as well as other values such as maintaining a healthy ecosystem. The intent was to balance the discussion of mercury control costs. Some reviewers objected to the inclusion of the Social Costs section partly because the impact of anthropogenic sources could not be directly and quantitatively related to these impacts (e.g., the declining Florida panther population). The section was consequently deleted. Is such a discussion appropriate for this study? How would the SAB advise the EPA to describe benefits of mercury reductions if a) the impacts of such reductions are not directly quantifiable, and b) the monetary value of such benefits are not easily quantified?

3. SOURCES

3.1 Source Simplification in Modeling Mercury Emission Patterns

In order to approximate future mercury emissions, the sources of mercury were simplified to model plants located to approximate current U.S. emission patterns. Question 2 of the Charge asked the Subcommittee to assess this approach for consistency with the best available scientific practice, and to consider the possible implications of this simplifying assumption.

The issue of the use of “source simplification” is best addressed by considering the current (existing) sources and the potential for new sources. According to EPA’s Table ES-3 (Volume I), current principal sources include fossil fuel combustors, incinerators, utility boilers, commercial/industrial boilers, and industrial sources. Will the regional distribution of incinerators in the country change significantly in the near future? Probably not. Will there be significant changes in the number and locations of utility and commercial/industrial boilers in the near future? Not very likely.

With the reduction of mercury use in existing commercial products, it seems unlikely that many major new uses will be discovered that will drastically change the emission scenario in the near future; **consequently the Subcommittee does not note any particular problems arising from the simplification approach, nor its presentation in the draft report.**

3.2 Modeling Sources of Mercury Emissions

The EPA limited the scope of its assessment to anthropogenic sources of mercury emissions. The modeling of local point sources did not include natural emissions, while the long-range transport modeling did incorporate a background level of mercury (to account for natural and re-emitted Hg) which has been measured over the open ocean. Charge question 3 asked for the Subcommittee’s findings on the major assumptions made, the statement of the supporting rationales, and the implications of using such an approach.

The role of natural sources of Hg and re-emission of "old" anthropogenic sources of Hg is recognized as being important on a global scale (Expert Panel, 1994). The EPA draft report acknowledges this, but with a lack of regional data and models to treat these sources specifically, was unable to include them in the overall analysis. Many caveats to this effect are stated, but the impacts of ignoring such sources on model results and interpretation are not clearly defined. In particular, it must be acknowledged that such sources cannot be readily controlled (if at all), and that the results of reducing U.S. anthropogenic emissions will be less than expected (with

respect to resulting exposure levels) because of these other sources. In other words, there will not be a 1:1 relationship between decreases in U.S. industrial emissions and changes in receptor exposure, with the possible exception of a site very close to a strong point source of reactive gaseous mercury. The Expert Panel (1994) estimated that 95% of the 200,000 Mg of Hg emitted since 1890 remains in surface soils and lake and oceanic sediments, so it only requires a re-emission of a fraction of a percent each year for this source to rival U.S. industrial emissions (see Lindberg *et al.*, accepted; Carpi and Lindberg, accepted A; and Kim *et al.*, 1995).

3.3 Speciation Profiles in Atmospheric Fate and Transport Modeling

Charge question 4 addressed the atmospheric fate and transport modeling conducted using both the Regional Lagrangian Model of Air Pollution (RELMAP) and the Complex Terrain and Deposition Air Dispersion Model (COMDEP), with specific attention to the speciation profiles used.

For its atmospheric fate and transport modeling, EPA used the speciation profiles based on European data from Peterson *et al.* (1995) for its baseline scenario. The Electric Power Research Institute and the U.S. Department of Energy have been working to improve methods for measuring the speciation of mercury emissions from coal-fired utilities. Data from these new studies have not yet appeared in the peer-reviewed literature and EPA cannot be faulted for not having included these findings in its draft. To our knowledge, there are no U.S. data on the species of mercury emitted from municipal or hospital waste combustors. The EPA also used an alternate speciation profile, which had a high percentage of mercury in the particulate form. Although it is useful to explore the sensitivity of the model to changes in the speciation profiles, the plausibility of this alternate speciation profile should be clarified. **Consequently, the speciation profiles used by EPA in its baseline scenario were not inappropriate, given the information available at the time. However, EPA should evaluate new speciation data as it becomes available, and revise its speciation profiles if necessary.**

Speciation is critical to the modeling of mercury fate and transport. It controls the predictions of the amount and location of deposition. It also controls the total loading at a given location, and affects the predictions of the eventual loading of methylmercury in ecosystems. Thus improvements in the understanding of mercury speciation are of the highest importance for improving the entire mercury risk assessment.

3.4 Anthropogenic Sources and Methylmercury in Ocean Seafood

In Charge question 5, EPA asked for an assessment of the evidence concerning the global relationship of human activity to methylmercury levels in ocean seafood, and if possible, the contribution of U.S. sources to methylmercury levels.

The upper layer of the ocean is estimated to have roughly a factor of 3 times the mercury content of pre-industrial times (Mason *et. al,* 1994). Total anthropogenic mercury emissions are estimated to be about twice global natural emissions. **Both of these estimates suggest that the anthropogenic contribution to ocean seafood may be substantial. However, because there is currently no detailed understanding of the quantitative relationship between the amount of methylmercury in ocean seafood and anthropogenic mercury emissions, we cannot quantify the anthropogenic contribution to methylmercury in ocean seafood.**

Seafood from coastal areas may be a special case. Seafood from U.S. coastal areas can be expected to be exposed to anthropogenic mercury from U.S. sources in much the same way as freshwater fish. Although U.S. emissions of mercury represent only about 5% of global anthropogenic emissions as of 1995, the impact of U.S. sources on U.S. coastal seafood can be expected to be larger than this ratio, due to the influence of local sources. However, the EPA's draft report did not attempt to model this pathway. Such an assessment should be considered in the EPA's revised report.

3.5 Modeling Mercury Fate and Transport

U.S. EPA relied on modeling to describe mercury fate and transport. In the Draft Report, the known Hg inventory served as the building block and was linked to the prediction models (which were themselves linked). Both local and regional impacts were assessed together (additive) and separately for both humans and wildlife. Modeled industrial plants were used as surrogates for actual facilities as well as hypothetical locations and populations. In Charge question 6, the Agency asked for guidance on the issue of using a case study approach using actual facilities rather than modeling; the Subcommittee's appraisal of the rationales for the selected modeling approach; and comments on the usefulness of measured data for estimating mercury exposures.

Clearly, a case study approach would not have been more appropriate than the modeling approach chosen by EPA. To the Subcommittee's knowledge, there are no case studies linking air emissions from a single specific point source to exposure in a specific water body. The Aquatic Cycling of Mercury in the Everglades (ACME) study, sponsored by a broad consortium of federal, state, and corporate entities, together with several other studies monitoring atmospheric deposition patterns in South

Florida, may be able to link the suite of South Florida sources to bioaccumulation and effects in the Everglades, but the study is not yet complete.

Case studies limited to relating emissions to deposition around individual facilities may have been useful in the report (Carpi *et al.*, accepted B; Stratton and Lindberg, 1995). However, we do not know if adequate case studies linking emissions, deposition, and exposure exist.

Considering the limitations in knowledge of the Hg cycle and Hg exposure modeling, the Subcommittee believes that it is important to use what limited measured data are available for estimating Hg exposures to both people and wildlife.

Although the Subcommittee agrees with EPA that it is necessary to rely on modeling to describe mercury fate and transport, the rationales for the selected modeling approach were not appropriately presented. The Subcommittee divided its consideration of the fate and transport modeling into two parts: air transport and deposition, and fate and transport after deposition and bioaccumulation within ecosystems.

The draft report's rationale and presentation of air transport and deposition modeling was reasonable overall, although it has some shortcomings. These issues are discussed in sections 3.7 and 3.8 of this report. However, the Subcommittee was disappointed with the models downstream from the deposition models, particularly the fate and transport in ecosystems and the bioaccumulation models. The consensus of the Subcommittee was that the rationale for the selection of these post-deposition models was poorly justified and inappropriate. **The Subcommittee felt that these weaknesses were the most serious in the report overall**. **Specifically, EPA's decision to model %MeHg (methylmercury) as constant across ecosystems, and to model fish bioaccumulation factors (BAF) based on total Hg (rather than MeHg) were most problematic.**

It is not possible at this time to produce highly quantitative models for MeHg production among ecosystems, starting with emissions or deposition. However, "quantitative modeling yielding qualitative responses" (an approach used in Vol. III and V to provide rough ideas of how deposition responds to source strength) *is* possible for modeling MeHg production and exposure in aquatic systems. The Indirect Exposure Methodology (IEM2) model discussed in Vol. III, which is mainly a watershed transport model, provides estimates for the total Hg concentration in water that is protective of wildlife (the Wildlife Criteria, or "WC") of about 0.5 ng Hg/L. This value is well below that of most natural inland waters at this time. The WC provided by the model has an extremely large associated error - 3 orders of magnitude between the 5 and 95% confidence intervals. The state of the science in 1997 provides an opportunity for EPA to make WC evaluations more ecosystem specific by explicitly including ecosystem

type and variability in the analysis (St. Louis *et al.*, 1996; Watras *et al*., 1995; Driscoll *et al*., 1994; Hurley *et al.,* 1995). By assessing %MeHg in surface water by ecosystem type, the EPA model could better capture variability among ecosystems. In addition, basing BAF on MeHg in water rather than on total Hg, and normalizing BAF by fish species, can also improve the credibility of the WC models. Even though many uncertainties in the transport and fate analysis will remain, these changes will improve the ability of the models to appropriately account for variations in WC. **By making use of existing models external to EPA, or by applying literature values of %MeHg among ecosystems to the existing EPA model, the report could be revised adequately, and fairly quickly.**

3.6 Nitric Acid as a Surrogate for Wet Deposition of Divalent Mercury

The Agency modified existing models to describe mercury atmospheric fate and transport, and, in the case of wet deposition of divalent mercury, used data on the deposition of nitric acid as a surrogate for mercury. In addition, classical Gaussian and Lagrangian puff models were adapted to reflect mercury chemistry as part of the overall modeling approach. In Charge 7, the Subcommittee was asked to comment on the adequacy of the modifications, as well as on the use of nitric acid as a surrogate for mercury.

In brief, the Subcommittee noted that:

a) Modifications made to RELMAP to model mercury transport, transformation, and deposition appear to be appropriate, but several areas (identified below) should be clarified in the report.

b) Modifications made to COMPDEP are not completely satisfactory. The dry deposition velocities for $Hg^{(II)(g)}$ should be amended to include the full specification found in Table D-17 of the draft report. Furthermore, a similar table should be developed and implemented for $Hg^{(0)}$. The scavenging coefficients for wet removal should be reformulated specifically to simulate below-cloud processes.

c) Application of COMPDEP to the model plants must be revisited, in view of the recommended changes to COMPDEP. In particular, the present study produces dry $Hg^{(II)(g)}$ fluxes that are most appropriate for land-use categories of water and barren land (see Table D-17). Dry deposition velocities to mixed forest/wetland areas can be 3 to 4 times larger! Variation in land use between the source and “critical receptors” in the simulations should also be considered. For example, depletion of the plume during transport due to dry deposition to forests (say at a velocity of 3 cm/s) will reduce the

near-surface Hg concentration available to dry-deposit to the surface of a distant watershed (at a velocity of 1 cm/s).

d) Although other studies have made this assumption, the use of nitric acid as a surrogate for the wet deposition of mercury may not be justified, given the chemical and physical properties of the two species.

The only justification given for EPA's assumption that available data on the deposition of nitric acid could be used to approximate the likely wet deposition of divalent mercury is that the water solubility of these two species is presumed to be "comparably high," in the words of Petersen *et al*. (1995), the paper which forms the basis for much of the deposition formulation used in the draft report. This high solubility implies that both vapors will rapidly dry-deposit to surfaces which they contact. Furthermore, for wet deposition, high solubility is expected to increase the washout efficiency. However, the presumption ignores the influence of associated anions on mercury solubility. Does it matter whether mercuric sulfate, oxide, hydroxide, or chloride nitrate is present in the aqueous medium? Most likely. The possible effects of complex formation on Hg solubility are also ignored. Differences between the ionic Hg(II) and molecular properties (NO_2) would also argue against the assumption: (a) HNO_3 is a bigger molecule than Hg(II); (b) the washout coefficient for the two species differ; c) the mass median diameter for the two species differ; and (d) the densities of the two species are different. **Consequently, although other studies have made this assumption, it may not be justified on the basis of the chemical and physical properties of the two species.**

Given the importance of the substantial estimates of wet and dry deposition fluxes of divalent mercury, the report should state the uncertainties involved with using the properties of nitric acid as a surrogate for divalent mercury, it should cite other studies which make this assumption when estimating fluxes of divalent mercury, and it should provide a discussion of the mechanisms by which high solubility enhances removal processes.

The report makes reference to the use of nitric acid as a surrogate for the deposition of divalent mercury vapor in discussing the Local Impact analysis (Chapter 6 of Volume III), and in the modeling details presented in Appendix D, but not when discussing the results of the Long Range Impact analysis (Chapter 5). Because the base-case versus alternate speciation simulations illustrate the sensitivity of deposition rates to speciation assumptions involving the presence of divalent mercury vapor, the basis for the deposition estimates should also be stated here (e.g. page 5-19).

EPA adapted classical Gaussian and Lagrangian puff models to reflect mercury chemistry in estimating deposition. As detailed below, the Subcommittee noted some problems in EPA's application of these models, particularly with respect to the use of

certain adjustment factors for local dry deposition. In the RELMAP model, injection of emissions into layer 1 (for "area sources") or layer 2 (for point sources) appears appropriate, but is only effective at night because during the day, RELMAP mixes all advected species throughout its 4 layers. At the same time, a local dry deposition factor is applied to particulate mercury emissions released into layer 1. The draft report states that **half** of the emissions into layer 1 are assumed to be dry-deposited within the local cell (nominally 40 km), based on a similar adjustment in Petersen *et al*. (1995) for their 1-layer puff model. This approach is designed to compensate for underestimating dry deposition fluxes for near-surface releases when near-surface concentrations are underestimated due to complete mixing in the vertical. At the public meeting, EPA staff stated that the final RELMAP simulations do not use this adjustment. **The report should be updated to remove the present discussion, and to replace it with the rationale for not including such an adjustment**. In particular, the discussion should address the effectiveness of the adjustment during the day compared to the treatment at night, and it should address uncertainties in selecting an appropriate removal factor, if it were used. Petersen *et al*. (1995) estimate this factor to be 0.5 for Hg(II)(g), and 0.025 for Hg(part). They obtain these estimates by assuming that the factor is proportional to the dry deposition velocity for each species, and use a deposition factor of 0.1 for SO_2 as a basis. With a dry deposition velocity of 0.8 cm/s for SO_2, and 0.2 cm/s for Hg(part), the factor is 0.025. The deposition velocity for Hg(part) used in RELMAP varies from 0.11 cm/s to 0.02 cm/s, so that deposition factors of 0.014 to 0.0025 would be estimated from this method. (Differences in the grid system will influence the value for this factor as well.)

Ozone reacts with elemental mercury, changing it to the divalent form (Hg^{++}), which is reactive with the environment, constituting a loss mechanism for atmospheric mercury. The question which must be posed is "How strong are spatial gradients in ozone aloft (as provided to RELMAP) during precipitation events, when RELMAP uses ozone in its wet scavenging algorithm for $Hg^{(0)}$?" That is, how important is ozone advection aloft on the aqueous phase chemical transformations?

Ozone concentrations aloft (layers 3 and 4) are specified for each cell, as computed from observed hourly surface measurements from the EPA's Aerometric Information Retrieval System (AIRS). The two midday 3-hour time steps use the corresponding 3-hr averaged concentration measurements. Recognizing that surface ozone measurements are not representative of ozone concentrations aloft at night, the average concentration over the period between 1000 and 1600 is persisted throughout the 18 hour period from 1600 to 1000 the next day. This procedure does not simulate ozone transport aloft. **The report should include a discussion/analysis of the assumptions concerning ozone gradients to the computed aqueous phase conversion of $Hg^{(0)}$ to $Hg^{(II)}$**.

Wind data used for advection in RELMAP are stated to be the wind field initialization data for the Nested Grid Model (NGM). The NGM uses a nominal 90 km grid. Results of NGM simulations were reportedly stored at 2-hr intervals for the 1989 year used in this study, but the Subcommittee understands that the NGM is initialized at 12-hour intervals. At the public meeting, EPA staff stated that 3-hour average wind data were used in the study. **The report should include a discussion that clarifies the source and characteristics of the meteorological data.**

Dry deposition velocities for soot were computed for a matrix of stability class/land use types using the California Air Resources Board (CARB) subroutine. This required an assignment of near-surface wind speed (nominally 10 cm/sec), and a roughness length. Wind speeds were assigned on the basis of the stability class, but the wind speeds associated with classes A and D (Table D-3) are substantially different from those typically used in the stability class typing procedure (see Table D-7). Speeds for class A are typically of order 2 m/s or less, not 10 m/s. And those for class D are typically greater the 6 m/s, not the 2.5 m/s reported in this study. Regarding the roughness length assigned to each land use category, several of the values in Table D-4 appear to be smaller than those typically used. Urban areas and forests are typically given a roughness length greater than 1.0 m, but a length of 0.5 is used here. Also, agricultural uses are given smaller roughness in the spring-summer than in the autumn-fall. Typically, the larger roughness is assigned for summer. The curves on which the CARB model is based do not include roughness lengths greater than 0.1 m, so deposition velocities obtained from this model may not fully characterize dry deposition to rougher surfaces. **The report should identify uncertainties associated with this use of the CARB subroutine**. Also, the rationale for the pollutant depletion rate of 5% per 3-hr time step chosen to represent the diffusive mass exchange out of the top of the model should be provided.

In the COMDEP, dry deposition velocities for $Hg^{(II)}(g)$ are said to be taken from the RELMAP implementation, and specified by stability class (COMPDEP was modified to allow such user-supplied deposition velocities as a function of stability class). However, a single value of 1.0 cm/s is used for classes A, B, and C, and a single value of 0.3 cm/s is used for classes D, E, and F, in spite of the presence of a full set of values given in Table D-17. The rationale for this scheme is not presented in detail, but the neutral/stable deposition velocity of 0.3 cm/s is said to represent nighttime periods when RELMAP uses 0.3 cm/s. Class D (neutral) occurs frequently both day and night, as it applies for the larger wind speed classes, so assigning all class D hours a “nighttime” deposition velocity will underestimate some daytime fluxes by as much as a factor of 3 to 9.**The values listed in Table D-17 should be used directly in the COMPDEP simulations, for the dominant land use prescribed for each site**. It would be preferable to adopt an existing gas phase dry deposition module, and place it into COMPDEP or other Gaussian plume model (GPM) for this study.

During the public meeting, one Member of the Subcommittee pointed out that dry deposition of Hg(0) is not zero, as assumed in the study. The Lindberg *et al*. (1992) report modeled dry deposition velocities (weekly averaged) to the deciduous forest at the Walker Branch Watershed that range from about 0.006 cm/s during the winter to about 0.1 cm/s during a few weeks in the summer. This increase is the result of leaf stomatal control of dry deposition during the growing season. Another effect of this control is the strong diurnal pattern in their computed deposition velocities, which vary from about 0.04 cm/s at night to 0.09 to 0.18 cm/s during the day for a simulated period in mid-June. **$Hg^{(0)}$ dry deposition should be included in the near-field modeling assessment**.

The precipitation scavenging treatment adopts the washout parameters of Petersen *et al.* (1995) for use in COMPDEP. However, the highly parameterized scavenging coefficient approach of this and similar models does not differentiate individual wet removal processes, such as in-cloud nucleation and aerosol growth, and below-cloud interception. Computed fluxes depend on vertically-integrated pollutant concentration, which increase rapidly as one approaches the source of a Gaussian plume. The efficiency of the scavenging process is assumed to be independent of the vertical scale of the plume. It is not apparent that the washout ratios used to estimate wet removal are appropriate for estimating the below-cloud removal of $Hg^{(II)(g)}$ and Hg(part) from highly localized plumes, in which case the algorithm will likely overestimate wet deposition fluxes in the near-field. **The scavenging coefficients should be modified to reflect below-cloud processes of importance near point sources**.

3.7 The Impact Of the Conversion of Elemental Mercury to Divalent Forms on Exposure Characterization

The mercury assessment neglects the potential conversion of elemental mercury to divalent forms in cloud droplets in both the local scale and the regional analysis; this decision was made because it was estimated that any such conversions would happen on a small scale and would have nominal impact on the ultimate exposure characterization. Charge 8 asks the Subcommittee to evaluate the rationale for this assumption, and to comment on the relevant uncertainties.

In estimating deposition, EPA states that it has chosen to neglect the potential conversion of elemental mercury to divalent forms in cloud droplets in both the local scale and the regional analysis. Many caveats re this approach are stated, but few uncertainties are shown (e.g., some modeled fluxes are given to 4 significant figures.).

The models used **do** include a form of $Hg^{\circ} \rightarrow Hg^{2+}$ conversion, but ignore the back reaction. This is acceptable for clouds with sufficient soot, and the model is probably reasonable for most of the U.S. The model ignores cloud aqueous chemistry

for non-precipitating clouds. However, the background levels of aerosol Hg are very low and not highly significant in Hg dry deposition. Use of background levels of aerosol Hg in the wet deposition model is appropriate.

In addition, dry deposition of Hg° is ignored in both near and far field models, and publications on dry deposition of Hg° were misinterpreted making the application of the alternate Vd in Table 6-39 invalid (Volume III p. 5-26). The model of annual mean air concentration is inadequate to estimate plant exposure and uptake because brief spikes control deposition. The compensation point is confused with no uptake, also as being a fixed value. The modeled internal plant Hg concentrations (Fig. 6-8) are low compared to measured data. There are 3 detailed field studies published on the dry deposition of Hg, (Sweden, Lake Champlain, Walker Branch) and all show dry greater than wet (Rea *et al.,* 1996, Iverfeldt *et al.*, 1996, Lindberg, 1996).

3.8 Assumptions Regarding Equilibrium among Mercury Species in Soil and Sediments

The Agency attempted to modify existing approaches to reflect the most recent science on estimating the temporal distribution of mercury concentrations in soil.. In Charge 9, the Subcommittee was asked to comment on the assumptions regarding equilibrium among mercury species present in soil.

The Subcommittee does not find the draft report's assumptions about the speciation of Hg in soils, and more importantly sediments of lakes and wetlands, to be appropriate. The major species are inorganic Hg^{II}, Hg^{0} and MeHg. Production of MeHg is the key step in bioaccumulation of Hg in food chains; production of Hg^{0} from $Hg^{(II)}$ is an important loss mechanism to soils and source term to the atmosphere. Rates of both reactions vary substantially among ecosystems, as functions of both ecosystem biogeochemistry and Hg loading (Watras *et al.*, 1994; Henry *et al.*, 1995; St. Louis *et al.*, 1996; Krabbenhoff *et al.*, 1992; Gilmour *et al.*, in press).

However, EPA chose to model MeHg as a constant percent of total mercury across all soil types and across all surface waters. The fraction of Hg as Hg^{0} was also set to a constant for all soils and natural waters. The report states clearly that this approach was chosen because of the complexity of the methylation processes, and the idea that MeHg production could not be adequately modeled. However, this simplistic approach is not appropriate, given the current level of understanding of this process. The predictive abilities of the IEM2 fate and transport, and the human and wildlife exposure models are weakened to the point where they have little predictive capability because the interecosystem variability in MeHg production is not considered.

The natural differences in MeHg production among ecosystems are at least as great as the differences due to Hg deposition. Considerable information is available in

the literature and should be reflected in the EPA's report (Benoit *et al.,* submitted; Watras *et al*., 1994; Driscoll *et al*., 1994; Hurley *et al.,* 1995). **The lack of use of available information on the Hg speciation in soils and waters is thus a major shortcoming of this report.** During the public review meeting, EPA stated that fate and transport and exposure modeling in the Hg report was done to provide information on Hg exposure that is "not available in the data." However, because the factors that affect Hg methylation and reduction were neglected in the models, the models actually provide much less information on MeHg production, bioaccumulation exposure than does the current literature.

A more sophisticated and up-to-date approach to modeling Hg methylation and reduction in soils and sediments should be taken, making use of the available information on the control of methylation and reduction processes. In fact, very significant progress has been made in understanding MeHg production in watersheds and water bodies in the last few years (much of it funded by EPA and the Electric Power Research Institute), and that information should be used by EPA in this report to provide improved estimates of Hg exposure and the potential to reduce that exposure through source regulation Gilmour *et al.*, 1992; Gilmour *et al*., in press; Driscoll *et al.*, 1994; Lee *et al*.,
1995). Nevertheless, many uncertainties will remain and will, for the most part, prevent accurate assessment of source-receptor relationships.

Certain types of aquatic ecosystems are sensitive to high levels of MeHg production and bioaccumulation including wetlands (e.g. St. Louis *et al.,* 1994, 1996; Hurley *et al.,* 1995; Krabbenhoft, *et al*. 1995; Lee *et al*., 1995; Branfireun *et al.,* 1996; Gilmour *et al*., in press; Heyes *et al.,* 1996); new reservoirs (Bodaly *et al*., 1984; Jackson, 1988; Kelly, *et al.* 1997) lakes impacted by acid deposition (Weiner, 1988; Weiner *et al.,* 1990; Gilmour *et al.,* 1992; Driscoll *et al*., 1994; Watras *et al*., 1995), lakes with high levels of disolved carbon (Watras *et al*., 1995) and lakes with anoxic hypolimnia (Henry *et al.,* 1995). Fish in smaller lakes may accumulate more Hg than fish in larger lakes of the same type (Bodaly *et al.,* 1993), possibly because warmer average sediment temperatures favor higher rates of MeHg production.

Among ecosystems not impacted by point sources of Hg, total Hg concentration is not a good predictor of MeHg in either water or sediment (Kelly *et al*., 1995). However, in lakes located near aquatic Hg point sources, MeHg concentrations in water and sediments, and Hg in fish, are generally elevated. Elevations in MeHg in water, sediment and fish are not proportional to the increase in total Hg concentration in these systems (Parks *et al.,* 1986, 1989; Henry, *et al.* 1995).

A number of recent studies have examined concentration patterns in estuaries (Coquery and Martin, 1995; Cosa and Noel, 1987). Estuaries and coastal waters appear less sensitive to MeHg production and bioaccumulation, probably due to sulfide

inhibition of MeHg production (Compeau and Bartha 1983, 1985; Craig and Moreton, 1983; Gilmour *et al*. 1992; Henry, 1992; Choi and Bartha, 1994; Benoit *et al* in press) .

The location of MeHg production within ecosystems has been fairly well defined. The interface between oxic and anoxic conditions (O/A boundary) in sediments (Gilmour *et al*., 1992; Gilmour *et al*. in press; Krabbenhoft *et al.* in press) or in the water column (Watras *et al.,* 1995) is a region of intense methylation activity because of the high availability of substrates (both organic matter and sulfate) for sulfate reduction in this zone. Within lakes, the O/A interface may move throughout the year as oxygen is depleted and replenished. Areas where S is rapidly reduced and reoxidized seem to be particularly important. For example, the top of the hypolimnion, where green and purple S bacteria supported reoxidation of sulfide, can be a very active area of methylation (Watras *et al.,* 1995). Littoral and epilimnetic sediments are often the favored site for methylation within lakes (Gilmour *et al*., 1992; Ramlal *et al*., 1993; Krabbenhoft *et al*. in
press) because of higher average temperatures and more available substrate than deeper sediments.

The first mass balance for Hg in was completed in the early 1990's using a hydrologically constrained seepage lake, Little Rock Lake (LRL), Wisconsin (Weiner *et al.,* 1990; Watras *et al*., 1994). The study included production of a sophisticated biogeochemical model (with minimal hydrology) parameterized from the experimental studies in the lake. The LRL study was also important in demonstrating the importance of acid deposition on Hg methylation and bioaccumulation, a factor that has not been considered in the EPA report . Work in LRL was later extended to other lakes and watersheds in the region - Pallette Lake (Hurley *et al*., 1994; Krabbenhoft et al. in press); Allequash Creek (Krabbenhoft *et al*., 1995); and interlake comparisons (Watras *et al*. b and c).

It is thus critically important to bring out the importance and inter-system variability of methylation in this report. Specifically, it is important to discuss and emphasize the methylation process, including intersystem variability in the report's executive summary; to detail the state of our understanding of methylation in Vol. III; to model (as well as possible) MeHg production and exposure among different ecosystems types using state-of-the-art transport and biogeochemical models in Vol. III; and to use the resultant information to model and discuss MeHg exposure to wildlife in Vol V.

3.9 Biogeochemical Issues in Modeling

EPA's Charge question 10 comprised a wide range of six separate questions on modeling the behavior of mercury in the environment and its uptake by plants. These questions addressed the selection of the model input parameters (such as the soil-to-

water partition coefficients); the estimation of the watershed and water body fluxes; estimation of fluxes in large lakes, rivers and other large water bodies also have been estimated; the treatment of the uncertainty surrounding assumptions about plant uptake

of mercury directly from the atmosphere; and the likely contribution of mercury from plants to soil.

The following discussion addresses the various specific questions in logical combinations.

The Subcommittee has significant reservations about the selection of model input parameters for the soil-to-water partition coefficients. Watershed type is extremely important in regulating metals transport to lakes. Land use/land cover characteristics can greatly affect fluxes and yields of Hg to a lake (St. Louis, *et al.*, 1994, 1996; Hurley *et al.*, 1995). The IEM-2 model presented is a high-quality watershed model, attempting to evaluate the effects of Hg deposition on partitioning and transport to a lake. The model is mainly soil-based and represents a watershed with untilled soils. While this approach can be used for upland soils, there is increasing awareness in the literature of the influence of wetlands on Hg cycling. In several regions of the U.S. and Canada where fish advisories exist for mercury, wetlands constitute a significant portion of the watershed. Recent evidence has clearly indicated that wetlands are zones of MeHg production(St. Louis, *et al.*, 1994, 1996; Hurley *et al.*, 1995; Kelly *et al.*, 1997). The modeling of watershed effects on Hg bioaccumulation, therefore, should evaluate contrasting watershed types. The model in the report only compares an eastern and western lake system that is dependent upon soil-water partitioning in the watershed. The IEM-2 fate and transport model used in the draft report is not designed to model transformations among Hg species (e.g., methylation and reduction). **As suggested above, a more rigorous comparison using simulations with different watershed characteristics, would be a better approach to assessing impacts of deposition on aquatic systems.**

The lack of published studies prior to 1994 with respect to soil-water partitioning led the authors to use a similar coefficient for $Hg^{(II)}$ and MeHg. The K_d used for soil-water is appropriate for the soil setting but is insensitive to any biogeochemical processes that may occur (for example, soil flooding or anoxia). Similarly, the sediment-water partition coefficient reflects similar values for $Hg^{(II)}$ and MeHg. A strength of the modeling effort was the calibration of chosen partition coefficients to existing databases.

The review also raised some issues regarding the estimation of the watershed and water body fluxes. The important partition coefficient for bioaccumulation is the K_{dw}, the suspended sediment-water coefficient. The test simulations indicated that this particular coefficient was insensitive to calibration test. Discussions with the EPA

modeling group at the public meeting revealed that the low suspended solids concentrations used for the simulations was the main cause for insensitivity. **This further strengthens the argument that a more rigorous water column model needs to be used to assess aquatic effects. Assessment of particle types (i.e., soil vs. phytoplankton) and amounts would provide additional important bioaccumlation simulation comparisons.**

It is unfortunate that soil and water loss degradation constants were not incorporated in the model. Several recent studies have shown that Hg^o production and evasion are common processes in soils and surface waters. Similarly, photodegradation has been shown to affect MeHg concentrations in surface waters. **The approach of using a set fraction of Hg species in lake waters (i.e., 15% as MeHg) is better replaced by a valid geochemical model, as mentioned above.**

EPA did not estimate fluxes in large lakes, rivers and other large water bodies. The Subcommittee does not, however, consider this to be a major problem. Rivers can be extremely important vectors for trace metal transport to lakes but modeling such efforts is undoubtedly beyond the scope of this report. Incorporation of large lakes and rivers complicates the assessment of atmospheric inputs to bioaccumulation because of the confounding effects of point-source discharges. Instead, tables in volume III should be expanded to include Hg and MeHg concentrations from selected river studies.

The Lake Michigan Mass Balance Model, funded by the EPA, should provide the first detailed large-lake Hg cycling model. The study quantified atmospheric and tributary inputs to the system and coupled this information with in-lake assessment of aqueous, sedimentary and biotic pools. This model, when completed, cannot treat riverine watersheds in the way that the IEM-2 model can, due to the effects of contaminated zones in rivers and harbors of Lake Michigan.

Sections of the draft report addressing assumptions about plant uptake of mercury directly from the atmosphere are adequate for the report's purposes, but could be improved. Most of the studies cited were conducted prior to 1990. The air-plant BCF (bioconcentration factors) was taken as the midpoint of the Mosbeak *et al.* (1988) study for a variety of plant types. However, several studies have been conducted more recently to assess accurately the effects of foliar uptake and release of Hg (Cocking, *et al.*, 1995; Hanson *et al.*, 1995; Munthe *et al.*, 1995). Detailed studies in specific foliar settings are being conducted to assess dry deposition and through fall of Hg. Since the model presented did not evaluate the effects of plant types on watershed processing of Hg, the effort is probably adequate.

Finally, the Charge asks if the likely contribution of mercury from plants to soil is

great enough to require adding such sources to the input for future models. **The Subcommittee recommends that a statement be incorporated into the report's text that specifies that both plant-to-soil and soil-to-plant pathways can represent important Hg transport processes.** Mass-balance studies that incorporate "through fall" in forest canopies have indicated that dry deposition onto plant surfaces can account for significant inputs of Hg to terrestrial systems. Similarly, evasion of Hg through the canopy can be an important loss mechanism and that decaying vegetation can be a significant source of Hg to soils.

3.10 Uncertainties in Atmospheric Modeling

Charge 11 asked for comments on a number of qualitative conclusions drawn from the results of the atmospheric modeling; in particular, the Agency was concerned about the effects of uncertainty.

A number of significant qualitative conclusions are drawn from the results of the draft report's atmospheric modeling. Chief among these are:

a) mercury species from combustion sources are transported over relatively great distances

b) mercury is deposited to soil and terrestrial vegetation, but at levels that do not result in human exposures likely to be detrimental to health though terrestrial exposure pathways

c) significant inputs of mercury in lakes and ponds result from both direct deposition of mercury compounds into lakes and ponds and run-off inputs of mercury compounds from the watershed land surface following land deposition

The Subcommittee considered three issues relevant to the question of whether uncertainties are adequately described: a) were the important uncertainties listed; b) is consideration given to how the qualitative conclusions could change as a result of the uncertainties; and c) what questions cannot be addressed because of the uncertainties?

As far as the Subcommittee could determine, the draft report does provide a fairly complete list of the important sources of uncertainty in the atmospheric model. However, the significance of these uncertainties and strategies for confronting these uncertainties in reaching conclusions are not addressed and should be. Although uncertainties and lack of data are discussed throughout the report, both the Executive Summary and other parts of the document need an emphasis on the fact that significant information is missing regarding the biogeochemistry of mercury species and that the

absence of this information limits the reliability with which any mercury control program can be evaluated.

It should be recognized that, in its current form, this document contains quantitative modeling for making order of magnitude estimates, but provides only qualitative treatment of uncertainty. There is no explicit quantification of uncertainties. We recognized that it may not be possible at this point in time to carry out a detailed uncertainty analysis. However, even without a quantitative uncertainty analysis, an effective way to communicate uncertainties is to state clearly: a) all the key assumptions made in the analysis; b) missing information; and c) how robust are the conclusions relative to the assumptions. **Perhaps the most important issue in this list is whether the conclusions are invariant with respect to parameter values that are missing or to the value ranges of parameters that are uncertain or have incomplete data. The uncertainties should be ranked in terms of their relative impact on the conclusions.**

3.11 Estimating the Bioaccumulation Factor (BAF) for the Aquatic Chain

Charge 12 sought comment on the BAF developed by the Agency, and its utilization in the models.

The Subcommittee agreed that the generation of the reference dose as currently presented for wildlife is flawed. The Wildlife Criteria (WC) was derived from a bioaccumulation factor (BAF) based on total Hg rather than methylmercury (MeHg), which is the species that bioaccumulates. As a result, the magnitude of the error in the BAF is associated with, and reflects, the wide variability in MeHg concentrations among ecosystems. This is inadequate to make predictions about the effects of Hg on wildlife, or the exposure of humans to non-farmed fish. The Subcommittee feels that EPA should calculate BAF and WC based on dissolved MeHg in water, and that BAF calculations be specific to ecosystem or water body type.

The draft report describes three approaches for calculating bioaccumulation factors (BAF). Each of these approaches represent state-of-the-art techniques for deriving a BAF, and the Subcommittee supports the preference of BAFs over BCF. The report clearly (and correctly) points out that field derived BAFs are preferred because they reduce the uncertainty in the number. BAF_3 x PPF_4 was chosen as the preferred method because it was based on field data for the BAF_3 and because the results showed less variability. The disadvantage to this approach is that the PPF multiplier is a fixed value. This value can vary from site to site and therefore utilizing a single PPF introduces uncertainty.

The uncertainty analysis conducted by the Agency was adequate although it did not include uncertainty that is due to analytical error. Understanding the

extent to which mercury is accumulated by various aquatic species is central to both the human health and ecological risk assessment. Unfortunately, both calculated and field measured BAFs show a great deal of variability in the numbers for the same species. The data shown in the draft report's Table 4-1 show that the field-derived BAF_3 and BAF_4 can vary by as much two orders of magnitude when comparing 5th and 95th percentiles. The variability is attributed to site specific parameters which control the extent of mercury methylation as well as sorption of mercury to suspended particles and dissolved organics. **One additional factor which should be included in deriving BAFs is fish age or size.** Calculation of BAFs for methylmercury as well as for total mercury would be useful and might help reduce the uncertainty.

For purposes of aquatic risk assessment, geometric mean BAF values were used, which is appropriate. However, it should be pointed out that the potential to overestimate or underestimate the BAF is significant and that the error may be an order of magnitude or more. This amount of error is sufficient to make a difference between risk and no risk. This amount of variability, in part, helps explain why some populations of sensitive aquatic species do not appear to be affected in the field while others may be affected.

3.12 Modeling the Terrestrial Food Chain

In Charge question 13, EPA asked for an evaluation of the models and modeling conducted for the terrestrial food chain.

The EPA's model does not appear to provide WC for mercury that approximate threshold (effect) values and hence the utility and accuracy of the value is questioned. The Subcommittee remains supportive of the approach used to derive the WC, but has reservations concerning the value derived for mercury and its subsequent universal application. Use of site-specific data in WC models, however, is supported. The SAB has, in previous reviews, supported the development of criteria for wildlife and continues to do so. However, reservations about model formulations have been expressed and still exist. The values provided by the model for several species are in the range of 0.2-0.4 ng/L (ppt) HgT. These values are a factor of 2-5 below levels in many lakes (1.0 ng/L) that have healthy populations of wildlife species including those selected as most at risk for mercury exposure. Derivation of WC as shown in the Report is overly conservative and not particularly useful for risk assessment. The value may be thought of in the same manner as a reference dose, that is, a concentration that is calculated to provide an adequate margin of safety for all species potentially at risk. Ecological risk assessments are based on comparison of threshold values with exposure values. **The WC do not appear to represent a reasonable threshold value. Therefore, it is recommended that they not be used for risk assessment purposes. The WC values appear to be overly conservative due to the two uncertainty factors and**

the large BAFs used in the model. The model input parameters, including those for methylmercury, need to be further evaluated.

3.13 Characterization of Wildlife Effects

Chapter VI of the draft report presented the Agency's current mercury risk characterization of wildlife effects. In Charge 35c, the Subcommittee was asked to comment on the appropriateness and environmental significance of the characterization.

The Agency identified the most significant laboratory and field toxicology studies which evaluated the effects of mercury exposure on wildlife. The findings are clearly presented in Volumes V and VI. These data were summarized to produce dose/ response relationships to methylmercury for wildlife species. The establishment of an avian Hg Lowest Observed Adverse Effects Level (LOAEL) of 0.064 mg/kg-day (0.5 μg Hg/g diet) is justified on the basis of Heinz's three generation study with mallard ducks (Heinz, 1979). However, an avian No Observed Adverse Effects Level (NOAEL) was not established. The Agency correctly established a mammalian LOAEL of 0.16 mg/kg-day and NOAEL of 0.05 mg/kg-day on the basis of Wobeser's findings of nervous tissues lesions in mink(Wobeser, 1973; Wobeser *et al*., 1976a; Wobeser *et al*., 1976b).

The methods used to calculate a wildlife criteria (WC) for mercury, using a wildlife reference dose and methods described in the Proposed Great Lakes Water Quality Guidance, are compromised by data deficiencies and numerous uncertainty factors in the model. **The uncertainty factors, questionable application of BAF ratios, and incomplete data on diet habits of target species produce WC for mercury which are not scientifically defensible.** The Agency should recognize that wildlife Hg exposure (as measured by egg, brain, muscle tissue Hg concentrations) differs by a factor of ten between most aquatic systems in North America and that the dose-response curve for methyl-Hg is unusually steep. **Applying uncertainty factors of 9-10 times to the test dose (TD) produces a reference dose which is so high that it is not likely to be encountered by most free-ranging piscivorous wildlife in North America.** Furthermore, other Members of the Sources Workgroup noted at the public meeting that water column total Hg concentrations are not predictive of fish methyl-Hg concentrations, an assumption made by the WC model. **Consequently, we recommend a BAF based on water column methyl-Hg concentrations and site specific BAF characterizations. Additional study of target species dietary habits is also needed (especially mink) and the inclusion of additional target species (i.e. common loon) is recommended.** The bottom line is that the Agency's own

estimate of WC for mink (Mercury Report to Congress, Vol. VI and Great Lakes Water Quality Initiative) ranges from 400 - 4000 pg/L. The same data sets were used to make the estimates, only the assumptions differ. This range of water column total Hg spans nearly the entire range currently measured in North American aquatic systems.

However, the Subcommittee believes that piscivorous wildlife are at risk to elevated mercury exposure and toxic effects in the areas of concern identified by the U.S. EPA. For instance, Hg concentrations in piscivorous wildlife tissue are greater in the areas of concern than in other regions of North America. Also, egg Hg concentrations of avian piscivores in the upper Great Lakes, mid Atlantic coast, New England, and Florida exceed levels associated with reproductive impairment. MeHg intake rates of common loons, osprey, and otter likely exceed the avian and mammalian LOAEL in many aquatic systems within these regions. Fish contaminant databases (developed for human consumption advisories) can be accessed to estimate Hg concentrations in many prey species consumed by wildlife. These estimates should be used to establish risk levels (in terms of probabalistic estimates incorporating confidence limits) for target wildlife species in the areas of concern.

The Agency should be cautious when using feather and liver total Hg concentrations as toxicological benchmarks. Interpretation of feather Hg concentrations as an index of exposure requires knowledge of feather type, molt pattern, and individual age. Interpretation of feather Hg concentrations as a toxicological benchmark for exposure is complicated by the fact that feathers are sites of methyl-Hg elimination and sequestration. Thus, feather Hg concentrations of piscivorous wildlife are expected to be greater than non-piscivores, even in the absence of toxic effects. Also, liver total Hg concentrations need to be interpreted with care as it has been shown that most liver Hg in piscivores has been demethylated and poses less risk than does methyl-Hg. Conversely, methyl-Hg is the primary form in egg, brain, muscle, and blood, which likely provide more meaningful toxicological benchmarks of exposure.

3.14 Evaluation of Wildlife Effects

Charge 36 asks the Subcommittee to evaluate the section of Volume V describes fairly significant wildlife effects (which are attributed to elevated mercury concentrations in some ecosystems). In particular, they sought comment on the scientific underpinnings of the evaluation, including its consistency with EPA's ecological risk guidelines.

The Subcommittee does not believe Volume V, in total, is based on the best available and sound science. To a large degree this chapter follows EPA guidelines for ecological risk assessment. However, it deviated in terms of

quantifying the risk. This is a critical component of risk assessment.

Risk assessment is the process of coupling exposure (or more explicitly, dose) and response (effect). It is the imputed relationship between biological effects and exposure to the agent(s) of concern. The draft report uses predicted exposures from computer models as the primary bases for exposure estimates (dietary mercury). This is not adequate for state-of-the-art risk assessment. **Site specific monitoring data are needed (and as noted in the draft report, are available for many sites).** These data could be used to provide more scientifically defensible examples of exposures at a few selected sites, for which risk quotients could be calculated to quantify the exposure/effects relationship (risk) at specific sites. Using this approach, one can define the potential for effects to occur at various sites and can perform probabilistic assessment of the potential for exposure to exceed designated threshold effect levels for species most art risk. These techniques are described in detail in SETAC (1994) and Solomon *et al.* (1996).

Volume V could be greatly improved through the use of calculated risk quotients for specific sites and species most at risk. There are sufficient data to do this for several areas and species. This requires calculating a threshold values from chronic laboratory feeding studies for the species of interest (e.g., threshold value is calculated as the geometric mean of the LOEL and NOEL). The threshold value can then be divided by the level of mercury assumed to be in the diet of a given species and a risk quotient for a given area is derived. An example follows for loons using the chronic data from a three generation feeding study with mallard ducks (Heinz, 1979) to derive a threshold value. The LOEL in this study was 0.5 ppm; a NOEL was not obtained, but it could be estimated by dividing the NOEL by 3 providing a value of 0.17 ppm. The geometric mean of the two values is 0.29 ppm. This value could then be used to calculate risk quotients for areas where dietary mercury is calculated from site specific mercury concentrations in fishes eaten by loons.

Care has to be taken in comparing mercury levels in tissues of animals that died or were collected in the 70s and 80s with samples taken in the 90s. Atmospheric releases of mercury appear to have declined somewhat over the past five years. Additionally, site specific characteristics are important in determining mercury methylation, fate, and transport; care should be taken in comparing site specific data and drawing conclusions relative to levels resulting from atmospheric deposition based on estimates derived from RELMAP.

In addition to these general comments on the wildlife sections of the draft report, the Subcommittee has identified some specific issues worth noting. These include:

a) Table ES-2 shows that <1% of the panther's range overlaps mercury areas of concern. This suggests that the potential for exposure to exceed

the effect level (i.e., risk >1.0) is low. This should be stated clearly. Conclusions drawn relative to the panther appeared to be based on two unpublished (non-peer reviewed reports). Although inclusion of these reports is appropriate, there are insufficient data to judge dose-response and significance of the field residue panther data. The data are anecdotal in nature, although indicative of the potential for increased exposure and increased risk to panthers from methyl mercury. Over reliance on the raccoon pathway for exposure is placed in this report. Multiple avenues exist for the panther, one of which is the raccoon. Concentrations of mercury in raccoons, may not always exceed those in other species. Risk statements could be drawn for panthers through the calculation of risk quotients for panthers using site specific data for the diet and a threshold effect level for cats based on a chronic feeding study (summarized elsewhere in this report).

b) Page ES-5 lists the five species identified as having the greatest potential to be at risk , along with the percent of the species' range that overlaps mercury areas of concern. This is a good start towards a risk statement. The report should complete the presentation by providing risk calculations, i.e., effect levels divided by exposure levels. **The statements on this page infer risk to the various species without presenting risk calculations. This is a serious short-coming to this report.**

c) Consistency as to comments on observed effects in the report is needed. Page ES-5 reports that Bald Eagle populations are improving in five states, yet the draft report later also infers risk to bald eagles from mercury and indicates that the Great Lakes is one of the areas of highest concern. This is a key area where eagle populations have been improving over the past decade in spite of mercury levels in fish. Page ES-11, however, indicates that "field data suggests that bald eagles have not suffered adverse effects toxic effects due to airborne mercury emissions." **The report paints a biased picture without taking advantage of the opportunity to test or verify the assessment with the analyses of field populations in the extant literature.** Once again, risk is inferred without a real risk calculation.

d) Page ES-8 indicates that "otter population declines do not overlap to a large extent with regions of concern; however, the area of decline does coincide with RELMAP predictions of high mercury deposition rate." It is apparent from these statements that the reasons for otter declines are not clear, yet risk is inferred without definitive risk calculations. A critical factor in risk assessment is the co-occurrence of the exposure and

effects. The data from RELMAP suggest that there may be increased exposure in areas where otters live, but this is strictly an inference and site specific/region specific monitoring data needs to be used. **The Agency should point out the weakness and lack of information to draw definitive conclusions about risk to otters or make the case based on risk calculations. The inference of risk based on exposure estimates overstates the case.**

e) Page ES-10 (second paragraph) states "...although causal links have not been established , mercury originating from airborne deposition may be a contributing factor to population effects on bald eagles, river otters, and mink. " Without a causal relationship, the above statement is unsubstantiated and does not suggest state-of-the-art ecological risk assessment. There are many factors affecting otter, eagle and mink populations, especially, the expanding human population in the U. S. (and trapping in the case of mink). The single biggest factor resulting in species loss in the U.S. is now recognized as habitat loss and habitat conversion due to human intervention.

f) Page ES-11, in several places, infers risk due to elevated mercury exposure levels (levels in the diet). Exposure by itself does not infer risk, it must be accompanied by an equally rigorous effects assessment and risk characterization. State-of-the-art risk assessment is not based on inferences. It is acceptable to draw conclusions, but they must be qualified as to the strength of the data on which they are based. Also, note that on page ES-11, lines 17-19, it is stated that "...field data are inconclusive to conclude whether the mink, river otter, or kingfisher have suffered adverse toxic effects due to airborne mercury emissions." **When this statement is taken together with a similar statement on ES-10 relative to bald eagles, one can conclude that field data demonstrating effects on the species most at risk are lacking. This is a key statement and should be brought forward for Congress to evaluate.**

g) Page ES-13 (last line) incorrectly states that "... the designation of an area as a region of concern implies an increased risk of mercury toxicity to wildlife." More correctly, designation of an area as a region of concern implies an increased **potential for exposure** to mercury for species that co-occur with the exposure. The consistent theme here is that exposure does not equate to risk!

h) Page 2-26 (2.3.3, second sentence) states "...the species are at high risk of mercury exposure and effects because they either are piscivores or eat

piscivores." This statement again infers that exposure = risk. Additionally, it states that the species are at **high** risk of both exposure and effects. This is a definitive conclusion without a risk calculation (risk quotient). On the other hand, one might more appropriately conclude, on the basis of the data presented, that elevated tissue residues can result in an increase in exposure for the species of interest and that this exposure could lead to effects if effect thresholds are exceeded. Better yet, if risk quotients were calculated, one could make a definitive statement about the apparent risk

relative to other species and other areas where mercury exposure levels and risk quotients are lower.

l) Page 2-28 (lines 5 and 9), page 2-27 (lines 24, 25, and 27) report units for Barr (1986) as ug/Kg (ppb), whereas they should be ug/g (ppm).

j) Page 2-28 (third paragraph) states "The viability of loon populations within their traditional habitats in the United States is unclear. None of the studies reviewed was able to demonstrate clear population declines on a regional or national level." This sentence should be brought forward to the Executive Summary for Volume V. It makes a clear summary statement and indicates that population trends are uncertain. Put in context with the sensitivity of loons and their potential for elevated exposure, further field evaluation appears warranted. It also appears that more definitive risk statements could be made which would show risk to loons if risk quotients were calculated (chronic threshold bird values for fish in the diet/dietary mercury; e.g., mallard duck chronic effects threshold value divided by mercury in the diet of loons at specific sites).

3.15 Linking Emissions and Wildlife Effects

The draft report makes the inference that exposure to mercury emissions is related to reproductive effects and neurobehavioral changes in fish consuming birds and mammals. These effects have been documented in the Great Lakes and in the Southeastern United States. EPA's models predict that regional hot spots (relatively high concentrations of methylmercury) would occur in these same areas. In question 37, the Subcommittee is asked to comment on the soundness of the analysis of the evidence linking emissions and effects.

The effort to link emission inventory to effects in piscivorous birds and mammals is a leap of faith with little actual scientific evidence to substantiate any correlations. The draft report recognizes that there is still considerable uncertainty as to the transfer mechanisms and rates of mercury from source to the target species. The following

major gaps in knowledge and/or model assumptions make it difficult to draw meaningful inference between source and effect:

a) Most of the mercury is emitted in inorganic form and there are large gaps in our understanding of the environmental movement and deposition of airborne mercury into aquatic ecosystems. The model ignores any re-emission processes which can amount to a large fraction of the deposited mercury.

b) Processes and rates involved in converting the inorganic mercury to methylated forms are only partially understood, although the current level of understanding is not reflected in the draft report.

c) The use of BAF to quantify the relationship between the dissolved mercury concentration in the water column and methylmercury concentration in fish does not seem to have much scientific justification. The BAF data used have a number of major limitations (nature of Hg in water, detection limit, and contamination artifacts).

3.16 "Hot Spots" and Wildlife Effects

Charge 38 deals with mercury concentration "hot spots" and associated wildlife effect (or lack of effects). EPA wanted to know if any "hot spots" have not shown evidence of wildlife effects, and if predicted "hot spots" correlated with methylmercury levels in fishery products.

The wording of the question on "hot spots" and wildlife effects pre-supposes that deposition hot spots are, in fact, reflected in wildlife Hg concentrations and effects. This also implies that in areas of low Hg deposition, we would not see wildlife impacts/or high fish concentrations. The actual situation is much more complex for several reasons. First, there is a small range (3x) in Hg deposition between the least and most impacted regions, while the effects on methyl Hg production caused by in situ factors (pH, SO_4^{+2}, watershed area, DOC, etc.) are much greater (>10x). Additionally, although it has not been demonstrated, anecdotal evidence suggests that the relationship between inorganic Hg input and MeHg production is not linear: i.e., as the total Hg increases by a factor of 10, methyl Hg increases perhaps only by a factor of two. This can be seen by looking at contaminated sites. For example, in the Lahonton Reservoir (NV) system, total Hg is 1000 ng/L, while piscivorous fish have 5 ppm MeHg by comparison; lakes in Wisconsin may have 1 ng/L Hg, but the piscivorous fish have 0.5 ppm MeHg. Onondaga Lake (NY) is in-between, having 25 ng/L total Hg, and fish with 1 ppm MeHg. Or, looking at deposition, we see that in Elephant Butte Reservoir (NM), an area with < 5 $\mu g/m^2$ deposition, piscivorous fish have 0.5 ppm MeHg, similar

to Northern Wisconsin, which has 10 µg/m^2, and upstate New York, which has 15-20 µg/m^2 (Driscoll *et al.*, 1994; Watras *et al.*, 1994; Henry *et al.*, 1995)

This is not to say that deposition "hot spots" have no impact on wildlife (the Subcommittee agrees that they might), but that a myriad of biogeochemical factors are at work in real systems which have not been incorporated into the model. It is not unlikely that each of the important factors (pH, DOC, SO_4^{+2}, HgT, watershed area, mean temperature, surface area to volume ratio, trophic state, etc.) has a temporally different, and non-linear effect upon the methyl Hg production in a given lake. Thus, aside from saying that MeHg will eventually go up if $Hg^{(II)}$ deposition is increased, we cannot say how much, or when. And, if two or more factors change at the same time (say, Hg inputs go up, but SO_4^{+2} goes down), predictions become very difficult. However, EPA has not taken advantage of the state of the science in the draft report.

3.17 Wildlife Effects as Warning Signs of Humans Effects

EPA asked the Subcommittee, in Charge 39, to advise it as to what wildlife effects (based on what metric) could be interpreted as harbingers of likely human health effects.

The Subcommittee's consensus was that wildlife epidemiology cannot serve to totally replace well defined laboratory studies (Kendall *et al.*, 1995). In the laboratory we are able to demonstrate, under controlled conditions, a true dose-range of exposure to the contaminant, in this case mercury, in a variety of wildlife species and generate critically needed dose-response curves. With appropriate laboratory species and well developed dose-response curves an opportunity then exists to utilize this information, even as developed on surrogate species, to better understand the potential exposure and subsequent tissue concentration that may exist in wild species. It is possible that surveillance of key wildlife sentinels, if appropriately chosen, may be extremely useful in the future to better understand impacts from environmental contaminants (Sheffield and Kendall, 1997). The generation of well designed laboratory studies to demonstrate cause and effect under a range of appropriate doses integrated with field exposure and perhaps effects measurements can be extremely important in the development of a wildlife ecological risk assessment (Kendall *et al.*, 1996).

Looking at mercury's effects in general, the classic case of "Minimata Disease" in Japan demonstrated that mehylmercury can have profound effects on humans as a teratogen and reproductive toxicant, as well as causing death in human and animals. Other forms of mercury have also been found to be toxic in humans and animals. For example, wildlife have also been killed by exposures to mercury compounds used to treat seeds used in agriculture. .

With sublethal exposure to mercury, a variety of toxicological endpoints may be manifested in wildlife that also could occur in human beings (Kendall *et al*., 1995). First of all, mercury can act as a reproductive toxicant, particularly as a teratogen which has been demonstrated with laboratory studies in wildlife. There is also concern as verified with Minimata Disease of teratogenicity with mercury exposure in humans. Mercury may act as an endocrine modulator in wildlife species. (Lower and Kendall, 1990; Kendall and Dickerson, 1996).

With regard to mercury acting as a reproductive toxicant in wildlife, of critical interest is its influence on population statistics. It is quite difficult in the field to measure the numbers of wildlife in their natural environment to understand their true population ecology (Kendall and Lacher, 1994). It appears that several wildlife sentinels, including wild mink and loons, may have experienced population declines correlated with mercury exposure. Future field studies of other species may identify additional species which could also serve as sentinels to identify reproductive and population impacts related to exposure to environmental mercury.

Mercury is also a potent neurotoxicant. The "Madhatters Syndrome" has been demonstrated in humans with severe neurotoxicological symptoms. In addition, sublethally exposed wildlife have demonstrated neurotoxicological responses to mercury.

Mercury existing as a strongly positive cation *in vivo* manifests its toxic action to a large degree through the disturbance of various enzyme functions, particularly those having sulfhydryl groups. In this regard, a variety of types of tissue damage, particularly in the liver and kidney, may occur with enhanced mercury exposure.

3.18 "Social Costs" of Mercury Contamination

The draft EPA report (Chapter VII) previously contained a section on the "Social Costs" of mercury contamination assessing the value of the fisheries in the U.S. as well as other values, such as maintaining a healthy ecosystem. The intent was to balance the discussion of mercury control costs. Some peer reviewers objected to the inclusion of the Social Costs section partly because the impact of anthropogenic sources could not be directly and quantitatively related to these impacts (e.g., the declining Florida panther population). The section was consequently deleted. In Charge question 41, the Agency asked the Subcommittee to comment on the advisability of including such a study, and to advise it the EPA how to describe best the benefits of mercury reductions if a) the impacts of such reductions are not directly quantifiable, and b) the monetary value of such benefits are not easily quantified.

The term "social costs," as used in the context of this Charge question (41) addressing the economics of Hg controls refers to the benefits of reducing mercury

emissions from a societal point of view. The supplementary material provided to the Subcommittee includes several pages deleted from a previous version of the mercury report that described social costs. This section was deleted following criticism received through an inter-agency review of the study. **We agree that the deleted discussion of social costs was inadequate.**

Nonetheless, the report is sorely lacking for a discussion of social costs (benefits). By including a discussion of the costs of reducing mercury emissions, but omitting discussion of the benefits of emissions reductions, the

Agency fails to provide a basis for weighing costs and benefits of any measures to reduce mercury emissions.

The control of mercury emissions is inter-twined with the control of other harmful pollutants. The benefits of controlling other pollutants should not be forgotten in the consideration of the benefits of mercury control. Even where the quantification and monetization of some potential benefits associated with reductions in mercury emissions is difficult, the description of benefits from the ancillary reduction in other pollutants that is achieved through mercury control may be readily available. These ancillary benefits should be described for consideration along with other benefits and with the costs of mercury control (McConnell, 1990).

Environmental benefits are often difficult to quantify, and indeed, the physical effects of pollution changes are often difficult to state precisely. Consequently, wherever possible, scientific analysis should characterize the effects of potential policy in probabilistic terms, rather than as point estimates. The state of the art in integrated assessment calls for the propagation of these probabilities through an entire model linking the source of emissions, their various environmental pathways, and endpoints that are of concern to humans and to the policy process. The result will be probability distributions describing the impacts of changes in emissions that can be combined with available information about willingness-to-pay for these changes, to provide a bound and range of potential benefits. Such analysis also is of tremendous use in exploring the value of additional information by identifying research needs that will yield the greatest "bang for the buck" through reducing uncertainties about the benefits of emission reductions.

The organization of a comprehensive integrated assessment along these lines is not achievable in a time frame that is available for revisions to the Mercury Study. However, as discussed below, a framework for such analysis should be included in the Study to guide further research efforts by the Agency.

It is not possible at the present time to describe the benefits of reductions in mercury emissions in monetary terms in a reliable fashion. In place of monetary

estimates, a rigorous framework for the consideration of benefits could be articulated. It should take advantage of the best scientific information available for the description of those benefits, and as importantly, describe how such benefit estimates could be achieved in the future. These benefit comparisons occur at the margin. Hence a discussion of the total value of an environmental asset or resource (such as was contained in the deleted material from a previous version of the Mercury Study) may be useful background but it is not relevant to the analysis of small changes in mercury exposure. Also, the framework should identify the various endpoints that in principle could and should be valued and it should identify the proper methodology for doing so

in each case. The benefits discussion should be accomplished in the time frame available before release of the final Mercury report.

For the case of mercury, the evaluation of social costs is particularly challenging because there is not a single peer- reviewed study that has attempted to evaluate specifically the social costs of mercury pollution. There is likely to be disagreement about the degree to which related valuation studies provide useful information pertinent to understanding issues regarding mercury. However, the existing literature on the valuation of related benefit endpoints should be organized and brought to the fore. There are other pollutants that pose generally similar threats to the environment or public health as mercury, yielding effects such as delayed child development, neurological effects in adults, and threats to species diversity and habitat. In supporting analysis for the regulation of lead, for example, these types of subtle effects have been studied for the purpose of economic valuation and contributed to the promulgation of regulations. Although lead is a very different toxicant than mercury, valuation estimates for these subtle lead effects may provide some useful information to describe the likely magnitude of economic benefits of reduced exposure to mercury. **More importantly, however, they provide immediately useful information for an evaluation of the methodologies available for estimation of the benefits for these type of effects, and they would help to establish priorities for research aimed specifically at valuation of benefits for mercury.**

Recent surveys that provide helpful background include Lee *et al.,* 1995; Haggler Billy Consulting, Inc. 1995; and the European Commission, 1995.

The review of costs of mercury control in Volume VII appears to have been done carefully, as far as it goes. However, it is flawed in two important ways. One serves to potentially overstate the private (out-of-pocket) cost of emission reductions by a large amount. The other serves to understate the social cost of government regulations. Interestingly, these two omissions are closely related, from the standpoint of options that might be considered by a policy maker.

The Study **overstates** the private cost of emissions reductions because it does

not comprehensively explore the range of management strategies available to the Agency for mercury emission reductions. **The Study limits its review exclusively to a set of post-combustion technologies of proven capability. It should be updated to consider emerging technologies for post-combustion control (Feeler and Ruth, 1996) and expanded to explore the opportunities for pollution prevention, such as strategies aimed at reducing the mercury content of fuels**. (PERI, 1997; EPA, 1996; Michigan Mercury Pollution Task Force, 1996). Although mercury differs from sulfur in that there is greater variation within a deposit, the average mercury content differs importantly among coal basins, providing a potentially low cost way of achieving sizable emission reductions from electric utilities.

More important, the analysis provides information that is organized for only a single management strategy—the implementation of Maximum Attainable Control Technology regulations. This approach is not one which is likely to achieve cost effectiveness in emission reductions. The Study only mentions in passing, and provides no analysis of, incentive-based approaches to achieving environmental goals. Incentive-based approaches that should be considered are deposit-refund systems (batteries, industrial uses of mercury), emission fees and tradable permits. Numerous studies of potential control of various pollutants have found that the costs of control can be decreased by 20 to 80% through the use of incentive based approaches in place of technology standards or inflexible emission rate standards (that is, emission rate standards that are calibrated to be achievable with a specific technology). (Tietenberg, 1985). The Study should put forward information about options in addition to the specification of emission guidelines (limits). However, in Volume VII the draft report states (p.4-15): "Other nontraditional approaches such as emissions trading or application of a use tax, or other market-based approaches may also prove feasible for mercury control. However, these options are not presented in detail in this Report as the control technology analyses focused on what might be achievable under the statutory language of sections 112 and 129 of the CAA."

A second flaw that leads to the cost estimates in Volume VII **understating** (potentially) the social costs of regulatory policies is the failure to acknowledge changes expected to occur in a general equilibrium setting. In brief, one can expect the existence of preexisting regulation and tax policy to cause the incremental social cost of additional policy to be greater than the private financial cost, due to its interaction with preexisting policy.

One can think of a new regulation as a “virtual tax” in that it depresses the real wage of workers in the economy by raising the cost of goods and services. Almost any tax has the unfortunate property, from an efficiency perspective, that it is expected to distort economic behavior. However, to an important degree, this problem can be remedied if a new regulation raises revenue (through a mechanism such as auctioned permits, or emission fees). For further background, see Goulder, *et al.* 1996; Goulder, 1995; Oates, 1995; and Parry, 1995.

The two ways in which the cost estimates are flawed invite the consideration of incentive based approaches to environmental policies. Cost effectiveness in attaining an environmental goal can be enhanced through such approaches. Further, the tax interaction effect and social costs in a general equilibrium setting are reduced as the cost of policies are reduced, and even further if such policy can be a source of revenue for government that might displace other taxes. Analysis that takes these issues into account, as well as consideration of the performance of alternative management strategies with respect to the costs of control, is essential to improving the scientific breadth and rigor of the Study.

3.19 Research Needs

In Charge 40, the Agency asked for suggestions to identify needed research.

With regard to the relation of anthropogenic mercury releases to human mercury exposure, the major research priority is to quantify the relationships between human mercury exposure and current and past anthropogenic sources of mercury. Quantification of these relationships would allow a quantitative prediction of the effect of mercury emissions control strategies on human mercury exposures.

Although there are many areas of uncertainty in the modeling of mercury fate and transport, lack of information about the methylation and bioaccumulation of mercury in various ecosystems is the area which contributes the greatest uncertainty to the overall modeling effort. Studies determining rate constants and factors affecting rate constants would lead to a more sound, defensible source-effect model. In addition, research is needed to understand better the link between lake acidity and mercury concentrations in fish, as well as watershed studies to evaluate the relative contribution of historical, versus current, deposition and the residence time of mercury in the watershed.

Additional study of target species' dietary habits is needed in order to better characterize wildlife mercury exposure in at-risk species. In order to better understand inter-relation of mercury sources to effects of mercury on wildlife, further research is needed to determine NOAELs and LOAELs, particularly in piscivorous avian species such as the cormorant, common loon, heron, osprey, etc.

3.20 Conclusions

The Sources Workgroup, after considering its discussions at the public meeting and developing the preceding report, reached the following conclusions about EPA's draft mercury report:

a) The emissions inventory of anthropogenic sources of mercury is largely sound.

b) The report does not address adequately the contribution of natural sources of mercury or of past anthropogenic mercury emissions, both of which may be important contributors to exposures.

c) The chemical form of the emitted mercury may have a significant effect on its fate. The fraction of mercury emitted in various forms is uncertain, although current research efforts may provide clarification. EPA should incorporate new speciation results as they become available.

d) The modeling of atmospheric mercury transport and deposition is largely sound. However, the treatment of dry deposition velocities should be carefully reviewed.

e) The modeling of the post-deposition fate of mercury in ecosystems is oversimplified and does not reflect recent advances in the science. This modeling should be revised, with the goal of having the report reflect current scientific understanding.

It is important to bring out the importance of MeHg production in ecosystems in the draft report. Because MeHg is the species that bioaccumulates in human and wildlife food supplies, understanding the methylation process is critical to modeling Hg fate and exposure. Mercury methylation and the variability in MeHg among ecosystems were neglected in the report, because of the perceived difficulties in modeling methylation. The report assumes that MeHg constitutes the same fraction of total Hg in sediments, soils and waters across ecosystems. This is not the case. Rather, the variability in MeHg production and bioaccumulation among ecosystem types is many orders of magnitude, and may be as large as the influence of Hg contamination. Without consideration of this variability, the report's fate and transport models, and the resultant exposure models and wildlife criteria models cannot predict WC with less than two to three orders of magnitude associated error.

The report should detail current understanding of Hg methylation process; MeHg production should be specifically included within fate and transport models; and these models should be specific for a suite of ecosystem types.

f) The derived wildlife criterion for mercury is a value that is below concentrations found in many lakes with healthy biota and the utility of the value is questioned. The risks to wildlife are not well characterized and should be revised.

g) Regarding the costs of controlling mercury emissions, the Report limits its assessment to end-of-pipe, post-combustion pollution control systems. Pollution prevention and market-based approaches should also be considered. In addition, the benefits from the simultaneous reduction of other pollutant emissions, which could result from some strategies, should be included in the cost/benefit analysis. Although the benefits of reduced mercury emissions can not, with the current-state-of-the-art, be quantified at this time, at least a framework to evaluate the benefits of reduced mercury emissions should be provided.

h) Even with revisions, the EPA should clarify that it is not currently possible to quantify the relation between anthropogenic sources of mercury and resulting mercury concentrations in fish or other biota. The EPA's approach was to use state-of-the-art models to provide a semi-quantitative link between mercury sources and mercury in biota. Given the limitations in the ability of fate and transport models to quantify mercury concentration in biota, the Subcommittee found the EPA's semi-quantitative approach to be acceptable, although critical biogeochemical processes were neglected. Further, by using better models, including existing models such as MCM or R-MCM, a respectable effort could be made at predicting effects. A more sound approach could have been taken in contrasting watersheds testing different ancillary parameters and loading rates.

4. Exposure, Doses, and Body Burdens

4.1 The Scientific Basis of the Volume 3 Exposure Assessment

The Subcommittee, in Charge 14, was asked to comment on the scientific basis of the exposure assessment, alternative approaches, and research priorities, and, as well, advise the Agency on how Appendix H of Volume 3 should be used, improved, or expanded.

The scientific methods used in the draft report's exposure assessment included estimates of population exposures based on fish consumption survey data and methylmercury concentration measurements in fish, scenario exposure estimates based on environmental transport and fate modeling to estimate concentrations in freshwater fish, and existing (albeit limited) data on mercury concentrations in hair. Based on these factors, and market basket survey data on methylmercury concentrations in food presented at the public review meeting, but included in the draft report, it was concluded that ingestion of mercury-contaminated fish is the major source of human exposure to methylmercury. Appendix H summarizes fish consumption information from several surveys of the general population and of special "high intake" populations. In addition, this appendix summarizes data on mercury levels in marine and freshwater fish and seafood. This methodology is scientifically sound and is consistent with approaches that have been used by EPA and other federal agencies for assessing the health risks posed by environmental contamination.

The Subcommittee's review of this portion of the document identified several areas where the exposure assessment could be strengthened or clarified. These areas are:

a) The Mercury Study Report concludes that there is "a plausible link between mercury emissions from anthropogenic combustion and industrial sources and methylmercury concentrations and freshwater fish." A critical question that still needs to be answered is "Do anthropogenic atmospheric mercury emissions significantly affect mercury levels in fish and seafood?"

   Answering this question requires an explicit multimedia transport/transformation assessment for mercury species. Only some of the relevant transport and source media are currently considered, i.e., air sources with transfer to surface waters by deposition. Other sources and cross-media transfers need to be considered.

   The overall question is only partially addressed in the draft report through the use of the RELMAP and COMPDEP models which were used to

predict the impact on of atmospheric releases on inland surface water. However, the models were not used to evaluate the impact of U.S. atmospheric releases on marine and estuarine environments, or to evaluate the impact of foreign emissions on U.S. waters.

Information about other sources of mercury to the aquatic environment were omitted from the report. Exclusion of this information creates the impression that atmospheric releases are the only source of mercury to the aquatic environment. This is not accurate, however, since municipal and industrial wastewaters which are directly discharged to surface water often contain traces of mercury. In addition, waste sludge from industrial processes or municipal sewage plants, which is often used to amend surface soil, can contribute to surface water contamination via runoff or following volatilization to air. Many readers of the final report will be aware of these sources and may wonder about their "relative contribution" to surface water. It would be wise to include some information about this in the final report. If it is impossible to estimate relative inputs from atmospheric releases vs. land disposal and surface water discharges, explain that to the reader. Perhaps this could be a future research issue.

b) Fish consumption rates were based on the Department of Agriculture's Continuing Surveys of Individual Food Consumption (CSFII) 3-day dietary history survey. This survey provides important information about fish consumption patterns within the general population. However, the 3-day survey has several limitations which are listed below:

1) The survey cannot be used to evaluate the frequency of fish consumption by an individual consumer.

2) Daily intake rates for participants who reported eating at least one fish meal during the survey period may be higher than actual since the weight of fish ingested was divided by 3 days to calculate a grams/day estimate.

3) More than half of those who normally ingest one fish meal per week would have reported no fish consumption during a 3-day period. Thus, the survey may not accurately reflect the percentage of U.S. residents who consume fish and seafood on a weekly basis. The survey provides very little information about patterns of fish consumption by individuals, i.e. how frequently a single consumer eats a particular species of fish; or about the geographic source of the fish he/she consumes. Therefore, the survey cannot be used to assess the randomness of a consumer's selection of

fish and seafood. This is problematic since the risk assessment for methylmercury in fish appears to be based on an underlying assumption that consumers eat a random selection of commercially-available and sport-caught freshwater and marine species -- an assumption the Subcommittee believes is incorrect. Members of the Exposure Workgroup have studied consumption patterns and found individuals eating very repetitive diets that include daily or weekly meals of the same species of fish that they obtained from the same commercial source or local fishery (Knobeloch *et al.*, 1995). This weakness in the survey data should be mentioned in the report and the assumption of randomness should be evaluated by future research. These inherent weaknesses in the survey design should be discussed in Appendix H. In addition, the authors should explain how the report compensated for these weaknesses; for example, by including information from other, longer dietary surveys.

c) Occupational, intentional, and accidental exposure to mercury are only partially covered in this report. Limited information on occupational exposure and exposure to mercury from dental amalgams is included, however the report does not cover other exposures, such as household spills, use of mercury for ritualistic or medicinal purposes, etc. The uneven and incomplete coverage of non-environmental exposure sources weakens the report. We recommend expansion of this section of the report to include a more comprehensive literature review. Several cases of mercury poisoning have been reported in the Center for Disease Control's (CDC) Morbidity and Mortality Weekly Report over the past two years. National databases could be used to determine the number of mercury poisoning cases that are reported to CDC or to Poison Control Centers annually. This information serves to confirm the importance of mercury as a cause of human illness.

d) The process of averaging mercury levels for several different subspecies of fish and shellfish to develop a mean level for each species may, in some cases, lead to inaccurate exposure estimates. When a small number of sub-species dominate the commercial marketplace the average mercury level for the species should be weighted accordingly.

In future surveys, it may also be useful to record the geographic origin of the marine and freshwater fish that are sampled for mercury analysis. This information could be used to weight mean estimates based on the percentage of the total catch that are harvested from each location (e.g., N. Atlantic vs Pacific). Correction for differences between mercury levels

in fish that are harvested from inland waters, estuaries, marine waters, and commercial fish farms would further refine the exposure estimates. Additional information on these topics should be identified as a research priority.

e) The average methylmercury intake estimates that are included in the Executive Summary do not provide the reader with a sense of the extreme variability of exposure that occurs within the U.S. population. A more accurate picture of exposure would be provided by citing a range of values such as the 10th, 50th and 90th percentile estimates.

f) Is information available that could be used to estimate mercury intakes among Native Alaskans that result from ingestion of marine mammals such as whales and seals? If so, this information could be included in Appendix H. If not, this could be identified as a data gap.

g) Humans and wildlife most at risk are those who repeatedly consume fish, aquatic mammals or birds from a single location that is contaminated with mercury. When sport-caught fish are involved, advisories are used to provide information on the safety of frequent or long-term consumption. Advisories are not used for commercially-sold species such as swordfish or shark. This report could address the appropriateness of labeling commercial fish species that are suspected of being high in mercury. The report might also mention the FDA's new Hazard Analysis and Critical Control Point Program (HACCP) designed to prevent control food safety problems. The HACCP, which goes into effect in December, 1997, monitors "Critical Control Points," which could reduce exposure to methylmercury in fishery products.

Appendix H provides an overview of fish consumption rates for the general U.S. population and for several "high risk" populations. Fish intake rates broken down by age-group and gender were used to estimate methylmercury intake rates for each subgroup based on mean mercury levels for freshwater fish. Mercury levels for freshwater fish were taken from Bahnick *et al.* (1994) and Lowe *et al.* (1985).

This appendix is a valuable addition to the report. It is best used as a summary of U.S. fish consumption data and tissue mercury levels. It could be improved by updating the fish sampling results and expanded by including information about fish consumption patterns by certain "at risk" populations, such as pregnant and nursing women, pre-school aged children, and the elderly; and by adding a section that addresses the randomness of fish consumption.

4.2 Characterization of the Exposure Assessment

Because of uncertainties inherent in the emissions inventory and the model, the exposure assessment was characterized as being a "qualitative assessment based on quantitative modeling." In Charge 15, the Agency asked if that was a reasonable characterization, and if the uncertainties and conclusions drawn from linking the models together were appropriately described?

In the view of the Subcommittee, EPA's characterization is not only reasonable characterization, but, given the quality and reliability of the information available very appropriate characterization. However, the Subcommittee noted that, even though quantitative modeling is used for making order of magnitude estimates, there remains only qualitative treatment of uncertainty. Since the qualitative conclusions are based on the quantitative results from models, it would be useful to put some quantitative bounds on the results presented. In addition, the Subcommittee observed that, in making qualitative conclusions, models are used more than data, and the data and models are not effectively compared or reconciled.

One area in which we believe the report needs to provide a better communication of uncertainties is in the use of an appropriate number of significant figures. Qualitative results do not have three significant figures! This is a problem both in the Overall Executive Summary, the Executive Summary for Volume II, and throughout Volume II. Too much precision is implied by the way the numbers are presented with so many significant figures. Most of the results in this report are only good to one significant figure, if that. For example in Tables listing sources of mercury a better qualitative presentation would be to list sources as major (i.e. 20 to 50%), significant (1 to 10%) and minor (<1%).

There should be more effort to make sense of model predictions relative to multiple observations of mercury deposition over land and water. These observations could be used to put some type of bounds on the model reliability. For example, the EPA could pose and test the premise that Hg emissions are essentially 80 to 90% accounted for and then test models and deposition data against this premise to see if it makes sense.

Comparing human and natural emissions of mercury carries with it the implicit assumption that human emissions have the same impact on human health and ecosystems as natural emissions. This assumption needs to be given more consideration. Do human emissions have the same biogeochemical cycle as natural emissions? Do they spread over the same spatial range? What is the relative persistence of human versus natural emissions?

One issue that is not well-characterized is how to distinguish between global average concentrations and local and regionally elevated environmental levels. This will be an important issue for interpretation of deposition data over land, lakes, and ocean waters.

Instead of simply explaining how the models work and showing the results, as is done in this report, it would be more useful to work through the logic of the models and identify where important uncertainties exist and how these uncertainties impact the source/receptor relationships derived from the models. The modeling and exposure evaluation process has an implicit tiered approach that should be made more explicit. In the report there are several modeling and evaluation scales, such as local models (within 10 to 20 km of the source), regional airshed/watershed models, continental scale models, and global scale models. In the absence of more data, simple bounding mass balance assessments are probably all that can be done given the current scientific understanding of the biogeochemistry of mercury and its compounds.

4.3 Methylmercury and Fish Consumption

The EPA has estimated methylmercury and fish consumption using both cross-sectional and longitudinal data for the general U.S. population. In these studies, EPA consistently finds that a portion (albeit a small one) of the population consumes very large quantities of fish. It is these individuals who face the largest risks from methylmercury exposure and who pose the greatest concern to the Agency. Charge 16 sought guidance to determine if EPA had adequately assessed the number and types of individuals who consume fish in these relatively large quantities. Related questions addressed the uncertainties associated with characterization of such small portions at the extreme end of the population distribution, and the possibility of a methodologic artifact.

The Subcommittee believes that the agency has adequately assessed the number and types of individuals who consume fish in these large amounts, given the state of existing information. As stated on page 3-35 of Volume I, the EPA estimates that between 1 and 5% of the population consumes more than 100 grams of fish per day. This estimate is supported by the 1973-1974 National Purchase Diary survey that identified the 99th percentile intake rate of 112 grams/day and by the 1989-91 CSFII survey that identified 95th percentile estimates of 118.9 and 134 grams/day for adult females and males, respectively; and 99th percentile estimates of 178-224 grams/day. In addition, several studies cited in Figure 3-6 (3-34) of special populations such as sport fishermen, Native Americans and Native Alaskans identified 90th and 95th percentile estimates that exceeded 100 grams/day. In fact, two independent studies of Alaskan Natives reported mean daily intake rates of 109 and 452 grams/day.

In addition, the Subcommittee finds that the uncertainties associated with characterization of such small portions at the extreme end of the population distribution are appropriately considered and presented.

The Subcommittee found the intent of Charge item questioning the possibility of a methodologic artifact affecting the estimate of 5% of the fish-consuming population as being high-end consumers to be unclear. All population distributions have an upper 5% tail. Therefore, any survey of fish consumption can be expected to define an upper 95th percentile subpopulation that consumes fish at a higher rate than the rest of the respondents.

The real issue seems to be, "Is the fish intake estimate for the upper 95th percentile population accurate?" This is a more difficult question to answer. Certainly the 3-day survey method could have overestimated the daily intake rate, however, several earlier surveys did find people with intake rates of 100 g/day or more (Humphrey, 1974, 1988).

4.4 Sources of Data for Mercury Concentrations in Marine and Fresh-Water Fish and Shellfish

The Agency relied on three nationally-based sources of data for mercury concentrations in marine and fresh-water fish and shellfish. Some of these data were obtained within the past three years, whereas other data were obtained as long ago as 20 years. Question 17 poses issue of the use of these older data, and the report's documentation of the limitations of this methodology.

There are several reasons to question older fish data, including a) concerns over analytical quality and documentability; b) representativeness of the sampling protocols; and c) whether, due to changes in Hg inputs to the systems, average values may have increased or decreased between the time of the survey and 1997. Overall, the data at hand can be used with confidence. Of course, if more recent survey data are available, it would be prudent to utilize those where possible.

It is fairly unlikely that significant analytical bias exists in any of the major fish surveys of **total Hg** collected in the past several decades. This is because techniques necessary to quantify total Hg in fish have long been available. Because fish tissue is relatively high in Hg (ppb to ppm), the risk of contamination is small (unlike the case for water samples, where contamination at the parts-per-trillion level is commonplace). Factors that could bias analytical data include the following: (a) how were the below the detection limits (BDL) values were handled in constructing mean values? (If less than detects were discarded, then an over-estimate of mean values will occur); (b) what were the BDLs of the earlier surveys? (The poorer the BDLs, the greater the risk of bias -- most likely in the direction of over-estimation of mean values); c) how were fish

processed prior to analysis--i.e., whole, filleted, skin on or skin off? (Inclusion of tissue other than muscle will result in an under-estimation of consumption of methyl Hg); (d) were the fish analyzed truly representative of the size, region, and species normally eaten by the American population?

It would be wise to look over the original documentation for these surveys to be sure that protocols were both appropriate and equivalent between surveys. Finally, it should be noted that if any of the data were of methyl Hg, rather than total Hg, there is a significant risk of bias too low, as earlier methyl Hg quantification techniques (solvent extraction/GC-ECD detection) are notorious for poor recoveries and reproducibility. Low recoveries for methyl Hg combined with the potential for contamination with Hg(II) has likely been responsible for the low bias in estimates of % methyl Hg in fish (70-90%) from the '70s and '80s, compared to estimates from the '90s (95-100%).

With respect to the representativeness of the sampling protocols, the Committee notes that Bahnick *et al.* (1994) sampled only 5 bottom feeders and 5 game fish from 314 sample sites selected based on proximity to either point or non-point pollution sources. Only 35 of the sites were considered remote. Data for the bottom feeders was based on analysis of the whole fish rather than edible portions. Although this information is indeed useful in monitoring site specific concerns, its application to a national consumption guideline including marine species is questionable.

Having made these comments, the Subcommittee regards the mean concentrations from the Lowe data set as too low, and suggests that the EPA/Bahnick data sets are more representative of fresh water fish levels. This position is based upon comparisons of species for which there are many additional studies (usually from the Midwestern states where these fish are mostly consumed), such as walleye, pike, and yellow perch. From the summary data, there is no indication as to why these data set means differ, but we suspect that looking into the primary data will show differences in the representativeness of the fish analyzed (e.g., regions, lake types, fish size). If no such assessment can be made for the report, we suggest dropping the Lowe data set in favor of the EPA/Bahnick data sets, and/or other more recent surveys. The mean Hg for marine species in the National Marine Fishery Service (NMFS) database appears to be appropriate, although a look at the underlying assumptions and analytical figures of merit would be worthwhile. It is of concern that the NMFS database is mostly unpublished data (although the report stressed that only published data were used), for which the level of quality control through time is not established. Of particular importance is verification that the named fish in the data base do indeed correspond to the same fish that people in consumption surveys think they are eating. This is important at least for mackerel, where a big discrepancy between the observed concentrations between surveys may be attributed to different species called mackerel being analyzed.

4.5 Fish and Shellfish Consumption

The U.S. Department of Agriculture (USDA) has published data indicating that fish and shellfish consumption have risen approximately 25% since the early 1970s . These consumption data were employed without adjustment in this report to estimate current fish consumption. Question 18 asks if these data should be adjusted to reflect the overall trends in fish consumption, if so, how would the estimates of very high consumption (above the 90th percentile) be adjusted.

As the Subcommittee interprets this question, the issue is whether the consumption data from the 1970s should be used without adjustment, even though recent data indicate that consumption of fish and shellfish has risen approximately 25% since the 1970s. Based on comparisons to other types of market information, the Subcommittee is of the opinion that the numbers used by EPA for fish consumption are representative and perhaps somewhat high for representing the mid-range fish consumer (this is discussed elsewhere in this review). The USDA report of increasing fish consumption is difficult to interpret in terms of its impact on the very-high fish consuming individual. It is typical in food-consumption surveys, that high-end consumers who make food choices based on economic and taste preferences are less likely to move up and down with market trends and diet trends as much as the mid-range population. Thus, high-end consumers are not likely to increase their consumption proportional to the mid-range fish consumer. The Subcommittee expressed the view that the fish consumption data for the high end consumers should not be adjusted to reflect the trend reported by USDA.

4.6 Calculations of Methylmercury Intake from Crab

Calculations of methylmercury intake from crab were grouped without specific consideration of the particular species. These data are then linked to dietary survey data which typically do not list the individual species of many fish and shellfish consumed. Question 19 asks if this approach might bias the final assessment, if the limitations of this approach are adequately characterized in the report, and if these limitations going to materially alter the assessment of health risk associated with methylmercury exposures.

EPA's calculations of methylmercury intake from crabs were made by grouping data without specific consideration of the particular crab species consumed. These data are then linked to dietary survey data which typically do not list the individual species of many fish and shellfish consumed. The Subcommittee agreed that this was not an issue of concern for two reasons. First, individual crab species values did not differ drastically from one to another (confirmed by data for Dungeness crabs collected by a Subcommittee Member), meaning that the mean value is relatively robust. More

importantly however, is that crabs make up a very small fraction of American fish and shellfish consumption. Thus, for any reasonable value for Hg in crab, there would be no discernible change in the overall human methylmercury consumption values. The methylmercury consumption for average Americans is overwhelmingly dominated by tuna, pollack, and shrimp. In the case of high end consumption of crabs, this can only realistically be assessed by identification of the exposed population and the particular crabs that they are eating.

A concern was raised, however, over the more general issue of averaging different species, or fish of the same species but from different locations, under a single common name. The risk inherent in this was noted above for mackerel, where an order of magnitude difference is seen in mackerel of different species --and it was pointed out that the species lower in Hg are not the species that are commonly consumed by mackerel eaters. As noted above however, for the purposes of national population exposure estimates, these issues will not affect a mean exposure that is so heavily weighted by three well-documented species (tuna, pollack, shrimp). In assessing the high end consumer groups, it is again critical to know clearly the exact species and lakes from which the fish are harvested, as order of magnitude differences can be seen over a few mile radius due to differences in water chemistry (*in situ* methylation rates).

4.7 Characterizing Total Population Exposure and Risk

In Volume III (Appendix H), the EPA characterized total exposure (and by association) total risk by considering methylmercury exposure from marine fish and shellfish together with consumption of methylmercury from fresh-water or estuarine fish and shellfish. The Agency, in Charge 20, wanted input as to how well the current approach characterized total exposure and dealt with associated uncertainties *vis-a-vis* sources of fish (inland freshwater versus marine).

The Subcommittee agrees that inland lake fish appear to represent the greatest acute source of exposure, but also notes that the contribution made by the marine environment is important and should not be ignored because it represents background or chronic exposure. Certain near-shore marine waters may also represent acute exposure sources.

The draft report correctly concludes that the exposure levels at which one infers risk for the general population are relatively low. However, total population exposure (all routes and pathways) and the related risk is not and cannot be fully characterized because of the large variability in human consumption of fish and interspecies and interregional mercury concentrations. Total risk cannot be characterized at this time because of the uncertainty of upper bounds exposure due to the variability found in existing data bases. For freshwater fish, there are only two surveys of “national” scope and the mean mercury body burden for all fish differed between them by more than a

factor of two. This large difference was also seen in the highest mercury levels recorded in the surveys (Lowe versus Bahnick). Although more data on marine fish are available, there appears to be limited information on near shore marine fish. These areas receive freshwater discharge and may well represent sources of acute exposure similar to certain inland freshwater lakes. Total population exposure/risk is difficult to characterize given the variability and gaps in existing data sets. These impact most significantly on the ability to accurately model and assess upper bound risk.

The draft report does provide a thorough and complete record of the existing data available. Many studies and data bases were found and reported in Appendix H. The uncertainties in and variability of existing information are also well presented (pages H-65-67).

Given the uncertainty in exposure assessment, especially for the upper bound of human exposure, we are not confident that accurate modeling of risk for this group can be performed. The assumptions used in Volume VI to model human risk may be overstated. Given the variability of mercury in fish and information gaps on "subsistence" or high consumers of fish, one must question use of the assumptions that these people eat trophic level 4 fish exclusively, that all trophic level 4 fish have 5-fold higher mercury levels than trophic level 3 fish, what fish mercury level should be used in the model and what is the actual size of the population at greatest risk. Overestimates in assumptions can show estimated human intake exposure in excess of that actually occurring in the field. The conclusions section of Volume VI (pages 6-1 to 6-3) acknowledges this problem.

4.8 Hair Mercury Concentrations

Some data exist on hair mercury concentrations in U.S. residents. Question 21 asks if this data base is adequate to predict the distribution of hair mercury in the general U.S. population.

Hair total mercury levels provide an index of blood total mercury when the major mercury exposure is in the form of organic mercury, particularly methylmercury. Hair mercury levels do not correlate well with blood mercury when exposure involves primarily inorganic or elemental mercury. There is a relatively small body of data describing hair mercury levels in U.S. residents. Most of the available data comes from research studies containing small numbers of individuals whose hair was measured in the course of studies on methylmercury exposure and disposition. There are many more studies involving hair analysis for mercury that have been conducted outside of the U.S. These also are research oriented and do not constitute population monitoring efforts. One exception is an unpublished study supported by the Food and Drug Administration which contained approximately 1500 U.S. residents from across the country. The draft report mentions this study but suggests that it does not have much

scientific weight because the variability in the data was not given. An expanded explanation should be given because this apparently is the largest attempt to measure mercury levels in the population and the data would appear to be useful.

The current draft mercury report correctly indicates that statistically representative population monitoring studies are not available at this time. The Subcommittee's Exposure Workgroup discussed the need to monitor the U.S. population for mercury exposure. Some Members felt that it would be beneficial and others thought that it was sufficient to monitor more highly exposed subpopulations such as subsistence fish eaters.

4.9 Hair Mercury Concentration as an Index of Methylmercury Exposure

The draft report identifies hair mercury concentration as the most appropriate available index of methylmercury exposure. Question 22 asks if this assumption is consistent with the available data, if the exposure estimate approaches used are relevant and appropriate, if the predicted exposure ranges are consistent with other published exposure analyses, and if the uncertainties of this assumption appropriately presented.

The preponderance of studies reviewed that are relevant to the developmental health endpoint, upon which the Reference Dose (RfD) for methyl mercury is based, have used total hair Hg concentrations as the most appropriate metric of exposure. The use of hair has practical advantages over utilization of body fluids or tissues given the non-invasive nature of such samples. In addition, Hg concentrations in hair provide an integrated measure of dose over time, as compared to concentrations measured in whole blood or some fraction thereof, which only provides levels existing at the time of sampling. In addition, there is a general correlation between total mercury concentrations in hair and blood, which support the assumption that hair analysis may be comparable in its validity as a bioindicator to blood, with the additional practical advantages described above. Finally, the current and proposed RfD is based on results from the Iran Hg poisoning episode, from which only maternal hair analysis data are available as an indicator of in-utero exposures. To this extent, the draft report is generally consistent with the preponderance of the studies, and presents some of the limitations regarding the RfD estimate. In addition, the authors have made an extraordinary effort at compiling and evaluating the available literature. They should be commended for this effort, given the difficulty and controversial aspects of this task. The comments that follow are not intended as a criticism but are meant to provide some guidelines to strengthen the review with respect to exposure-dose issues.

Most of the discussion on the appropriate metric of dose is presented in Chapter 2 of Volume IV: Health Effects of Mercury and Mercury Compounds, with further reference in Chapter VI which presents the risk characterization for the U.S. population.

Estimated exposures for the U.S. population based on emissions and multimedia transport models are presented in Volume III. The document could benefit from a section dedicated exclusively to exposure and exposure-dose relationships, either as an additional Chapter in Volume III, or as the first Chapter in Volume IV. This section should address specifically some of the issues that are not discussed in the present format of the document, or that are presented in a diffuse manner throughout Chapter IV. These issues include:

a) clear definitions of what metric constitutes an indicator of exposure, dose, or effect and how these metrics relate to each other. In its current version, the draft document (and the preponderance of the past and present population-based studies) uses the number of fish meals as the main indicator of exposure while exposure should be the concentration of methyl mercury present in the fish times the amount of fish consumed during a day, week, etc. The number of fish meals is a surrogate for exposure and, as such, could lead to misclassification. The most appropriate exposure indicator would be the amount of methyl mercury ingested via the food chain over a relevant period of time. Since the concentration of methyl mercury varies by type of fish, where it is caught, and what parts of the fish are eaten, the number of fish meals consumed over time may or may not be a good indicator of the exposure depending on the other determinants of exposure, as mentioned above.

   The use of number of fish meals could lead to individual misclassification of exposure. For example, inspection of the data presented in Table 2 of Grandjean *et al*. (1992) shows that if the only information available for exposure classification were the number of fish dinners consumed per week, we would be likely to place individuals in the wrong “exposure” category according to the blood or hair levels because the range of the latter measurements is relatively broad. In part, individual variability in compartmental distribution and disposition of methyl mercury could account for the lack of better predictive validity. However, since the number of fish dinners consumed per week has not been demonstrated to be a good indicator of exposure (based on actual Hg concentration and fish consumption data), we cannot determine if only individual variability is important in explaining the potential for misclassification. Mercury concentrations in blood, urine or hair could be indicators of exposure if it can be shown that they are correlated with exposures as determined above. On the other hand, mercury concentrations in biological fluids or tissues could be used as markers of effect if they were shown to be associated with particular effects in a consistent manner. The current document uses mercury concentrations in hair for dual purposes, that is, as a marker of exposure (as indicated by number of fish meals consumed)

and developmental effects produced by in-utero exposure. EPA has an opportunity in the future to evaluate the association between exposure and the appropriateness of using the concentration of Hg in biofluids and tissues as indicators of exposure by better estimating actual exposures (that is, beyond number of fish meals consumed) using the recently completed and on-going population studies. The investigators in these studies should be able to derive those estimates which can then be related to the bioindicator data. Perhaps it would also be useful to combine the data from the various studies in New Zealand, Peru, the Faeroe and Seychelles Islands using a meta-analysis type approach, if possible, so the exposure-bioindicator relationships could be evaluated in more detail as a function other population variables.

b) broaden the discussion of limitations on the usefulness of hair mercury concentrations to include practices among the U.S. population that may affect these concentrations. Besides the limitations discussed in the document (e.g., acute vs. chronic exposures, genetic differences, etc.) that may affect the usefulness of this bioindicator in U.S. populations, there are cultural practices that could also be important (and for which data are probably lacking). Populations in developed countries, particularly women in the U.S., engage in chemical treatment of their hair for cosmetic purposes far more that those in developing countries. Do treatments such as permanents, straightening, bleaching, etc. alter the concentration of metals present in hair, including Hg? If this is the case, the usefulness of mercury concentrations in hair would have limited applicability in the U.S.

c) related to b) above, discuss the usefulness of hair analysis given multiple exposure pathways to different forms of Hg. Exposure to Hg in the U.S. may be dominated by other than methyl mercury in foods, for example exposures to elemental Hg emissions from Ag/Hg dental amalgams. Would this affect the applicability of analysis of mercury in hair as an indicator of in-utero, methyl mercury exposures?

Other issues that the document should address include:

a) since brain development does not end at birth but continues well into childhood, there could be a potential for subtle developmental effects due to ex-utero exposures, for example via breast milk. There is no RfD for children. Is there evidence that exposures after birth could affect development and, therefore, should there be a guideline for children's exposure?

b) a more careful attempt at trying to identify U.S. sub-populations that may be at increased risk of exposures, particularly since the “average” individual is not at risk.

4.10 Linking Mercury in Fish and Current Anthropogenic Emissions

Although the modeling exposure assessment focused on anthropogenic emissions, the fish consumption analysis considered measured mercury concentrations in fish tissue regardless of the mercury’s origin. Thus, there is considerable difficulty in assessing or describing how much of the mercury in fish is attributable to current anthropogenic emissions. Questions 23 addresses the approach taken by the Agency in this assessment, asks the advice of the Subcommittee regarding the differentiation between current emissions and their impacts relative to the “body burden” approach of the fish consumption analysis.

This Charge issue, addressing the exposure assessment, goes to the very heart of the prime objective of the EPA report: Can a quantitative linkage be established between patterns of anthropogenic atmospheric emissions and mercury concentrations ultimately manifested in fish?

As the various specific questions in this issue point out, it is extremely difficult at this time to determine such a relationship in quantitative terms, although the report concludes a "plausible link" exists between this proposed cause and effect. Therefore, a quantitative linkage was not established in the EPA study in a real sense based on comprehensive field data, but a qualitative linkage was postulated based on theoretical models and limited field data.

Why was this not done? At least two reasons are responsible for this shortfall. The first of these is the protracted time course of mercury effects in the context of the global mercury cycle. There are many dynamics in the relationship between atmospheric mercury and methylmercury levels in fish, and the various steps may span long time periods, making the quantitative description of the linkages between steps all the more difficult. This problem is understandable and perhaps deserves a bit more emphasis in the EPA report.

The second reason for the shortfall is the lack of field data, covering the full spectrum from emission through deposition to methylation and finally appearance in fish, near U.S. anthropogenic sources of concern. Few experimental studies exist that precisely document the cascade of changes that occur when mercury emissions from a given source are varied. A 100-year mercury emission elimination experiment would be a revealing, albeit completely impractical, research project to address this question. Perhaps more feasible would be an historical analysis of mercury deposition changes,

using core samples in lake beds and ocean bottoms. Many such studies, based on sediment cores from lakes, oceans, and ombrotrophic bogs are available (Hurley *et al.*, 1994; Rada *et al.*, 1993; Rada *et al.*, 1989; Compeau *et al.*, 1985; Choi, S.-C. and R. Bartha, 1994; Gagnon *et al.,* 1996) These data could be used in geochemical/ecological models to predict the down-the-line changes that should have occurred given what we do know about the linkages. The model outputs could then be compared to data on historically relevant changes, such as fish methylmercury levels (where known), and adjusted accordingly. But this is intended as a research recommendation, not a currently feasible analysis.

Given these problems, therefore, it is reasonable and appropriate that EPA took the approach that they did. Advice on dealing with this issue follows:

a) Although EPA should not necessarily try to quantitatively estimate the contribution of current air emissions to mercury in consumed fish, it should nevertheless provide some analysis of natural and old anthropogenic emissions, using the above mentioned sediment studies, so as to indicate the effect that might be expected in a reduction of current emissions.

b) In doing so, EPA should showcase localized studies, especially on point-source emissions in freshwater systems (and perhaps marine/estuarine cases like Minamata), where a direct linkage between field data of mercury emission and human effects is demonstrable because the temporal and spatial scales are limited.

c) EPA should stress in the report the global picture: U.S. emissions contribute to total global atmospheric mercury and the resulting deposition in the oceans and on land. This ultimately must contribute to total mercury loads in fish, since elemental mercury in the environment is neither created nor destroyed.

   Because methylation is complex and not well understood, however, it cannot be assumed that a change in total mercury emissions will be linearly related to any resulting change in methylmercury in fish, even taking into account the role of natural and old anthropogenic sources. It should be made clear that the variability in MeHg production among ecosystems may be as large as the effect of Hg contamination Therefore, EPA should emphasize to decision-makers the difficulties of quantifying the linkages, while underscoring the plausibility of the qualitative connections on a local scale and the certainty of a linkage on a global scale.

4.11 The Biokinetics of Methylmercury in Grain and Fish

In its assessment, U.S. EPA assumes that the biokinetics of methylmercury from contaminated grain approximate those resulting from methylmercury from fish. In Question 24, it asks if this assumption consistent with the available science.

There is no compelling evidence to suggest that the toxicokinetics of methylmercury (MeHg) ingested in grain (as in the Iraqi poisoning episode) is different from that resulting from ingestion of fish (the typical exposure route of humans). The best evidence for this is a study in which cats were fed contaminated fish, control fish, or MeHg in a non-fish diet (Charbonneau *et al.*, 1974). No differences were observed in degree of MeHg neurotoxicity, latency to toxicity (ataxia), tissue levels or distribution of Hg. Some discussion in the EPA document focused on potential for Selenium (Se) to protect against MeHg neurotoxicity, since Se levels may be higher in fish than most other foods. While co-administration of MeHg and Se apparently results in decreased MeHg concentrations in kidney, Hg levels in brain and liver are increased (Suzuki and Yamamoto, 1984; Brzenicka and Chmielnicka, 1985; Komsta-Szumska *et al.*, 1983). Se also increased methylmercury staining in spinal cord and nerve cell bodies (Møller-Madsen and Danscher, 1991). A positive correlation between brain Hg and Se levels was observed in monkeys exposed to MeHg with no exposure to Se other than regular diet (Björkman *et al.*, 1995); the mechanism for this is unknown. The apparent protective effect of Se against overt high-dose MeHg toxicity has been attributed to the decreased accumulation of MeHg in kidney in the presence of Se (Stillings *et al.*, 1974). It is doubtful that this effect on kidney is relevant at environmental levels of MeHg. It has also been suggested that the formation bis (methylmercury) selinide may render MeHg less toxic (Naganuma and Imura, 1980), but there is no direct evidence for this. In addition, although increased fish consumption was associated with a very modest increase in (cord) blood Se levels in a fish-eating population, the blood Hg levels increased much more dramatically (Grandjean *et al.*, 1992). Grain may also contain substantial levels of Se, depending on the soil in which it is grown. Based on the questionable relevance of any protective effect of Se against high-dose MeHg nephrotoxicity, the fact that increased Se intake results in increased brain Hg levels following MeHg ingestion, and a complete lack of data on the Se status of the human (Iraqi) population exposed to MeHg via grain, there is no reason to postulate that ingestion of MeHg in a fish matrix would result in decreased toxicity compared to ingestion in a non-fish matrix. Indeed, the study that addressed this directly found absolutely no difference in toxicity or tissue levels when MeHg was administered as contaminated fish or added to a non-fish meal (Charbonneau *et al.*, 1974).

4.12 Uncertainties in the Fish and Grain Consumption Analyses

Charge question 25 asks if the uncertainties in the fish and grain consumption analyses are adequately and consistently presented in the draft report.

A major uncertainty in the fish consumption data are that the current supply of 'fish' for U.S. consumption has significantly changed through the last decade and projected trends and predictions indicate continuing changes which must be accounted for in any national projection to address methyl mercury consumption in the United States. The EPA report relies on methyl mercury assessments focused on fish from United States environments, rather than existing markets. This approach is understandable in a report also attempting to link mercury sources with contaminated foods, but it only accounts for foods from domestic sources. Since the 1980's, nearly 70% of the seafood, including fish, consumed in the U.S. are imported and this supply trend is predicted to increase in response to steady-state domestic sources and increasing restrictions on both commercial and recreational harvest. Likewise, aquaculture sources, both domestic and international, have grown to represent nearly 20% of U.S. seafood, including fish, consumption. Aquaculture remains the most plausible source for future fish supply to meet domestic demands. The EPA report does not account for this segment of consumption, which is based on cultured products grown in shorter duration in more controlled conditions for water quality and feed composition. Although there is no evidence to suggest that MeHg levels are substantially higher or lower in imported fish than in fish from domestic environments, this should be noted in the report as an additional source of uncertainty.

In addition, the EPA cautions against consumption of certain aquatic predators, i.e. swordfish, shark, and barracudas. Recent federal and state-based fishery management plans since 1990 are restricting the production of such fish due to conservation concerns, recreational plans, and separate food safety issues. For example, harvesting of sharks about Florida is soon to be prohibited; many recreational billfish practices have adopted, and enforced catch-and-release programs, and concerns for ciguatera have banned harvest and commercial sales of barracuda in regions of southern Florida, Puerto Rico, etc. These supply changes, which favor the reduction of risk from consumption of fish from the United States, should be noted in the final report.

The Committee particularly wishes to emphasize and alert EPA to all of these ongoing changes in the sources of fish in American diets and to recommend that EPA be prepared to address such changes in future risk assessments.

EPA's methods for determining the methyl mercury load in "fish," as documented in the draft report are confusing and difficult to understand in several places**.** Section 2.1 in Appendix H (p. H-45) exemplifies the confusion. This is a critical paragraph in the

report and warrants correction and clarification. Part of the problem seems to stem from typographic errors:

a) Line 9,...from Table H-36 (Consumption of freshwater fish.. .) does not correspond with Table H-36, page no. H-51.

b) Use of methyl mercury data from limited freshwater fish alone (p. H-45, section 2.1) to estimate the range of [national] exposure from total fish consumption is not appropriate. The vast majority of fish consumed is from marine sources. In fact, the EPA reports that the CSFII 89/91 survey reported less than 31% of the identified 'fish eaters' ate freshwater fish (page. no. H-8). In conflict, the Executive Summary (page no. 3-33) states that the CSFII 89/91 survey found 33% of the 'fish and shellfish' eaten came from freshwater and estuarine species. It is not clear how shellfish and estuarine species only boost consumption by 2% (31%+2%=33%).

The report offers no definitions for marine, estuarine, river and freshwater fish. This distinction is important, particularly for certain subpopulations considered to be at higher risk. For example, would the Alaskan salmon be marine, estuarine or river fish? Would commercial at sea harvest differ in concern for the same fish taken in river migration? Simple reference to 'fish' complicates interpretation of some parts of the report. Addition of some definitions is recommended; the text should also be reviewed and edited to reflect the added definitions.

It is also not completely clear how the NMFS methyl mercury data for marine species was used. The Executive Summary (p. 3-33) mentions a "mixture of fish/shellfish reported in CSFII 89/91 to be consumed by persons surveyed is 0.134 ppm." How the 'mixture' was calculated is not clear in Vol. III on Section H. There are also concerns that the NMFS data are not easily accessible and lack peer review.

Portions of the report and subsequent discussions by EPA staff during the public meeting mention use of weighted intakes for methyl mercury based on matching the 'fish eaters' reported fish vs. the respective reported methyl mercury levels for the respective fish. No such comparisons are offered in the report and if available would be subject to critique for a) proper fish identity, and b) appropriate source/comparisons. It is highly probable that some of the recall survey data on the type of 'fish' consumed is inaccurate. The proper identification is limited by the persons' knowledge, use of local vernacular, and/or reliance of package labels or restaurant menus that are also suspect. Product mislabeling in retail and restaurant settings has been measured as high as one-third of the commercial events in certain states. Increasing use of imported products further complicates this problem. Thus, aligning 'recalled' fish consumption by fish type with estimated methyl mercury concentration is compromised

by proper product identity. The report should note this source of uncertainty explicitly.

A concern that the EPA report placed too much reliance on CSFII 89/91 and failed to incorporate data from other consumption surveys has been repeatedly expressed by numerous reviewers. The survey, by virtue of its short (3-day) sample and division by 3 days per amount eaten, tends to overstate consumption for an infrequently consumed product. It also tends to understate the total number of consumers. This survey also extrapolated data on 'recalled' species and amount of fish generally consumed in a single meal to an estimate of daily exposure over an extended period. There is no data to support such an extension. The only way such an estimate should be valid is by assuming a consumer eats the same species and amount in each and every three day period throughout the year. Data from CSFII 89/90 does provide good information on average amounts consumed in an eating occasion. Utilizing this information with other surveys which indicate frequency of fish eating occasions over a longer period of time would produce a better estimate of fish consumption and methyl mercury intake.

4.13 Biokinetic Parameters for Children vs. Adults

The EPA assumes the biokinetic parameters for children are identical to those of adults. The Subcommittee was asked, in Question 26, if such an assumption introduces bias into the assessment, if the uncertainties were adequately and consistently presented in the draft report, if the conclusion that children's lower body weight results in higher exposure than to adults, and if using 3-day consumption survey data could introduce an artifact affecting the findings.

There are no published data which indicate that the biokinetics of mercury differ between children and adults. On the other hand, there are data which indicate that the blood mercury concentrations of newborn humans or non-human primates are approximately 1.5 - 1.8 times higher than those of their mothers, suggesting that the fetus may become a sink for mercury following maternal exposure. This is also consistent with the concept that the fetus and new born probably experience higher exposures due in part to lower body weight and given the above data, this concept is probably not an artifact of the 3 day consumption data. The uncertainties regarding this concept are adequately addressed in the EPA's draft document. It should also be noted that fetuses and newborns may be at greater risk for mercurial toxicity since there are a number of mercury sensitive cellular and molecular processes which are highly activated during this period. For example, methylmercury interferes with cell migration in the brain, a process which occurs during fetal development in humans.

4.14 Methodologies for Estimating Body Burdens of Mercury

Charge question 27 asks if methodologies other than hair concentrations could

be used to estimate body burdens of mercury.

At steady-state exposure to methylmercury, hair and blood mercury levels are highly correlated. Both of these biological materials can be used to estimate an individual's mercury exposure. The principal advantage of using hair as a biomarker is the ability of segmented samples to provide an exposure history. The major disadvantage is that hair is not routinely collected or analyzed. Therefore, researchers who limit their analyses to hair will be unable to use existing biological specimens that were collected for another purpose such as the National Health And Nutritional Examination Survey study for mercury exposure assessment. In addition, since hair mercury
analyses are less commonly done than blood and urine mercury levels, many laboratories are unable to perform the test and costs may be higher than for blood.

Concerns have also been raised about the ability of hair to adsorb mercury from the air. This is most likely to occur in an occupational setting. Unless the hair is carefully washed to remove surface-deposited mercury, measured mercury levels are likely to overestimate dietary intake rates for some individuals. The Subcommittee's preference is to use hair and blood mercury levels in combination to assess an individual's exposure since neither is a perfect predictor by itself.

4.15 Priority Areas for Research

In response to Question 40, the Subcommittee recommends the following research priorities in exposure assessment:

a) Exposure measurements to better delineate the upper or high end of the distribution of population exposures should be a high research priority.

b) Exposure measurements of pregnant women should also be a high priority since this will enable EPA to address exposures to the most vulnerable population - fetuses. It should be possible to obtain statistically selected samples of blood and/or hair from pre-natal clinics and analyze these for mercury. Complementary data on fish eating and health of the baby should also be obtainable for this population. This will also provide information on potential high end exposures in the population.

c) Research is needed to estimate exposures of the population to inorganic mercury since these exposures can add to the risks.

d) Research is needed to better delineate biological susceptibility in the population. Even among highly exposed populations, not all subjects

experience adverse health effects, suggesting that there are differences in susceptibility.

e) Given the rapid changes in the types of fish being consumed and their sources, e.g., changes in international sources of marine fish, over fishing of some species, and increasing supplies of farm-grown fish, the Committee recommends that EPA and FDA cooperate to provide surveillance of fish for environmental contaminants such as mercury.

f) More long-term research is needed to better understand the dynamic behavior of mercury in the environment. Such research should included integrated and iterative development and use of models and environmental measurements. Opportunities for international cooperation and coordination in such research should be sought since there is a global component to environmental mercury contamination.

4.16 Conclusions

The Subcommittee's major conclusion, based on the existing data and the analysis of these data, is that the majority of the population is not experiencing methylmercury exposures that are of concern. The Subcommittee also agrees that the high end of the distribution of methylmercury exposures is very uncertain with respect to exposures, total number of people (and percent of the population) who may be experiencing exposures high enough to cause adverse health effects, and the actual sub-groups who are highly exposed. Additional comments on the human health aspects of the EPA's draft report will be found in Section 5 of this report.

With respect to the modeling linkage between emissions from anthropogenic sources and human exposures, the Subcommittee agrees that it is plausible that current anthropogenic emissions are contributing to human exposures. However, the relative contributions of current anthropogenic emission sources, global backgrounds, recycling of old emissions and natural background to human exposures of methylmercury are highly uncertain. Furthermore, the time constants for intermedia transport are not known. **Nonetheless, since mercury does not degrade in the environment, current anthropogenic emissions will add to various sinks as well as to the fraction of global mercury that is actively circulating in the biosphere, surface waters, soils. In addition, emissions from both the U.S. and from other countries can impact the U.S. environment and exposures of humans and wildlife.** The estimated exposures (based on transport and fate environmental modeling) are consistent with other lines of evidence regarding population exposures. However, this section of Volume III of EPA's draft report is not clearly written and confuses environmental transport and fate modeling with exposure analysis.

The Subcommittee concurs with the conclusion that fish are the major source of methylmercury exposures for the human population. This is supported by the exposure analysis based on methylmercury concentrations in fish and fish consumption data. The market basket survey data of methylmercury in various foods consumed by the population also provide strong support for this conclusion.

The exposure analysis based on fish consumption must be regarded as a "snapshot" in time. The species of fish that are being consumed and their sources are both changing rapidly due to over fishing of some species, changes in the global market in marine fish and more domestic fish supplied by fish farms. The impact of local anthropogenic sources of mercury is likely to be greatest on freshwater and estuarine fish. There are, however, two potential biases to the exposure analysis based on fish consumption which should be checked in order to provide greater confidence in the analysis. First, we recommend that the consumption data from the CSFII survey should be checked against production data. These will not agree exactly but should be reasonably consistent. Second, the average concentrations of methylmercury in fish used for the exposure assessment were provided by the National Marine Fisheries Service. The Subcommittee recommends that EPA determine how measurements of methylmercury in fish which were below the analytical limits of detection (BDL) were statistically treated in arriving at the mean concentrations. If the BDL values were excluded, than the means are biased high. If BDL values were included in the estimation of the mean using one of the standard methods for this, then the means can be considered good estimators. However, if a very large percentage of the measurements for any fish species were BDL, then the estimates of the means are much less reliable.

The Subcommittee strongly recommends that EPA edit and shorten Volume III on Exposure to eliminate redundancies and clarify the logical sequence of the exposure analysis. The basic questions that should be addressed in the volume on exposure are:

a) What is the distribution of exposures of the U.S. population to methylmercury?

b) What are the exposures of wildlife to methylmercury?

The introduction of this volume should more clearly lay out the three approaches that are used to estimate exposures to methylmercury -- fish consumption data combined with methylmercury concentration measurements in fish; scenario exposure estimates based on environmental transport and fate modeling to estimate concentrations in freshwater fish; and existing, albeit limited data on mercury concentrations in hair.

Environmental transport and fate modeling is used in two ways in this volume, and it is presented and discussed in a confusing way. First, the volume should be revised to clearly distinguish between environmental transport and fate modeling and exposure analysis modeling (which are confused in this document). These two techniques are not the same thing. Secondly, transport and fate modeling is also used in two ways in this volume. It is used to estimate of methylmercury concentrations in fish for human and wildlife exposure estimation. It is used as well to provide a basis for linking domestic anthropogenic emissions of mercury to methylmercury exposures of the U.S. population and wildlife. These two different applications need to be clearly

distinguished. Finally, the materials on mercury measurements in hair should be in Volume III since they provide a biomarker of exposure.

In the Subcommittee's opinion, EPA's Dioxin Risk Assessment report (EPA, 1995) provides a very good model for the organization and analysis of information on mercury.

EXPOSURE APPENDIX 1

General Comments

Volume III should be rigorously edited for greater clarity, improved logical flow and elimination of redundancies. This volume is now written with an emphasis on the transport and fate modeling of emissions, rather than an objective scientific analysis of human (and wildlife) exposures to MeHg. The central question that this Volume should be addressing is "What is the distribution of exposures of the U.S. population?" Some suggestions for reorganizing and editing this volume are as follows:

a) The Introduction should present an overview of the three different approaches used to estimate exposures of the population to MeHg and explain that each had a somewhat different purpose. The introduction should also present a clear road map of the overall flow of the arguments to be made. This would help the reader enormously. As now written, the reader must figure this out the hard way - read through the entire volume and then go back and re-read sections to make sure he/she understands what it's all about. These three approaches and their purposes are:

   First, transport and fate modeling is used to estimate the possible contributions of anthropogenic sources of Hg to MeHg in fish. Long-range transport and fate modeling is used to estimate the "average" or background concentrations of MeHg in fish, etc., from emissions that are dispersed over long distances. The contributions of local sources are added to the "background" contributions to estimate totals. Exposure scenarios are then used to evaluate the potential contributions of anthropogenic sources to exposure through the food chain. This should be explained succinctly in the introduction.

   The second approach is to combined diet consumption data with the concentrations of MeHg measured in food in order to estimate the average exposure for the population. This is probably the most important and extensive analysis of exposure presented. It"s the only one that gives an estimate (and it is reasonably robust) of the average exposure of the population. This should not be relegated to an Appendix (H).

   The third approach is to examine the concentrations of Hg in hair to see if they are consistent with the estimates of average exposures from the dietary analyses. The Hg in hair data should be included in Volume III. These data, while not as statistically representative as the dietary exposure assessment, provide important supporting evidence that the dietary exposure assessment is correct.

b) The overall organization of this volume is very confusing. We suggest that a more logical organization would be as follows:

Present the environmental measurements first, as Chapter 2. The purpose of presenting these data is to show the levels in different media and conclude that air, water and soil are NOT major exposure concerns. However, the food measurements do indicate that fish is the major source of exposure. The tables that are presented should be only those need to provide the evidence that these are scientifically sound conclusions. It may also be possible to eliminate some of the tables in this section, particularly those that are redundant with tables in Appendix H.

Also, the section on the chemical properties would be more logical in Volume 2, before the discussion of source emissions. (See the Dioxin Report).

Chapters 3 & 4 should present the transport and fate modeling, with an explanation of the purposes of the modeling. The environmental concentration predicted by the modeling can be compared to the existing measurement data, where appropriate, to demonstrate that the models and measurements are consistent (one purpose). The second purpose is to use the modeled concentrations in scenario estimates of potential human exposures.

Chapter 5 should then be the exposure analyses for the scenarios. This chapter also provides some upper bound estimates of exposures.

Chapter 6 should present the population exposure assessment based on dietary data. It"s very surprising that this ends up in an appendix instead of being a main feature of the exposure assessment volume. This and the hair Hg are much more immediate estimates of human exposure than multi-media models that depend on many input parameters that are not well known or not known at all.

Chapter 7 should present the Hg in hair data and compare these data to the data from Chapter 6 and from the scenario modeling (Chapter 5).

Transport and fate modeling is used to understand the processes by which the pollutant is transported through the environment and finally comes into contact with humans or wildlife. But it is not exposure assessment *per se*! Exposure analysis requires the additional step of estimating contact between the pollutant in an environmental medium with a human (or animal).
It is strongly recommended that the definitions of exposure and dose, which are given in this volume, be used correctly and consistently throughout the

volume and that transport and fate modeling be clearly distinguished form exposure analysis.

Specific Comments

The term "exposure" is frequently confused with (and used interchangeably with) transport and fate modeling in this volume. These are not the same. Exposure is defined correctly on p. 1-9 and 1-13 but then not always used correctly throughout this volume. For example, p. ES-2 - "Exposure Assessment of Local Deposition of Mercury" - delete "Exposure." This section discusses deposition of Hg, not exposure. Another example, on p. 1-10, paragraph 2 - direct measurements of mercury concentrations in source emissions DO NOT provide an estimate of exposure - unless the human is inhaling or ingesting the emissions.

H-4 First full paragraph is confusing. Why is the default value 6.5 g/day used by EPA if the overall consumption rate from the NPD survey was 14.3 g/day? Which rate is the last sentence referring to?

Table H-1 Do men and women over age 75 really report serving sizes that are 12% larger than those consumed by working aged adults? Has this pattern of consumption changed over the past 20 yrs?

Table H-2 Title could be improved to better describe the table contents. The no. and (%) reporting would be useful in second column, e.g. 70 (17%).

Table H-3 Shows grams per day in each column. Why aren't children aged 2-11 included?

Table H-4 Why are 2-9 yr olds omitted? It would be helpful to include lower consumption rates in table so that the columns total to 100%.

Tables H-6 and H-8. The footnote indicates that the data were weighted to be representative of U.S. population. How was this weighting accomplished? Some explanation of the weighting procedure should be included in the text.

Table H-10 Includes the Peterson *et al.* study. The percentage of males and females that reported eating 3 or more fish meals in this study are inaccurately listed as 0.15 and 0.26%. The percentages were actually 15 and 26%.

Pages H23 and H24 discuss the dependence of Alaskans from subsistence economies on marine wildlife including marine mammals. However, there is no attempt to quantitate dietary mercury intake for this susceptible population and no mention of the

source of mercury to the habitat of these animals. Such information would be a valuable addition to this section of the report.

Page H-24. The Peterson *et al*. study is again cited. Again, the percentages are listed as 0.15 and 0.26%. These should be corrected to 15 and 26% as in Table H-10 (see comment above).

Page H-26 First sentence - the word *anadromous* should be defined since it is likely to be unfamiliar to many readers. Second full paragraph - something appears to be wrong with the units in this paragraph and in Table H-19. The passage states that the finfish consumption rate for male members of these tribes was 14 times the default rate of 6.5 g/day. [6.5 x 14 = 91 g/day]. The next sentence indicates that the 50th percentile for these tribes was 32 g/kg bodyweight/day. [32 g/kg x 70-kg = 2240 g/day] Later in the paragraph the author states that the daily fish consumption rate for both tribes was 73 g/day. None of these values appear in Table H-19. Instead most of the values in this table are well below 1 gram/day.

Table H-20. Suggest changing the title to “The percentage of nursing women who reported consuming locally-caught fish.”

Table H-21. Fish purchases are reported in pounds per year. All other tables in this appendix have used metric weights of kilograms per year or given both units.

Tables H-22, 23, 24, 26 & 27 The listing of a mean values would be more meaningful if the number of samples tested and the standard deviation were included. The title should be revised to indicate that the values are averages.

Page H-42. The discussion of the “National study of chemical residues in fish” appears to have focused on mercury levels in fish caught at sites that were selected based on their proximity to contamination sources. Most of these contamination sources appear to have posed a threat via surface water discharges or groundwater seepage. This should be discussed in the report since the mercury levels measured in these fish are unlikely to be related to atmospheric deposition.

Tables 29 and 30. Please include an explanation of how the methylmercury exposure levels were calculated. It might also be helpful to explain why the estimated mercury intakes are essentially the same when calculated using data sets compiled by Bahnick and Lowe, and to explain how the data were weighted as mentioned in the footnote.

Page H-65 second paragraph. This paragraph was confusing and difficult to follow.

5. HEALTH ENDPOINTS AND SUSCEPTIBLE SUBPOPULATIONS

5.1 EPA's Assessment Methodology

The EPA reports available data demonstrating increasing severity and frequency of nervous system effects (particularly impairment in visual-motor integration) among pediatric subjects with increasing levels of maternal hair mercury. In question 28, the Agency requested comment on the soundness of its assessment methodology, and on the presentation of the uncertainties in the characterization of potential effects in the draft text.

The U.S. EPA has established an RfD for ingested methylmercury (MeHg) at 0.1 µg/kg-day based on the presence of the developmental delay or neurological deficits in infants exposed prenatally to MeHg in Iraq. The RfD in the draft report was based on the calculation of a benchmark dose approach that does not assume or require a No Observed Adverse Effects Level (NOAEL). A benchmark dose was estimated using a Weibull model on grouped data with a 95% lower limit on a 10% response level. These calculations yielded a benchmark dose of 11 ppm concentration of mercury in maternal hair. This was then converted to a mercury blood level assuming a ratio of 250:1. An uncertainty factor of 10 was used to account for variability in the human population, variation in the biological half-life and variation in the hair to blood ratio. All these assumptions were extensively documented. Additional analysis was performed using different groupings of the data which yielded similar benchmark dose levels. Basing the RfD on the Iraqi study is not ideal. This study involved an acute high level exposure from contaminated seed grain, rather than the chronic low level exposure from fish consumption that is the principal risk the RfD is designed to protect against. The report cites several studies involving chronic exposure from fish, including the New Zealand and Cree studies (see Table 2, below), from which benchmark doses have been derived, which are very similar to that derived from the Iraqi data. Moreover, recent risk assessments derived from experimental animal data (Gilbert and Grant-Webster (1995; Rice, 1992; 1996) supported a similar RfD. **The conclusions of the draft report would be strengthened considerably if the authors were to emphasize the convergence of these data from multiple studies based on different ethnic populations and species, exposures and developmental endpoints, all suggesting similar** RfDs. The Subcommittee has prepared a summary of the study data that is overwhelmingly supportive of the EPA RfD (see Table 2 -- prepared in part from a table presented by EPA at the meeting).

Investigators conducting two new major prospective longitudinal studies-- one in the Seychelles Islands the other in the Faeroe Islands-- have recently begun to publish findings in the literature and are expected to continue releasing their findings during the next 2-3 years. These studies have advantages over those cited in the previous

Table 2 Summary of Estimates for the Effects of MeHg in Humans and Animals

Study	Duration of Exposure	N	Exposure	Endpoint	Analysis	Maternal Hair Level (ppm)	Hair: Blood	Dos
Iraq	ST - seed grain	81	in utero	all developmental	BMD	11	250	1.1
				all developmental - "timing" endpoints	BMD	15	250	1.5
				all developmental	NOAEL	7-10	250	1.0
				delayed walking	LOAEL	14	250	1.2
				all developmental	LOAEL	11? (44 µg/L blood)		0.7
				delayed walking	threshold	10		
				delayed walking	threshold	80		
				delayed walking	threshold	>100?		
New Zealand	LT - fish	237	in utero	IQ (WISC-R), language	threshold	5-15	250	0.8
				used a PBPK model	BMD	10-31 (17)		1.7
Cree Indians	LT - fish	247	in utero	tendon reflex	LOAEL	10-20	250	1.0
Amazon natives	LT	29	adult	visual discrimination	LOAEL	20	250	1.0
Minamata	LT?	986	adult	Minamata disease	threshold	20	250	1.0
Peru	LT	131			NOAEL	30		
Data review	Animal & Human		in utero		LOAEL	10-20	250	
Data review	Animal & Human		in utero		LOAEL	10	250	

Adapted in part from slide presented by EPA at the Subcommittee's public meeting.
LT - Long-term; ST Short-term

paragraph in that they have much larger samples sizes, a larger number of developmental endpoints, potentially more sensitive developmental endpoints, and control a more extensive set of potential confounding influences. On the other hand, the studies have some limitations in terms of low exposures (to PCBs in the Faeroes) and ethnically homogenous societies. Since only a small portion of these new data sets have been published to date and because questions have been raised about the sensitivity and appropriateness of the several statistical procedures used in the analyses, the Subcommittee concluded that it would be premature to include any data from these studies in this report until they are subjected to appropriate peer review. **Because these data are so much more comprehensive and relevant to**

contemporary regulatory issues than the data heretofore available, once there has been adequate opportunity for peer review and debate within the scientific community, the RfD may need to be reassessed in terms of the most sensitive endpoints from these new studies.

The EPA draft document provided an extensive review of the uncertainties associated with the studies cited. The reanalyses of the Iraqi data using various grouping factors is commendable. **However, we recommend that the EPA consider information that suggests that the uncertainty factor be increased.** It is striking that no new data are available for risk assessment. For example, the Faeroe Islands data (also animal data) indicates that the fetal exposure may be greater than maternal exposure. In this study fetal cord blood mercury levels averaged 80.2 ppb while maternal blood levels were only 38.1 ppb. Animal data supports that the fetus may act as a sink for mercury. The report extensively reviews blood mercury kinetics but has little to say about fetal brain mercury levels. Although the data are slight there are indications from recent monkey studies that the brain mercury half-life is very long (Vahter *et al.*, 1995). The RfD for MeHg is based on results from an acute exposure study while most MeHg exposure is thought to be long term. This may be an additional reason to increase the uncertainty factor. There are also indications of age related changes where MeHg may accelerate neurodegeneration associated with aging from human data (Igata, 1993) and animal data (Rice, 1989a; 1989b). In evaluating neurotoxic effects from low exposures such as with methyl mercury, it must be remembered that few individuals may actually demonstrate clinical signs of disease but many individuals may suffer subtle changes which can produce total population effects.

5.2 Alternative Neurological Endpoints

Data from experimental animals (including primates with long-term exposures to methylmercury) show methylmercury-induced nervous system damage, particularly on the visual system, although the animals appear clinically normal. The traditional RfD methodology neglects such impairment. In question 29, the Subcommittee was asked to determine if these data are important endpoints, and if they are appropriately characterized in the draft report.

The reviewers were impressed by the draft report's thoroughness of the review of the animal literature as it existed in 1994. The document appropriately distinguished among the different forms of mercury (elemental, organic, and inorganic) and it distinguished between adult and developmental exposure. The tables identifying LOAELS/NOAELS in animal studies were most helpful, although a few errors are noted below. We are generally in agreement that the comments below can and should be addressed quickly, but we also agreed that timely publication is a high priority. Answers to the specific questions, and critiques of the discussion of the animal literature are provided below.

The endpoints described in the animal literature are important and they have been induced by dosing protocols that are relevant to human exposures. In experiments using nonhuman primates, sensory (visual, somatosensory, auditory), cognitive (learning under concurrent schedules, recognition of faces), social play, and schedule-controlled operant behavior (not referenced in the tables) are all identified as having been affected by methylmercury. The sensory, cognitive, and motor deficits appear reliably over a consistent range of doses in nonhuman primates exposed to methylmercury during development. Subtle, but believable and important deficits appear in several functional domains. The draft document calls these 'subclinical,' which is true only in the sense that they are not overtly obvious upon casual observation. These are identifiable signs when appropriate testing conditions are applied, conditions that could be applied in clinical settings.

The rodent studies buttress these conclusions in general, though the results are not always consistent. The rat is the most common rodent species used and the endpoints identified to date have usually been less specific than those examined in the primate literature, but schedule-controlled operant behavior (Bornhausen *et al.,* 1980; Schreiner *et al,* 1986) and subtle characteristics of motor function (Elsner, 1991) have been examined. The latter two approaches represent some of the more sensitive endpoints in the rodent literature, but these papers are not without their difficulties. The Bornhausen experiment used such low doses that replication is called for before too much weight is given to that study. Elsner's study used sophisticated endpoints on rats that could be trained to perform the task with extensive analysis conducted on the best performing subjects. In that study, performance on a task in which the methylmercury-impaired rat was required to produce a carefully defined force with its forepaw was affected. This procedure was sensitive, the effects are consistent with some effects identified with humans and nonhuman primates, and are consistent with the accumulation of mercury in areas of the nervous system important to motor function. Many of the other rodent studies used less sensitive screening measures, but nevertheless deficits have been identified, and in a range of doses consistent with the different blood-brain ratios usually assumed for the rat (0.06) as compared with the nonhuman primate (2-4).

Where studied, there is some overlap in the effects of mercury vapor and methylmercury, but there are important differences, too. Appropriately, the draft document keeps the different forms of mercury (organic, elemental, and inorganic) separate.

The sensory and motor deficits imply directly that the exposed individual is missing the full complement of important capabilities. **Moreover, recognition that forms of learning and reading dysfunction in people can be traced to subtle alterations in sensory systems is growing, so these findings raise concerns about deficits in functional domains not traditionally linked directly to sensory**

function. The motor deficits are consistent with neural systems that are affected by methylmercury and therefore indicate important deficits. Whether the cognitive endpoints are traceable to this sensory loss remains to be determined but some, such as the learning deficits under concurrent schedules or alterations in fixed-interval schedule performance may be independent of such loss.

The description of the relevant endpoints misses, in places, the importance of the endpoints studied. In this sense the coverage is more encyclopedic than interpretative. Similarly, describing the visual contrast sensitivity function as simply a measure of spatial vision misses the point of the investigation. This approach to visual psychophysics provides a rich lode of information about function and dysfunction in the visual system. Contrast sensitivity functions enable links between important features of visual function as expressed in behavior and the neural mechanisms underlying vision. The learning impairments observed in behavior under concurrent schedules not only raise concerns about cognitive effects of methylmercury exposure but also point to behavioral mechanisms by which these effects occur. The primate studies out of the University of Washington can make contact with cognitive and visual impairment. Deficits in visual recognition of faces make contact with well-established areas in the primate visual cortex that are tuned to identify complex features such as faces. Results suggesting deficits in the visual recognition of faces make contact with well-established areas of neuroscience that show how higher-order functioning is accomplished in the primate sensory (including visual) cortex. Although somewhat preliminary, these results could point to links between the integration of complex visual information and higher order cognitive abilities.

The rodent studies generally find effects at doses that might be predictable based upon the kinetics of methylmercury in these species and the sensitivity of the procedures used. Some of the studies, e.g., those by Elsner, are sensitive, consistent with other known effects of methylmercury, and should be taken quite seriously. The authors of the draft report have provided a comprehensive review of all studies, both positive and negative. However, it would be helpful if they provided further interpretation of how the studies on rodents relate to human risk.

The most disappointing aspect of the section on the health effects of mercury (elemental, inorganic, and organic) is that it fails to link the animal studies to the risk assessment process. The effects of methylmercury in these studies are important ones and the doses at which they occur are consistent across studies. Where the human epidemiological studies are non-experimental in nature and therefore contain confounding variables and unknown terms which may make it difficult to determine causality; the animal studies are experimental in nature and provide better control over potential confounding factors. **As pointed out at the public meeting, however, the animal studies are poorly integrated into the general document.** This is unfortunate because the animal studies have much to offer to the risk

assessment process.

First, laboratory studies can be drawn upon to examine critically the absence of effects in human studies. For example, if contrast sensitivity functions, high-frequency hearing, or learning are especially sensitive to methylmercury, then the absence of an effect in an epidemiological study can be interpreted only if these functions are examined directly. Human studies that rely on relatively insensitive screening measures rather than refined measures of functions known to be affected by mercury should be interpreted cautiously if refined measures are absent. The primate studies, and even some of the rodent studies are clear in showing that subtle features of behavior are affected in animals that show no gross impairment.

Second, these studies can be used to resolve ambiguities in threshold estimates. Some estimates from epidemiological studies are so heavily dependent on the statistical model that order-of-magnitude differences in the estimated threshold arise. These disagreements can be resolved by a review of the animal literature. For example, many pages are devoted to detailed discussions of statistical models used to characterize four cases of delayed walking in the Iraqi study but not a single line draws from the large and growing animal literature to support the different arguments, even though empirically grounded interpretations from well-controlled experiments are available.

Perhaps most important, an independent risk assessment can be conducted with the animal studies. This has been accomplished recently (Rice, 1996, Gilbert and Grant-Webster, 1995) and the RfD's recommended there are lower (but within an order of magnitude) than those recommended by the U.S. EPA. This lower estimate coupled with the long half-life of mercury elimination from the brain (Vahter *et al.*, 1995) raise the
possibility that an additional uncertainty factor might be considered to account for accumulation and possible neurodegenerative effects.

As an additional note, the summaries of the animal studies, and especially some of the primate studies, are accompanied by criticisms about the small sample size used. A small sample size is a problem if one is trying to determine a benchmark dose, but in many regards the small sample size is a strength. This experimental tactic permits the use of refined endpoints to identify effects of low exposure levels, can point to mechanisms of toxicant-induced behavioral disruptions, and facilitates links to other studies, such as kinetic or in vitro experiments. Because of the refined analysis permitted by smaller studies, these studies, especially the primate ones, identify LOAEL's that can form the basis for a comparative risk assessment between species.

The Subcommittee offers the following specific recommendations, while urging that timely publication of the document be given the highest priority:

a) Integrate a discussion of risk based estimates upon the animal studies that have been published. Do so by drawing on papers published since this document was written (Stern, 1993; Rice, 1996; Gilbert and Grant-Webster, 1995).

b) Update tables and other descriptive information with papers that have been published describing animal studies since the document was written. We limit this recommendation to the animal literature because of uncertainties in how to interpret recent human epidemiological studies. Some studies are listed below.

c) Implement suggested corrections and clarifications found in the Appendix of this report.

d) Where it is possible to correct interpretations of the animal literature do so quickly. Don't delay the document too long by rewriting entire sections

5.3 Fish Consumption Patterns and the "Developmental Window"

The draft report provides information on fish consumption drawn over relatively short time periods (e.g., days). These data are used to extrapolate consumption patterns over longer periods (e.g. a month). Although the exact developmental window affected by methylmercury in humans is not precisely defined, it is thought to be less than three months. The Subcommittee was asked, in question 30, to advise if such an extrapolation was appropriate in this case, and if the draft document appropriately presented the limitations of this methodology.

The Subcommittee noted that data from studies of humans and animals presented in the draft report do not support the notion of a precisely defined 3 month window of vulnerability for the effects of methylmercury on the developing fetus or child. **In contrast, the Subcommittee indicated that there is sufficient data to conclude that the developing organism is vulnerable during the entire period of development and that i*n utero* as well as early postnatal exposure to methylmercury is of concern.** The Subcommittee also indicated that intermittent or short-term exposure to methylmercury at a critical period in development should also be considered. Exposures prior to pregnancy may also be of concern given the half-life of methylmercury.

The draft report presents some but not all of the limitations of the methodology used to assess Hg exposure from fish consumption. The report notes that available data are frequently based on samples gathered up to 20 years ago; it should also state that, although Hg levels in marine species appear to have remained fairly stable over the past 20 years, levels in freshwater fish have fluctuated considerably. Information

on recent changes in marketing that have led to increased consumption of non contaminated farm-raised fish should also be incorporated. More emphasis should be placed on the paucity of data on high level fish eaters who are likely to be the only populations at risk and particularly on the dearth of data on exposure of women of child-bearing age. One study of Mohawk Indians in upstate New York indicates a dramatic decrease in fish consumption among women of child-bearing age upon learning of its potential health hazards.

5.4 Subtle Endpoints Versus Traditional Metrics of Child Development

Volume 4, Section 6.3, and Volume 6, Chapter 2, Sections 2.1 and 2.2.21 of the draft report present EPA's interpretation of the data demonstrating increasing severity and frequency of nervous system effects (particularly impairment in visual-motor integration) among pediatric subjects with increasing levels of maternal hair mercury. In question 31, the Agency sought the Subcommittee's comments on the possible biases introduced into the assessment by focusing on subtle endpoints of neurobehavioral function, rather than the traditional metrics of child development and on establishing the conditions under which such subtle measures should be employed. Advice was also requested as to whether the available data indicate that children are more sensitive than adults to the effects of methylmercury.

The Subcommittee's findings on these issues are herein summarized (Detailed discussion follows below):

a) Subtle neuralbehavorial measurements should be used even if traditional metrics are within normal ranges.

b) No specific biases are introduced by the use of subtle neuralbehavorial endpoints. However, given the questions about the Iraqi study, the EPA report should clearly acknowledge the potential significance of these issues.

c) The data are unequivocal in indicating that the fetus is more susceptible to mercury toxicity than is the adult

The Subcommittee interprets the term "subtle endpoints" to mean scores yielded by individually-administered sensory-motor or neuropsychological tests. Focusing on subtle endpoints versus ".... traditional metrics of child development" such as age at achievement of milestones (e.g., walking, talking) will not introduce bias in the usual sense of distorting the estimate of the magnitude of an association because of selection bias or confounding bias.

Insofar as the wording of the question posed to the Subcommittee implies the

equation of "subtle" with "more sensitive to performance variation within the subclinical range," a statistical test involving a more subtle endpoint may have greater statistical power if the gain in sensitivity is not matched by a loss in specificity and thus be more likely to detect a non-zero association with the index of exposure, should one actually exist. The key issue would seem not to be one of bias, but of interpretation, namely whether the performance differences found using more sensitive endpoints are important enough to act on. The lead and PCB literatures provide useful lessons for thinking about this issue. Neither compound would probably be viewed as a developmental neurotoxicant, at least at low levels of exposure, if reliance had been placed solely on "traditional metrics" such as developmental milestones. This experience with other neurotoxicants indicates that the answer to the question "Should these indicators be dismissed if traditional metrics are within normal ranges?" is clearly "No."

Use of traditional metrics such as milestones of development requires consideration of several measurement issues. Ages at milestone achievement are necessarily based on the reports of an observer in close contact with a child, and often a considerable amount of time may separate the achievement from solicitation of the report. As
such, these reports are subject to a number of errors, both non-differential (random) and differential (systematic), that are attributable to characteristics of the reporters.

The possibility of non-differential misclassification arises because the reports depend on the intensity of the reporter's "diagnostic surveillance" for the target behavior, the acuity of the reporter's observational skills, the criteria used by the reporter to identify when the milestone was achieved (e.g., when is a verbal approximation accepted as a "word"?), and the accuracy of the reporter's memory of the milestone achievement. The distributions of responses provided by the Iraqi parents about the ages at which their children walked and talked suggest that some of these factors may have influenced these reports. The most notable feature is a clear digit preference for both judgments. For "age at walking," 70 of 78 values are even numbered months, and 50 or nearly 3 of 4 responses are multiples of 6 months (i.e., 12, 18, 24, 36, 60, and 72). This is true for "age at talking" responses as well (70/73 are even numbered months). These patterns are unlikely to have occurred by chance alone and suggests that the respondents were giving "ball park" responses. Depending on the way Iraqi nomads mark the passage of time, it may also indicate that the interviewers had to suggest response categories for the respondents (The report does indicate that no particular significance is ascribed either to the onset of walking or to date of birth in this culture). This may not be a big problem if the data are analyzed categorically[3] (since distinctions within the groups below the cut point or above the cut point are irrelevant). As noted in the EPA report, however, response misclassification

[3] Especially if the category includes a preference point as the middle of a category.

will be a problem when it occurs in the neighborhood of the cut point chosen as "abnormal". Various analyses summarized indicate the extreme sensitivity of the threshold of effect to the choice of cut point. Without having Iraqi norms for ages at walking and talking, it may be inappropriate to designate any cut-offs for identifying an "abnormal" response (particularly if that “point” represents a preference number). Treatment of age at milestone achievement as a continuously distributed variable would reduce the problem of misclassification in the neighborhood of the cut-point. It would be interesting to learn about the estimated ages of the Iraqi children at the time they were identified. Was the age of the child at the time a respondent was interviewed associated, either positively or negatively, with age at which milestones were reported to have been achieved? If so, the next issue to address would be whether child's age at time of interview was associated with estimated mercury burden?

The draft report says that the data were collected 30 months after the episode, although this is difficult to reconcile with the fact that one child was reported to have been 6 years old before he or she walked or talked and another 2 to have been 5 years old. If the interval really was 30 months, one would expect some censoring of the data, i.e., missing data because some children had not yet achieved the milestones at the time of the interview. Some data are missing, but these are not identified as due to censoring.

Differential misclassification is a type of systematic bias arising when a respondent's judgment about whether or when the target behavior occurred is affected by knowledge of exposure status, i.e., a mother who knows that she consumed more contaminated food grain than most other women tends to overestimate the age when her child began to walk or talk. It is not possible to evaluate the extent of this type of misclassification in the Iraqi data set.

Aspects of the Iraqi data raise doubts about its quality, but do not clearly suggest whether the problem is non-differential or differential misclassification. For "age at walking," 46% (36/78) reportedly did not walk until 18 months of later. In the standardization sample of the 1969 version of the Bayley Scales, 95% of children met the criterion for "walks alone" (at least 3 steps without support) by age 17 months (Bayley, 1989). In the Iraqi sample, 37% of the children (27/73) did not produce 2 or 3 words until 24 months or later. In the U.S. standardization sample for the MacArthur Communicative Development Inventory, a parent-completed checklist, the median age at which children were speaking 2 or 3 words was 10-12 months(Fenson *et al.*, 1993). At age 24 months, the 5th percentile for Vocabulary Production was 70 words for girls and 48 words for boys, and by this age, 89 of girls and 83% of boys were combining single words into rudimentary syntactic structures.

The data presented by Marsh *et al.* (1987) may accurately mirror Iraqi norms, or may reflect a sample in which children with developmental delays are greatly over-

represented (even among infants with low maternal hair mercury levels).

Besides being more sensitive than caretaker memories of ages at milestone achievement, assessments of more subtle sensory-motor or neuropsychological endpoints are generally less subject to these sources of classification error because they typically involve standardized administration of items, clear definitions of the target behavior and criteria for response classification, and can be completed by an individual blinded to exposure status and whose performance can be monitored by some quality control procedure.

The issue of endpoint sensitivity also bears importantly on the question of whether one is interested in drawing inferences about the individual that is exposed or the population that is exposed. An individual-centered approach would frame the public health impact of exposure in terms of clinically significant impact on a particular child (e.g., a delay in walking or talking that would warrant a referral for further evaluation). A population-centered approach would frame the public health impact in population terms. A 5 point decline in the IQ of an individual child, roughly 1.5 times the standard error of measurement of full-scale IQ, is unlikely to have clinical import for that child, i.e., to move the child's score out of the normal range. Weiss' example of the implications of a shift of 5 points in mean IQ on the population distribution of IQ scores shows that this might result in a doubling of the numbers of the children with scores in the clinically meaningful range (Weiss, 1988).

The Subcommittee recognizes that there is little EPA can do at this point to address these concerns about data quality in the Iraqi studies and, specifically, to reduce the uncertainties attending their interpretation. The EPA report should, however, more clearly acknowledge the potential significance of these issues and their potential impact on the results of the risk assessments conducted.

We assume that use of the term "childhood exposure" here excludes fetal exposure, referring only to postnatal exposure. The data in humans and in several animal models are unequivocal in indicating that the fetus is more susceptible to mercury toxicity than is the adult. One of the most important lessons learned from the Minamata and Iraqi episodes of congenital methyl mercury poisoning is that fetotoxicity can occur in the absence of clinical signs or symptoms in the mother. In contrast, little evidence is available on the relative susceptibility of children versus adults. In most human studies, it is impossible to discriminate the effects of fetal exposure from those of lactational exposure or to exposure incurred by the postnatal child by virtue of his or her own patterns of consumption. Animal data appear to suggest age-related changes in mercury metabolism that would likely be expressed as increased vulnerability in the early postnatal period (e.g., greater retention of ingested mercury by suckling rats compared to adults, especially in brain) (Null, *et al.*, 1973). In addition, data from animal models and human neuropathology studies clearly indicate that the immature

brain is more sensitive than the mature brain to methyl mercury Rheul, *et al*., 1979). In the adult, selective focal damage to the visual cortex, granule layer of the cerebellum, and somatosensory cortex may be seen following high dose exposures**.**. In contrast, damage to the developing brain of the fetus and infant is diffuse and widespread, resulting in microcephaly, broad gyri, shallow sulci, ectopic neurons and enlarged ventricles. Animal models confirm that methyl mercury can cause late mitotic arrest in proliferating neurons (Sager *et al.*, 1984). Examination of the brains of adult, infant, and fetal victims of Minamata disease clearly show a strong relationship between developmental stage at the time of exposure and the extent of cortical and subcortical damage (Takeuchi, 1968; Takeuchi et al., 1979). Another reason to assume an age-associated decline in vulnerability is the fact that many of the developmental processes presumed to underlie neurotoxicity in the fetus continue into the postnatal period, including myelination and organization of the neuronal cytoarchitecture involving processes of cell proliferation, migration, and organization of cellular layers (Rodier, 1994). A similar inference is supported by the available evidence regarding the molecular bases of mercury neurotoxicity, which include interference with Ca^{2+} homeostasis and ion channel function (particularly the PKC pathway), with neurotransmitter function, and with microtubule function, all of which may ultimately affect the fine structure of the nervous system (Rodier, 1994). It should also be pointed out that these effects are clearly less severe than lead encephalopathy and may not require the conservative safety factors that are applied when such severe sequelae follow exposure to other neurotoxicants.

5.5 Uncertainties in the Characterization of Potential Effects

Charge question 32 asked if the uncertainties in the characterization of potential effects were accurately described in the draft text.

The Subcommittee found, that the draft report included a very good discussion of the uncertainties in the characterization of the potential effects of MeHg. There are some specific issues requiring discussion, however.

Appendix D (volume 4) presents a comprehensive set of complex highly quantitative simulations and sensitivity analyses to assess the impact of differing levels of uncertainty (e.g.,producing a series of cumulative bootstrap threshold distributions multiplied by values of the dose conversion distributions). In that Appendix, the report states "The principal uncertainties in calculating the reference dose arise from the following sources: the variability of susceptibilities within the Iraqi cohort; population variability in the pharmacokinetics processes reflected in the dose conversion; response classification error; and exposure classification error."

The text seems to assume (p. D-2, D-3) that the only type of exposure misclassification of concern is classifying an unexposed child as exposed because of

uncertainty as to whether the period of exposure overlapped with the developmentally critical

period. The same uncertainty could result in the inverse classification error of assuming that an exposed child was unexposed.

Considerable attention is focused on the assumptions underlying the bootstrap method used to generate the threshold distributions (e.g., p. D-5: assumes that “...the observed sample was a random sampling of a larger population and that each observation was equally likely to occur in additional samples." In the Subcommittee's view, greater consideration should be given to the sampling mechanism that generated the Iraqi mother-infant pairs, to issue of whether this data set can support analyses of the sophistication and precision of the bootstrap models.

The draft report does a better job identifying the uncertainties in the purely toxicologic factors than it does the uncertainties associated with epidemiologic design issues.

One uncertainty mentioned but dismissed is selection bias in the Iraqi sample. The sample of mother-child pairs studied by Marsh *et al*. (1987) appears to be a convenience sample insofar as no sampling frame or referral mechanism is described to indicate how the pairs contributing data came to be included in the study. One concern is that the characteristics of those who were selected (or self-selected) for study differed systematically from those who were not. One uncertainty, for instance, is whether the likelihood of participating was associated with the severity of outcome in the child. If so, this would distort an estimate of the association between mercury exposure and the endpoints of interest. On the other hand, if the mother-child pairs who make up the data set were identified by some specified mechanism, the data would permit estimation of the population distribution of both hair mercury levels, ages at which children achieve developmental milestones, and the prevalence of abnormal findings on neurological examination. These can be known only if all members of the base population have an equal probability of being selected (rarely achieved).

Some of the problem stems from the absence of a denominator. The draft report states that, "...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" and "Whether or not those who obtained medical care represented a more sensitive subpopulation is not known."

Is it possible that mothers who elected to participate in the study had particular concerns about their children's developmental delays? The sample would suffer from

selection bias if there were women in the population who did not participate, who had equally high hair mercury levels, and whose children did not manifest developmental delays, and so did not seek to participate in the study. By the same token, were there women who did not participate, perhaps because they did not eat much contaminated grain and knew that was the investigators' focus, and whose children had significant developmental delay?

This is important because calculation of a threshold, benchmark dose, or reference dose depends on having a denominator for the size of the exposed population, and a background prevalence of the adverse health impact of interest. The concept of "added risk" also requires an accurate estimate of background prevalence insofar as it represents " ... 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" (vol, 6, 2-6). On what basis can a 10% incidence in response be hypothesized if the background prevalence is not known? Any quantitative estimates will be biased in ways that are not known. From the data presented by Marsh *et al.* (1987), the background prevalence of abnormal development appears exceedingly high, at least using U.S. data as a reference. The prevalence of delayed walking ($\geq$18 months) among children whose mothers had hair mercury levels <10 ppm) was 11/31 (36%) (versus 5% in the U.S. population), and the prevalence of delayed talking ($\geq$24 months) was 6/27 (22%). In the U.S. standardization sample of the MacArthur Communicative Development Inventory, more than 95% of 24 month old children were producing 48 words or more (Fenson, *et al.*,1993). By 24 months of age, 89% of girls and 83% of boys were combining single words into rudimentary syntactic structures (Fenson, *et al.*, 1993).

5.6 Risks among Subpopulations

Traditional methods for estimating potential human health risks from environmental hazards do not distinguish risks among subpopulations (e.g. racial or ethnic) groups. Question 33 asks for advice on dealing differential response across population groups, and how this factor could be addressed in the report. The Subcommittee was also asked to determine if factors such as nutritional status, life-styles (e.g., substance abuse), or economic status play a role is mediating these differences between groups.

Effect modification occurs when, at a given dose of a neurotoxicant, an adverse outcome is observed in some members of a population but not others. Epidemiologists seek to define the characteristics of sensitive and insensitive subjects. Those individuals who are affected may possess one or more distinctive characteristics such as age (stage of development), gender, social class, or certain premorbid health factors (e.g., diabetes, liver disease, pulmonary dysfunction) or genetic predisposing factors that are not well represented in unaffected members of the population.

Unfortunately, most studies of environmental chemical influences on child development have treated potential effect modifiers as covariates or confounders in multiple linear regression models without interaction terms models, or as matching variables in comparing so-called “exposed” and “unexposed” groups. Interactions are infrequently explored by pediatric neurotoxicologists and, when they are found, their significance is often dismissed as a symptom of “data dredging.”

However, the animal model literature is brimming with examples of neurotoxicity enhancement or buffering as a result of species, strain, drug, and physical and social environmental interactions. This is the “experimental system” that has been largely ignored in environmental neuroepidemiology (Bellinger, 1995).

An example taken directly from the methylmercury literature is the phenomenon of male vulnerability. Several epidemiologic studies have shown that the relative risk of perinatal morbidity and mortality is higher in males (Abramowizc and Barnett, 1970; Naeye *et al.*, 1971), including the risk of poor reproductive outcomes and postnatal development due to fetal exposure to industrial pollutants (Scragg *et al.*, 1977; McKeown-Eyssen *et al.*, 1983). Males also have a higher rate of mental developmental disability in the general population (Gross and Wilson, 1974; Schaffer *et al.*, 1985) and display more profound intellectual deficits as a result of cortical lesions (Bornstein and Matazarro, 1984; Inglis and Lawson, 1981).

Gender-related differences in susceptibility to perinatal methyl mercury exposure were originally reported in a study by McKeown-Eyssen in the early 1980's (McKeown-Eyssen *et al.*, 1983). An interesting sexual dimorphism was observed with male infants in particular presenting with dose-related deficits in sensorimotor behaviors as assessed by the Bayley Scales of Infant Development (Bayley, 1989). Furthermore, the prevalence of abnormal muscle tone and deep tendon reflexes was positively associated with methyl mercury dose in males but not females. An examination of cases from the Iraqi episode confirmed that more severe neurological effects were observed in males (Marsh *et al.*, 1987). Animal experiments have also observed sex differences in neurodevelopmental vulnerability. Thus, for example, Sager *et al.* (1984) administered a single dose of methyl mercury to neonatal mice. At the lower doses, only males evidenced mitotic arrest in cells of the granule layer of the cerebellum.

The episode of pediatric elemental mercury poisoning via medicinals earlier in this century supports the concept that organismic and environmental factors may modify the severity of this metal’s developmental neurotoxicity. Thus, while many were exposed to these iatrogenic preparations, only a relatively small number of children developed the complex of cutaneous, neurologic, and psychiatric symptoms that clinicians have called “acrodynia” (Warkany and Hubbard, 1951).

One of the important lessons of mercury neurotoxicology is that a substantial

amount of interindividual variability in the response of fetuses and children to equal doses of an environmental contaminant can be expected. These differences in response may be due to genetic, nutritional, maternal, metabolic or other premorbid factors. The difficult task is identifying these factors in rigorous epidemiologic studies and animal model experiments.

There is evidence that lifestyle factors such as the quality of the home environment and nutrition play a role in the expression of developmental neurotoxicity. Although social interactions have not been extensively investigated in the mercury literature, lead studies have found deeper neurocognitive deficits in exposed individuals from the poorest families (e.g., Bellinger *et al.*, 1989; Dietrich *et al.*, 1987; Harvey *et al.*, 1984; Lansdown *et al.*, 1986; Winneke and Kraemer, 1984).

Positive nutritional factors associated with a seafood diet may be one reason for the greater delay in the onset of the Minamata as compared to the Iraqi outbreaks. Early results from the Faeroe islands studies have shown an unexpected positive association between cord blood methyl mercury concentrations and birth weight (Grandjean, *et al.*, 1992; Grandjean *et al.*, 1995). The authors attribute the finding to the benefits of n-3 polyunsaturated fatty acids in a high seafood diet. Selenium may also play a protective role against methyl mercury neurotoxicity. Infant hair methyl mercury concentrations at 12 months were also positively associated with the attainment of motor developmental milestones. The authors attributed this unexpected correlation to the benefits of breast-feeding which, in itself, can lead to higher methyl mercury intake by the infant.

The protective effects of genetic and environmental factors may be evident in the most recent results of the studies performed by the Rochester/Seychelles group (Davidson, *et al*, 1995). One of the most intriguing aspects of this study is the overall performance of the Seychelles infants on the Bayley Scales and other measures of sensorimotor development. Thus, for example, at 19 and 29 months scores on the Psychomotor Development Index (PDI) were very negatively skewed. The mean PDI scores at 19 and 29 months were 1.7 and 1.3 standard deviations above the United States means of 100 +/- 16 points respectively. That is, the Seychelles means for the PDI are well above what would be classified as “accelerated performance” on these scales. Furthermore, the inexplicable developmental health of this sample is also reflected in the incredibly small number of subjects attaining “abnormal” scores on the Denver Developmental Screening Test-Revised when compared to samples in the United States. Only three out of 737 individual examinations or 0.4% were rated as abnormal (i.e., below the 10th percentile for U.S. norms). Developmentally, this appears to be an extremely robust sample of infants. Accelerated motor development has been noted in previous studies African cultures and is also observed in African-American infants under two years of age.

The apparent neuromotor developmental precocity of this sample leads one to question the negative results of the initial studies. On the older version of the Bayley Scales, both the MDI and PDI are highly influenced by the motoric skills of the infant. It is conceivable that, by virtue of culture, nutrition, genetic factors, or some combination of these variables Seychelles infants are buffered from the adverse neuromotor consequences of low level *in utero* methyl mercury exposure. For now, this remains a matter of conjecture and debate.

All of these factors notwithstanding, the data regarding effect modification in human epidemiologic studies of mercury poisoning are currently too meager to base separate estimates of human health risks or establish different RFD's for various subpopulations.

5.7 Estimating Risks to Fetuses, Children, and Adults

Many assessments of methylmercury risk clump risk to fetuses and children together with risk to adults. Charge question 34 asks if this approach is scientifically valid for methylmercury.

The RfD has been set for neurodevelopmental effects on the fetus, which is currently believed to be the most sensitive endpoint in the most sensitive subpopulation. This approach is in accordance with current RfD methodology. Both human epidemiological and animal experimental data suggest, however, that it may be appropriate to consider a second, higher RfD for adult males and adult females beyond child-bearing age. In other words, although there is strong scientific justification for the current RfD for the fetus, there are no data justifying such a low RfD for adults. The fetal RfD would, of course, continue to be a criteria for risk management pertaining to Hg levels in air, but a two-tier RfD may be more appropriate for issuing fish consumption advisories. Dual-criteria fish advisories are commonly issued by state agencies, and these advisories would benefit from rigorous EPA risk assessments for both the more and less vulnerable populations. The original EPA RfD of 0.3 ug/kg/day, which was based on adult paresthesia in Iraq, provides a basis for deriving an RfD for the less vulnerable adult population, but other new studies, including those on effects of long-term Hg exposure on dentists and dental hygienists, should also be considered.

Unfortunately, there is a paucity of data on long-term chronic effects of lifetime Hg exposure, particularly as the individual ages. The concern with Hg effects on older adults is heightened by the recognition that over time MeHg may be demethylated in the body and the Hg may be preferentially stored in the nervous system. Because the current RfD is based primarily on the chronic short-term Iraqi exposure, we recommend noting in the Report that future risk assessments might consider an additional uncertainty factor to take into account possible effects of lifetime exposure. With

regard to possible differences in sensitivity to MeHg among different ethnic groups, the committee concluded that such differences should not be considered in assessing human health risks unless clear evidence indicating racial/ethnic differences in sensitivity emerges in the future.

5.8 Wildlife Effects as Harbingers of Human Health Effects

In question 35a, the Agency asked the Subcommittee to recommend what wildlife effects (based on what metric) could be interpreted as harbingers of likely human health effects.

Beyond the obvious behavioral, reproductive, and immunologic effects that should be monitored in both sentinel wildlife and laboratory studies, there is considerable evidence to support a stronger use of wildlife data. In 1991, the National Research Council (NRC) published Animals as Sentinels of Environmental Health Hazards. That monograph clearly outlines the use of wildlife, food animal, and companion animal data for human epidemiology.

First in the introduction, the history of the use of wildlife in human toxicology is described beginning with the canary in mines and then concluding with Table 1-1 listing the environmental toxicants first identified in animals as human hazards. In Table 1-1 mercury epidemics in animals included cats in Minamata Japan developing "dancing cat disease" in the 1950s prior to general recognition of the human epidemic; birds in Sweden (1950s) becoming ill from eating mercurial treated grain; and (1954-1971) pigs developing neurologic disease and death following ingestion of mercury treated grain in the U.S. These reports clearly depict that animals can provide important indications of human health risks. Specifically, Chapter 5 provides an in depth discussion of "Fish and Other Wildlife as Sentinels." Table 7-1 depicts the advantages and disadvantages of animal sentinel systems for risk assessment. The EPA should consider including the sections of the NRC monograph listed here possibly incorporating the section as an integral part of the EPA report to Congress.

However, we must recognize that wildlife studies will provide little if any insight into mechanisms of action and cause/effect relationships. Laboratory animal studies will be imperative to answer those types of questions. The data from both wildlife and laboratory studies should be used to calculate comparable RfDs to give us more confidence in our human data. Such calculations were published earlier by other Members of this Subcommittee.

As a final note, we believe that EPA should be cautious in assuming that wildlife studies are inherently less sensitive than human studies. Wildlife populations are constantly operating at the limit of their resources and therefore stressors such as mercury on those systems may display population effects at levels less than those for

either laboratory or human studies. As demonstrated at Minamata, stray cats were overtly affected long before the problem was identified in humans. Conversely, protective mechanisms such as concurrent uptake in selenium may serve as a natural buffer against adverse health effects of mercury in wildlife or in humans. Complex dietary interactions are difficult to test in the laboratory setting. Therefore, generalizations should be avoided, and all three types of data must be considered (wildlife, laboratory, and human).

5.9 Unaddressed Human Health Issues

In Charge 35b, the Agency asked for the Subcommittee's advice on human health issues not addressed in the coming epidemiologic studies (such as toxicokinetics).

The Subcommittee identified several significant human health issues not being addressed in ongoing epidemiological studies (i.e.,Seychelles, Faeroes, the Agency for Toxic Substances and Disease Registry, Canada, and Brazil):

a) Studies of the long term effects of neonatal exposures to methylmercury

b) reproductive toxicity, with an emphasis on germ cell effects and transgenerational effects

c) immunological effects

We see the highest priority for research in human populations as:

a) Research on the long term neurobehavioral effects of mercury exposure, including measures of neurosystem stability, recovery of delay, and the appearance of progressive or long latency effects.

b) Measurements of neurobehavioral development, based on a presumptive biological mechanism to assess relative vulnerability depending on age of exposure (especially from prenatal to puberty)

c) Effects on germ cells and other genotoxic markers (lymphocytes) and relevance to reproduction (not just fetal development)

d) Immunologic effects (T- and B-cell functions; cytokines, immunoglobulines) and relevance to host immune status and resistance

e) Understanding basic Hg kinetics and blood:hair ratios in diverse populations (e.g. differences between Seychelles and Faeroes)

5.10 Research Needs

In terms of overall research needs, the Subcommittee notes the following areas in response to Question 40 of the Charge:

a) Biomarkers of integrated and/or past exposure to methyl mercury

b) Understanding variability in response

c) Long term (even latent) neurotoxic effects; interactions of aging with earlier mercury exposure

d) Reproductive toxicity (not developmental), especially related to published data on germ cells, pre implantation embryo, and distribution to the pituitary

e) Low dose dose/response studies in models appropriate to the research design and issue under study.

f) Nature and significance of immunologic effects

g) Effects of pregnancy and lactation on distribution of mercury

h) Distribution and accumulation of mercury in brain/cellular and regional), de-methylation in brain, role of glia in neurotoxicity

I) Improve linkage between animal and human neurobehavioral measures.

5.11 Conclusions

The U.S. EPA has established a RfD for MeHg of 0.1 microgram from the International Agency for Research on Cancer Monographs Programme on the Evaluation of Carcinogenic Risks to Humans (Preamble, pp7-8, Volume 67, 1996). The RfD is based on neurological deficits and developmental delay in Iraqi children who ingested contaminated seed grain. A benchmark dose was estimated for this population based on the level of 11 ppm of mercury in maternal hair which was extrapolated to an equivalent dose by an ingestion route. The Subcommittee noted that the Iraqi population had some limitations for purposes of setting standards for several reasons. Possible selective factors may have been involved in determining

who participated in the original study which could bias the data. The exposure in this instance represented an acute toxicity rather than a chronic exposure which populations have from chronic exposure to fish with a mercury burden. Other flaws in the epidemiologic study have been reported such as the fact that there is little information on the background performance scores for the normal Iraqi population, a concern which has arisen because of the very low performance of the children in this population versus children in the U.S. However, the Subcommittee generated a table reflecting the maternal hair level in other studies which was partially based on the data provided by the EPA at the meeting and found that the Iraqi data and those from other sources are compatible. This reassured the group that the use of this database is adequate for setting the RfD in the absence of newer data.

The data from the animal literature was appropriately characterized in regard to the available published data at the time of the writing of the report. The major deficit in this review was that the report's authors did not adequately tie the animal data to the human data. The animal data have identified sensory, cognitive, social play and schedule-controlled operant behavior deficits related to mercury exposure. The data also indicate that there are changes in the brains of animals exposed in the fetal and infant periods which suggest that there are wide spread changes in brain including microcephaly, broad gyre, shallow sulci, and other abnormalities which indicate that there may be differences in effects based on age at exposure.

The data, although scanty , suggest that there may be differences in response of human populations based on various biologic factors other than age. For example the male of most species appears to be more susceptible than the female. It would be important in further studies to examine those factors that, like sex, appear to influence the risk of demonstrating neurologic deficits.

The Subcommittee was briefed on the current status of the studies in two populations which have high MeHg exposure by virtue of fish ingestion and which have been under study for several years. Because the current results from these studies have not been published the populations have not been used for setting the RfD. The studies raise issues about the important influence of other factors such as genetics, nutrition, and metabolism in determining the detectible effects of mercury on fetuses and infants. The Faeroe Island population have demonstrated a positive relationship between levels of MeHg and both birth weight and motor development. The unexpected result may be related to breast feeding. Additionally, data from the Seychelles have shown a very low rate of developmental abnormalities compared to the normal U.S. and an accelerated Psychomotor Development Index which may be attributed to the precocious motor development of children with African heritage. These influences of other factors on the neurologic performance of infants exposed to MeHg will need to be considered further in any future analysis.

HEALTH APPENDIX.

Volume I. Executive summary.

The units are confusing in places. Units of ppm and µg/g, are used interchangeably, for example, as though they represent different measures. To complicate further the reading of the summary, units of 10^{-4} are used instead of one of these measures. In other places abrupt changes among biomarkers such as blood and hair make it difficult to follow the argument. It would help to summarize the argument using a single biomarker, even if it requires a calculated estimate. If such an estimate is called for then, of course, it should be clearly stated that such an estimate has been made. Attending to the inconsistencies in units of measure could make the discussion on pages 3-19 to 3-23 more readable.

Volume IV: Health Effects of Mercury and Mercury Compounds.

Page 2-12. Table 2-2. The detection limit for atomic absorption spectrophotometry is in the ppb range, not 0.5 ppm.

Page 3-31. The reference to the Fredriksson *et al* (1992) study incorrectly lists brain levels as 1700-63000 µg/g. The true values are 0.017 to 0.063 µg/g.

Page 3-31. Newland *et al*., 1996 can be added to Table 3-27 describing developmental toxicity of elemental mercury.

Page 3-64. First paragraph. Bornhausen(1980) gave doses of 0.01 and 0.05 mg/kg 5 times, not once as implied in this paragraph.

Page 3-91, Table 3-68. Omits Rice, 1992. Also, consider adding Rice and Gilbert, 1995 to this table.

Page D-4 Only three cases of delayed walking are listed below 100 ppm hair mercury. Four cases are shown in the figure from Cox *et al*. that has been published from this study.

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