APPENDIX A

SUMMARY OF THE SCIENTIFIC PEER REVIEW

1. OVERVIEW OF THE REVIEW PROCESS

Ensuring the quality of scientific underpinning actions by U.S. EPA has been a major thrust of Agency policy. In order to ensure top quality science, U.S. EPA has been advised by review bodies including its Science Advisory Board (SAB) to consider peer review of its programs, methods and products to be a top priority. To this end Administrator Carol Browner issued a memorandum requiring expert review wherever appropriate and requiring U.S. EPA Programs and the Office of Research and Development (ORD) to develop specific guidelines for scientific review. The ORD final guidelines for review of scientific products were issued in November 1994. These were used as the basis for the peer review plan for this Report. The Mercury Study Report to Congress was considered by ORD and the Office of Air Quality Planning and Standards, Office of Air and Radiation (OAQPS/OAR) to be one of U.S. EPA's major and most visible outputs. As such the Report was considered to fall into category 1, requiring the highest level of scientific peer review. The components for category 1 review include the following: approval of the peer review plan by the Assistant Administrator of ORD; review of the product by appropriate U.S. EPA scientists; review of the product by appropriate scientists external to the Agency; convening a peer review meeting; and stringent recordkeeping on all phases of the review process.

Because of the wide scope of the Report and the interest in mercury by many stakeholders, it was felt that the process of generating the Report should be open to external input. Meetings with U.S. EPA Report authors were held with members of the public at their request; for example, during early stages of Report generation, U.S. EPA staff met on a quarterly basis with scientists and engineers representing the Electric Power Research Institute (EPRI). Meetings were also held with the Portland Cement Association and with other requestors. The Agency accepted and reviewed submissions of data and mercury assessment material throughout the study period; these were used as was considered appropriate by U.S. EPA scientists.

In order to gather input and critiques on preliminary assessments, several of these were presented at conferences and scientific meetings. Early results of the emissions inventory (found in Volume II) were presented at both regional and national meetings. Draft health assessments were also shown for purposes of discussion at scientific meetings on mercury. In January of 1994 a review draft of the emissions inventory was made publicly available.

Internal scientific review of a draft of the entire Report (minus Volume I, Executive Summary) was begun in November of 1994. Following procedures for review and clearance established for the Office of Health and Environmental Assessment (now the National Center for Environmental Assessment, NCEA) within ORD, the draft was reviewed by four scientists from that Office. In addition, the draft was reviewed by a U.S. EPA Mercury Study Work Group consisting of staff from the following U.S. EPA offices: Office of Science, Planning and Regulatory Evaluation (OSPRE/ORD); Office of Health Research (OHR/ORD); Office of Policy Analysis and Review (OPAR/OAR); Office of Water (OW); Office of Solid Waste and Emergency Response (OSWER); Office of Prevention, Pesticides and Toxic Substances (OPPTS); Office of Policy, Planning and Evaluation (OPPE); and Region V. Scientists representing the State of New York and the State of Michigan also participated in the Work Group and in this phase of review.

Included as part of the Report are summaries of human health risk assessments which comprise parts of the Agency's Integrated Risk Information System (IRIS). IRIS is a publicly available computerized data base which provides U.S. EPA consensus health risk assessment information. IRIS files must undergo specific forms of internal and external review before they are made available on the system. The IRIS documents on mercury were reviewed as part of the Mercury Study Report to Congress. The following six IRIS summaries were distributed to reviewers as Appendix B of Volume

IV of the Report: reference concentration for elemental mercury; cancer assessment for elemental mercury; reference dose for inorganic mercury; cancer assessment for inorganic mercury; reference dose for methylmercury; and cancer assessment for methylmercury. Internal review for the IRIS documents consisted of the appropriate Agency Work Group discussion and closure (referred to as "verification"). The Work Groups charged with reviewing IRIS information and achieving consensus on its validity are comprised of U.S EPA scientists from a variety of disciplines relevant to human health risk assessment and who represent ORD, the Regions and the Program Offices. The two Work Groups have been organized around either the assessment of carcinogenic effects (the Carcinogen Risk Assessment Verification Endeavor (or CRAVE) or the assessment of general systemic toxicity (RfD/RfC) Work Group). To enhance the mercury expertise of the Work Groups and to allow for discussion of alternate risk assessment approaches, scientists from FDA, ATSDR and the State of New Jersey were invited to participate in the RfC/RfD Work Group discussions; they were not part of the consensus process, however, and did not participate in Agency decisions on the assessments. After consensus on the assessment was achieved, IRIS documents were revised and received external review (see below) as part of the external review draft of the Report. Following external review and revision the IRIS documents were either reviewed and cleared by the Work Group chair (RfDs and RfC) or given a pass-around review by the whole Work Group (CRAVE).

External review of the Mercury Report to Congress and the appended IRIS documents was done in two steps: a Federal interagency review and a non-Federal external review. A meeting of Federal reviewers was held at the U.S. EPA, Washington DC on January 9, 1995 to discuss scientific issues in the Report. Representatives of the following Agencies were invited to attend and to submit written comments at the time of the meeting: ATSDR, NIEHS, NOAA, USDA, DOE, FDA and the National Biological Survey. The names and addresses of the reviewers can be found at the beginning of each volume of the Report. Written comments were received from all Agencies participating in the review. A summary of reviewer comments, consensus opinion of reviewers and U.S. EPA's response to comments can be found in this Appendix.

The second phase of external review included comments from non-Federal experts. Reviewers were chosen based on scientific expertise and availability. An attempt was made to include representatives of a spectrum of groups with interest in mercury: academe, research groups, State agencies, industrial concerns and environmental groups. The names and affiliations of reviewers can be found at the beginning of each volume. All reviewers were required to submit written comments on the report including the IRIS documents. A public review meeting was held January 25-26, 1995 at U.S. EPA in Cincinnati, OH. A notice of the meeting was published in the Federal Register, and there was time set aside each meeting day for members of the public to comment. The pre- and post-meeting reviewer comments, synopses of meeting discussions and conclusions of the meeting comprised the external review report. Examples of external review comments are in Appendix A to this Volume. In response to reviewer comments, specific changes were made in the External Review Draft. As the Risk Characterization (Volume VI) was revised, a second review of that volume was done.

One revised component was reviewed in advance of the remainder of Volume VI; this was the estimate of population size, amount of fish consumed and measured amount of mercury in marine and freshwater fish. This assessment (now included in Volume III, Appendix H and summarized in Volume VI) was sent to two external reviewers expert in statistics and demographics. These reviewers were selected by a U.S. EPA contractor who was provided with criteria for reviewers and a list of potential candidates. The entire revised Risk Characterization was subjected to internal and external review. Scientists in ORD, OAQPs and Office of Water were sent the volume and requested to submit comments. Four external reviewers were selected by a U.S. EPA contractor based on criteria provided by U.S. EPA. Among these criteria were that two reviewers be included who had commented on the External Review draft. Written comments on the risk characterization were provided by these four

external scientific reviewers. Copies of all review comments and external input are archived at the National Center for Environmental Assessment in Cincinnati, Ohio.

This appendix summarizes the major comments provided by external and Federal interagency reviewers, along with U.S. EPA's responses. Section 2 presents an overview of the charge to the external and interagency reviewers. Section 3 provides a summary of the external review process, the non-Federal, external reviewers comments and U.S. EPA's disposition. Finally, Section 4 summarizes U.S. EPA's notes and responses to comments from Federal interagency reviewers.

2. CHARGE TO REVIEWERS

Reviewers were asked to focus on that portion of the report that matched their area of expertise. The following are issues or questions considered by the reviewers, including the development of premeeting comments.

All Volumes

- Are additional data or analyses available that would have a major impact on the conclusions presented in any volume of the report?
- Are arguments and conclusions presented clearly and in a logical manner?
- Do the Research Needs chapters of particular volumes present a program of research projects that will address uncertainties in the evaluation of mercury impacts?

Volume I: Findings and Recommended Actions

- Does the summary adequately reflect the conclusions of the other volumes?
- Is additional information presented in the report that should be added to the summary for clarity or completeness?
- Is the summary sufficiently clear and informative to function as a stand-alone volume, or does it rely too heavily on familiarity with the report as a whole?

Volume II: Inventory of Anthropogenic Mercury Emissions in the United States

- Please critique the emission factors approach used in the inventory.
- Are you aware of information for source categories identified as having insufficient data for evaluation?

Volume III: An Assessment of Exposure From Anthropogenic Mercury Emissions in the United States

- Please critique the conclusions of the exposure modeling. Are the conclusions well supported by the analyses presented in the text of Volume III?
- Is there material in the text of Volume III that would be more appropriately presented in an appendix?
- Please critique methods used and assumptions made for the local impact analysis.
- Do the appendices provide necessary supporting information concerning methods described in the text?

Volume IV: Health Effects of Mercury and Mercury Compounds

- Is the information provided on pharmacokinetics sufficient for evaluating human health effects associated with mercury?

- Please critique the weight-of-evidence categorizations for carcinogenicity, developmental toxicity, and germ cell mutagenicity. Is the level of detail in the report descriptions in Volume IV sufficient to permit evaluation of these endpoints?

- No quantitative dose-response assessment was conducted on carcinogenicity for inorganic or methyl mercury. Are the arguments against conducting a quantitative assessment presented cogently and are they supported by the information given in this volume?

- Are the reference doses (RfDs) and reference concentrations (RfCs) properly calculated? Were the appropriate critical study and endpoint(s) chosen? Were the proper uncertainty factors and modifying factors used?

- Are there any factors modifying mercury toxicity in humans that have not been addressed in the volume?

Volume V: An Ecological Assessment for Anthropogenic Mercury Emissions in the United States

- Please critique the methods used for generating a trophic level three BAF and a trophic level four BAF.

- Please critiques the methods used for generating an uncertainty analysis.

- Were appropriate endpoints and studies selected for generating wildlife RfDs?

- Were appropriate assumptions used in developing wildlife water criteria?

- Are there other species of concern that should be considered in this volume?

- Are there other geographic areas of concern that should be included in this volume?

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

- Are the summaries of human and wildlife risk assessment sufficient for a scientific critique?

- Are there major areas of uncertainty, defaults, or assumptions that were not discussed?

- Please critique the uncertainty analyses.

- Please critique both the methods and results of the comparative discussion of risk presented in this volume.

Volume VII: An Evaluation of Mercury Control Technologies and Costs

- Are you aware of any quantified benefits of mercury control? Please specify.

- Are you aware of data on the efficacy of materials separation programs or other pollution prevention measures other than that presented in this volume? Please specify.

- Please critique the cost analysis presented in this volume.

3. SUMMARY OF NON-FEDERAL EXTERNAL REVIEWERS COMMENTS AND U.S. EPA DISPOSITION

On January 25-26, 1995, a 1½-day workshop was held at the U.S. EPA's Andrew W. Breidenbach Environmental Research Center in Cincinnati, Ohio, to provide external review of the draft *Mercury Report to Congress*. A draft report was prepared by U.S. EPA's Office of Air Quality Planning and Standards and Office of Research and Development in response to Section 112(n)(1)(B) of the Clean Air Act Amendments of 1990, which requires U.S. EPA to submit a report to Congress on mercury emissions. The draft report consisted of six volumes at the time it was distributed for review:

- Volume II: Inventory of Anthropogenic Mercury Emissions in the United States.
- Volume III: An Assessment of Exposure from Anthropogenic Mercury Emissions in the United States.
- Volume IV: Health Effects of Mercury and Mercury Compounds.
- Volume V: An Ecological Assessment for Anthropogenic Mercury Emissions in the United States.
- Volume VI: Characterization of Human Health and Wildlife Risks from Anthropogenic Mercury Emissions in the United States.
- Volume VII: An Evaluation of Mercury Control Technologies, Costs and Regulatory Issues.

Volume 1, the Executive Summary, was not yet complete and ready for review along with the other volumes. In preparation for the workshop, Eastern Research Group, Inc., providing contractor support to U.S. EPA, identified 15 independent external scientists to review the document. The reviewers' expertise covered a variety of subject areas relevant to the report, including mercury emissions and sources of mercury emissions; the transport to and fate of mercury in the environment; the physicochemical and biotic transformation among mercury forms in environmental compartments, particularly of inorganic to methylmercury; exposure of human and ecological populations to methylmercury and other mercurials; human and ecological toxicology; quantitative risk assessment; and risk management. Each reviewer was asked to focus on that portion of the report that matched his or her area of expertise. Reviewers prepared and submitted premeeting comments on the report prior to the workshop.

Fourteen reviewers,[1] 10 U.S. EPA representatives involved in writing and/or revising the mercury report, and 39 observers attended the workshop. The agenda included plenary sessions and breakout groups. The first day of the workshop began with a presentation, by the two breakout group chairs, of summaries of the reviewers' premeeting comments for Volumes II, III, IV, and V. The participants then broke into two groups — one to discuss Volumes II and III, and the other to discuss Volumes IV and V. During a plenary session at the end of the first day, the breakout group chairs presented a summary of their groups' discussions and observers commented on the report.

The second day of the workshop consisted of a half-day plenary session. Two reviewers presented a summary of the premeeting comments on Volumes VI and VII, and all the reviewers then

[1]One of the 15 original reviewers was unable to attend.

discussed these two volumes. Following this discussion, additional observers presented their comments on the mercury report.

A summary of the major comments provided by external reviewers along with U.S. EPA's responses is presented in the following sections: a report of the workshop chair (Section 3.1); summary of premeeting comments (Section 3.2); summary of breakout group discussions (Section 3.3); overview of reviewer discussion in the plenary session (Section 3.4); and the summary of revisions made in response to reviewers comments (Section 3.5).

3.1 Report of the Workshop Chair - Paul Mushak, Ph.D.

Overview

The draft report and reviewers' comments clearly show that, while we do not know nearly as much as we would like to about environmental mercury, we know a lot. In fact, we know more about environmental mercury than about most contaminant metals or metalloids of concern.

The principal challenge for both the authors and external reviewers of the draft report was to critically evaluate the problems associated with integrating what we do and do not know into a scientifically credible synopsis. One of these problems appears to be that the extensive database for mercury is mainly available as discrete blocks of information within various scientific disciplines, while the congressional mandate requires U.S. EPA to establish and quantify linkages between these blocks of data. For example:

- Information in one block tells us that the forms of mercury addressed in the draft report — particularly methylmercury — are intrinsically toxic, with a relatively high degree of toxicological potency to humans and various other biological receptors. The types of toxic responses known or anticipated in both ecological and human populations are qualitatively recognized.

- Information in a second block tells us that mercury is emitted to the environment from a variety of sources, and that one can generally determine the relative contribution of different anthropogenic mercury source categories.

- Information in a third block tells us that some fraction of the mercury emitted to the atmosphere from a point source will eventually be deposited by precipitation processes onto land and water bodies. Direct or indirect post-depositional processes not only will impart mobility to the contaminant but also will transform mercurial species.

- Information in a fourth block tells us that inorganic ionic mercury entering certain environmental compartments will undergo biomethylation to methylmercury, and that methylmercury will accumulate and biomagnify in the human food web, particularly in high-trophic-level predator fish. Data in this block also show that mercurial forms can contaminate several environmental media, depending on the exposure particulars.

These examples of what we know clearly indicate that the difficulties in synthesizing all this information into a coherent statement about the potential health and ecological risks posed by mercury in the United States are rooted in uncertainties about how to quantitatively link these blocks together. Areas of uncertainty include, for example:

- How much of current anthropogenic atmospheric emissions is deposited in various environmental compartments?

- What is the link between natural and anthropogenic mercury in terms of proportional contamination and subsequent impact?

- How much of this post-deposition mercury is converted to highly toxic methylmercury?

- How much of any increased toxicity risk associated with consumption of methylmercury-contaminated fish can be traced back to anthropogenic atmospheric emissions of mercury?

The draft report was variably successful in dealing with the numerous complexities, uncertainties, and data gaps connected with quantifying linkages. The essence of the reviewers' comments concerned whether the report under- or overstated these uncertainties, particularly with reference to risk characterization.

General Review Panel Assessments of the Report

In their comments before and during the workshop, the peer reviewers recommended revisions to strengthen the report's scientific credibility. Reviewers generally agreed that the report would serve a useful purpose once it had been revised and improved in the various ways they had suggested. Few, if any, reviewers felt the report should not be submitted at all, and no reviewer thought the report should be transmitted without revision.

The review panel generally agreed that some portions of the report underestimated the uncertainty associated with modeled estimates or pathway analyses. The panel suggested that one way to better acknowledge this higher uncertainty was to use a range of values rather than point estimates in the estimating exercise; some panel members also argued that a more refined point estimate could be presented in certain cases—for example, in deriving the reference dose (RfD) for methylmercury.

On the other hand, the panel also generally agreed that the draft report conveyed too much uncertainty by failing to include important peer-reviewed data available in the recent scientific literature. For example, the exposure breakout group generally agreed that data do exist to indicate a relationship between point-source mercury emissions and gradients in mercury deposition consistent with a point-source contribution.

The review panel was similarly concerned about including or excluding available information on other topics in the report. The panelists felt that the authors should revisit the most recent scientific information to close any gaps that affect quantification of the linkages noted above.

Reviewers also were concerned about the role of modeling in the report. However, they had different opinions about how much data from the recent literature could be used to complement the model estimates. Panelists generally agreed that the report volumes should be more consistent and integrated, particularly concerning information relevant to risk characterization.

3.2 Summary of Premeeting Comments

This section presents the summary of the premeeting comments for the following Volumes of the draft Mercury Study Report to Congress:

- Volume II (Emissions) and Volume III (Exposure)— Gerald Keeler, Ph.D., and Paul Mushak, Ph.D;
- Volume IV (Health Effects)— Steven Bartell, Ph.D., and Paul Mushak, Ph.D;
- Volume V (Ecological Effects)— Steven Bartell, Ph.D., and Paul Mushak, Ph.D; and
- Volume VI (Risk Characterization)— Pamela Shubat, Ph.D., and Paul Mushak, Ph.D.

3.2.1 Volume II (Emissions) and Volume III (Exposure)— Gerald Keeler, Ph.D., and Paul Mushak, Ph.D.

Reviewers felt that Volume II probably was the best of the four volumes reviewed. The approach used to characterize emissions was reasonable. However, the volume provides no estimates of natural and baseline emissions and ignores several potentially important sources. Specific comments on the various sections are provided below.

Natural Emissions

The inadequate coverage of natural sources of mercury detracts from the entire report. Chapter 2, *Natural Sources of Mercury Emissions*, which consists of only a single page in Volume II, is incomplete and misleading. The topic of natural sources of mercury is controversial and qualitative at best. If the authors want to include this topic in the report, they should provide a more complete and defensible assessment of natural emissions. Reviewer William Fitzgerald, Ph.D., recommended that natural emissions could be roughly calculated using an approach similar to that of Mason et al. (1994).[2] This approach suggests that natural emissions in the United States are approximately 20 percent of anthropogenic emissions. A recent estimate of natural emissions in Europe gave a similar result of 25 percent of the total emissions (Axenfeld et al., 1992).[3] However, the quantitative data concerning natural emissions are very limited, and there are numerous problems with the estimates in the literature.

Anthropogenic Sources

The report's list of source categories for mercury emissions is complete with respect to the major source categories. Many of the source categories discussed have relatively low annual mercury emissions. For a few source categories for which insufficient information was found, the report provides no emission estimates. Emission factors and data are missing for several potentially important sources, including hazardous waste incinerators, primary mercury production, mercury compounds production, by-product coke production, refineries, and mobile sources. In addition, Volume II provides no information or discussion on emissions from iron-steel production and primary zinc production. Emission factors and data are available for European sources and could be used to estimate the U.S. emissions to determine their potential importance.

The report to Congress provides only very limited information on emissions of various physical and chemical forms of mercury. Better information is needed on mercury speciation in both emissions and environmental samples. These could be identified as research needs.

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[2]Mason, R.P., W.F. Fitzgerald, and F.M.M. Morel. 1994. Aquatic biogeochemical cycling of elemental mercury: anthropogenic influence. *Geochim. Cosmochim. Acta* 58:3191-3198.

[3]Axenfeld, F., J. Munch, and J.M. Pacyna. 1991. Europaische Test-Emissionsdatenbasis von Quecksilber-Komponenten für Modellrechnungen. Dornier Report. Friedrichshafen, Germany.

The report could be strengthened by adding maps showing the actual location of point sources for categories like utilities (by fuel type), incinerators (sludge, municipal), iron-steel production, coke ovens, and cement production. The spatial distribution of the gridded emissions presented at the workshop by report author Martha Keating should also be included.

Lastly, the report lacks information regarding seasonal or temporal variations in emissions by source category. While utilities may have fairly constant emissions both diurnally and seasonally, other sources do not. Operations involving multiple steps over different time periods will probably have time-varying emissions.

Exposure to Mercury

A comprehensive quantitative assessment of the relationship between anthropogenic mercury releases to the atmosphere and the potential exposure of people, wildlife, and terrestrial and aqueous systems to these releases may not be possible due to the apparently limited state of knowledge of the mercury cycle in nature and the environmental consequences from anthropogenic emissions of mercury. The report states that the exposure assessment is a "qualitative study based partly on quantitative analyses." As noted by reviewer William Fitzgerald in his premeeting comments:

> …this important exposure assessment provides a valuable guide for research. Although the results and conclusions are qualitative, this extensive and essential modeling effort provides a credible means for evaluating the present sparse data base, and for identifying major gaps, inconsistencies and weaknesses associated with major aspects of the biogeochemical cycle of Hg at the Earth's surface….

As the report confirms, human exposure to methylmercury is almost exclusively from consumption of fish and fish products. Intake of methylmercury through consumption of nonlocal fish and seafood should be evaluated. Such intake should not be considered "background," as the mercury found in coastal environments and in saltwater fish may be of anthropogenic origin. The report lacks an assessment of the exposure of the marine environment—especially the coastal zone—to anthropogenic mercury emissions and of the effects of such exposure.

The report suffers from a general lack of recent information and actual measurement data in the recent peer-reviewed literature. References will be provided by the reviewers, and the *Monterey Mercury Meeting Book* will be provided by Donald Porcella (Electric Power Research Institute). Inclusion of more recent information will address such comments as "There is a general recognition of uncertainty," "So much is said about uncertainty that it appears as if we do not know much about mercury," and "Little of the most recent knowledge has found its way into this report."

The modeling results should be "ground-truthed" where possible. The report's estimates of deposition and water concentrations often are more than an order of magnitude greater than any actually measured in the United States.

The meaning of some key terms used in the report, such as "total emissions" and "background," was confusing. The peer reviewers strongly recommended that the authors add to the report the definitions provided in the *Atmospheric Mercury Expert Panel Report* and that they use the various terms consistently throughout the report based on these definitions.

3.2.2 Volume IV (Health Effects)— Steven Bartell, Ph.D., and Paul Mushak, Ph.D.

Several of the reviewers' key premeeting comments concerned the major sources of intake and exposure in human populations. Some reviewers suggested that the report should address the contributions to human mercury exposure of dental amalgams containing mercury. Similarly, reviewers recommended that the drinking water pathway be further examined, including the potential human health risks associated with drinking water at locations known to have elevated mercury concentrations in ground water. The report should clearly explain why particular papers concerning human health endpoints are cited while others were omitted.

Reviewers also commented on the subject of mercury disposition among biological indicators of mercury exposure, particularly exposure to methylmercury. The derivation and use of a constant ratio of mercury in hair to mercury in blood for estimating blood levels of mercury may require additional attention. Reviewers expressed reservations about the time-scale differences implicit in comparing blood mercury with hair mercury—namely, that mercury concentrations in hair reflect exposure over a longer time scale, while mercury concentrations in blood may correspond to a shorter time frame. The reported variability may reflect interindividual variability rather than just measurement error as Volume IV suggests. Reviewers identified an error in the equation used to calculate the methylmercury concentration in blood; an additional term defining blood volume is needed to make the units in this equation work out to those stated.

The quantitative linkage of mercury intake by exposed populations and the expression of some toxic endpoint is mediated through the toxicokinetics—i.e., the uptake, distribution, and retention/excretion—of the particular mercurial. The modeling of the systemic behavior of methylmercury is particularly critical in this regard. The reviewers felt that the derivation of the parameters used in the pharmacokinetic modeling needed additional explanation and justification. For example, the elimination rate or half-life used to describe methylmercury conversion to inorganic mercury and its subsequent removal from the body in feces is an important model parameter; reviewers disagreed about the most appropriate value. Differences in this parameter can result in appreciable variability in the modeled mercury concentrations for the human populations of interest.

Chapter 4 on toxic effects of various mercurials, particularly methylmercury, was the subject of several comments. The organization and presentation of toxic endpoints in the chapter could benefit by progressing from lethal through acute effects to subchronic and chronic effects. Distinct subsections organized along this framework would improve the presentation. The rationale for selecting the set of core studies of toxic responses should be clarified.

Not surprisingly, many comments involved the chapter on dose-response relationships. Several reviewers were concerned that the current RfD for methylmercury might not be protective, particularly for more subtle neurotoxic endpoints such as neurobehavioral and neurodevelopmental endpoints. One reviewer pointed out some confusion regarding the interpretation and presentation of the apparent association between maternal methylmercury exposure and abnormalities in deep tendon reflexes in their male children. Two reviewers recorded their disagreement regarding the adjustment of No Observed Adverse Effect Levels (NOAELs) and Lowest Observed Adverse Effect Levels (LOAELs) to lifetime exposures for different exposure pathways (e.g., inhalation, ingestion) in the derivation of RfDs and reference concentrations (RfCs). Exposure resulting from these pathways would be more realistically described as intermittent, shorter-term events. There was apparent confusion regarding the derivation and use of uncertainty factors (UFs) and modification factors (MFs). The values were not carried through the analysis according to the usual protocols. Reviewers pointed out some confusion and inconsistency regarding the relative sensitivity of adult and fetal developmental toxicity used to derive overall human health assessment endpoints.

Reviewers disagreed with the presentation regarding the possible interactions between mercury and selenium, particularly the implication that interaction with selenium may mitigate the human toxic effects of mercury.

3.2.3 Volume V (Ecological Effects)— Steven Bartell, Ph.D., and Paul Mushak, Ph.D.

Reviewers were concerned with the efficacy of the overall approach to the report's ecological assessment, which involves defining overlapping areas of potentially high mercury exposures with the distribution of sensitive piscivorous birds and mammals. For example, the life history and distribution of the Florida panther differ considerably from those of the mink or kingfisher. Failure to address life history and migration patterns in developing this overall approach might lead to inaccurate assessments of risk.

Reviewers also pointed out the report lacked a consideration of mercury effects on organisms at lower tropic levels (e.g., plankton, invertebrates). Additional reservations were expressed over the absence of wading birds, particularly species of declining abundance that are known piscivores. Effects of mercury on fish and reptiles should also be explored, or their omission should be further justified.

Reviewers were concerned about the report's dependence on assessment approaches and data that emphasized the Great Lakes and upper midwestern lakes, for example, in developing the bioaccumulation factors (BAFs). Concern also was expressed regarding the removal of surface waters with pH > 5.5 from regions of concern. This approach would exclude the circumneutral waters of the Florida Everglades that are suspected of posing mercury-related risks to resident populations of birds and mammals.

A major review issue focused on the use of NOAELs as endpoints for developing the wildlife criteria for the ecological assessment. This approach removes any consideration of a dose-response relationship from the assessment. If measured or modeled mercury exposures exceed the wildlife criteria values, we would not know the nature or magnitude of the expected response. Also, this approach implies different time scales between the shorter-term toxicity data used to develop the wildlife criteria and the longer-term exposure values. The fact that limited data were used to develop NOAELs for the selected wildlife species also calls into question the efficacy of the report's overall approach for estimating ecological risks.

In developing the BAF values, the report essentially ignored the complex chemistry of mercury in surface waters. Instead, these factors were developed using constant ratios of methylmercury to total water column mercury. Reviewers expressed serious concerns with this assumption, which ignores the complex environmental chemistry of mercury. Also, in developing the BAF values, the assumption was made that the selected piscivores restrain their feeding to specific "trophic level" fish. This assumption is certainly open to question; it remains unclear what the impacts of this assumption are on the resulting estimates of BAFs and wildlife criteria used as endpoints for the assessment. The assumption of a simple linear food chain implied by this approach was similarly of concern; the draft does not address spatial and temporal variations in diet and feeding behavior that might increase or decrease exposures for the selected piscivores.

It was not clear what the exposure models (RELMAP, COMPMERC) really provide to the assessment. The different spatial scales of these exposure models were not related to the spatial scale of the distributions of the selected species.

Finally, the reviewers noted that the sensitivity/uncertainty analyses did not comprehensively address all the components of the equations used to develop the BAFs or the final wildlife criteria

values. The reported analyses addressed some of the models' structural uncertainties (e.g., correlations), but did not adequately address parameter uncertainty. The results of the sensitivity analyses do not lend themselves to defining future research needs in relation to reducing uncertainty on the endpoints of the assessment.

3.2.4 Volume VI (Risk Characterization)— Pamela Shubat, Ph.D., and Paul Mushak, Ph.D.

Reviewers agreed that Volume VI fell short of expectations for a risk characterization of health and ecological effects from mercury emissions. One reviewer felt that the necessary data to conduct a risk assessment are lacking, considering that a risk characterization should estimate the probability of health effects.

Reviewers noted that the volume should have compared the measurements of fish mercury levels and the incidence of health effects in populations to the volume's assumptions and results. The volume assumed a body weight and a fish consumption rate for each species; it also assumed a NOAEL and LOAEL for the selected species and derived a fish concentration that would permit consumption without exceeding the NOAEL or LOAEL. Reviewers felt that more data were needed to support this approach, and they expressed particular concern about the NOAEL and LOAEL selected for each species.

Reviewers felt that the assumptions, in the relative exposure ranking, that a given lake has only a single mercury concentration and a single trophic level were not accurate. The exposure rankings for the eagle, kingfisher, otter, and other species should be compared to measured values in tissue samples from these species.

3.3 Summary of Breakout Group Discussions

This section presents the summary of breakout group discussions on the following volumes of the Mercury Study Report to Congress:

- Exposure Breakout Group (Volumes II and III)— Gerald Keeler, Ph.D., and Paul Mushak, Ph.D; and
- Effects Breakout Group (Volumes IV, V, and VI)—Steven Bartell, Ph.D., and Paul Mushak, Ph.D.

3.3.1 Exposure Breakout Group (Volumes II and III)— Gerald Keeler, Ph.D., and Paul Mushak, Ph.D.

Volume II (Emissions)

Panelists suggested that the "minor sources"—i.e., those not included in the quantitative assessment—may contribute as much as an additional 20 percent to the total amount of mercury emitted annually. European emission factors should be used to improve the accuracy of this assessment of the minor sources.

Reviewers stressed that, to provide a complete picture of the atmospheric flux of mercury and to properly assess anthropogenic contributions to environmental mercury, the report should assess natural sources of atmospheric mercury as well as the reemission of mercury previously deposited on both aquatic and terrestrial environments by anthropogenic emissions.

Reviewers suggested that a national network of atmospheric mercury monitoring be established to validate emission data and to provide necessary information on trends in mercury deposition.

The panel felt that the division of sources into point and area source categories should be improved. For example, mercury emissions from residential heating furnaces should be defined as area sources, while crematories and medical waste incinerators should be categorized as point sources.

The panel agreed with the appropriateness of the emission factor approach. Many of the emission factors are based on actual test data and measurements, which contributes to the accuracy of the inventory. The emission estimates, when compared on a per capita basis, are quite similar to those in selected industrialized countries in Europe. In addition, the total U.S. anthropogenic mercury emissions are similar in magnitude to those of other industrialized nations in the world.

Volume III (Exposure Assessment)

The exposure volume utilized state-of-the-art methods in investigating the relationships between mercury emissions and exposures. Nevertheless, only plausible relationships between anthropogenic emissions and exposure could be defined.

The draft report does not assess the impact of anthropogenic mercury emissions in coastal environments. However, since fish consumption is the dominant exposure pathway, seafood or saltwater fish should be included in the total exposure estimates.

The analysis presented in the report supports the conclusion that current levels of emissions from major combustion/industrial sources result in incremental exposures above background to both humans and wildlife through the consumption of contaminated freshwater fish.

The group discussed the use of exposure estimates derived from the RELMAP and COMPMERC models. The discussants felt that the report should better describe how the model estimates were added. After questioning the modelers directly during the breakout group, the reviewers suggested that the authors consider alternative strategies for the risk assessment. For example, decoupling the regional impact provided by RELMAP from the local-scale exposure scenarios may improve the site-specific risk analysis and provide a clearer definition of the uncertainties in the exposure estimates utilized in the risk assessment.

Reviewers recommended that actual observations (i.e., measured mercury concentrations) could be used to "ground-truth" the model estimates or could themselves be used in the local-scale risk assessments. Although a wealth of high-quality atmospheric mercury data or mercury deposition data is not available, enough data are available from the Great Lakes programs to perform a risk assessment at a similar or better level of accuracy than the models provided. The only drawback to this approach would be the lack of assignment of risk to specific source categories.

Additional suggestions for improving the assessments include:

- Evaluate the existing exposure to methylmercury via seafood consumption. Base this evaluation on existing data and not the model results.

- Perform the risk assessment and exposure to methylmercury from existing freshwater fish data. (This could be time-consuming because so many data are available.)

- Utilize existing wet and dry deposition data as input to the Indirect Exposure Model (IEM) to see what is predicted. This approach would remove two of the greatest uncertainties from the modeling and could be used to estimate the risk in the risk characterization.

- Attempt to identify a better indicator of the central tendency (perhaps the median) from the exposure assessment uncertainty analysis, which used the distributions rather than the high-end (maximum) estimates.

In conclusion, the panel members felt that the accuracy of the estimates decreases as the report moves from the initial emissions inventory through the exposure modeling using RELMAP and COMPMERC to the risk assessment phases. This results in a risk assessment that may have relatively large uncertainties and, therefore, may not provide a sound basis for decision- or policy-making.

The report would be improved by providing linkage between the risk management and the emissions inventory. The type and cost of mercury control technologies depend largely on the form of mercury in an emission and, thus, on the source category being considered for emission reduction.

3.3.2 Effects Breakout Group (Volumes IV, V, and VI)—Steven Bartell, Ph.D., and Paul Mushak, Ph.D.

Volume IV (Health Effects)

After some discussion, all or most group members generally agreed with the views and recommendations reported below. Dissenting views on key issues, where they occurred, are noted.

The group expressed several concerns about the organization and accuracy of Volume IV. Chapter 4 is difficult to follow, but group members generally agreed that its goal was to provide toxicity data for a human health risk assessment.

The description and discussion of lipophilicity of mercury compounds was not entirely accurate. The term is simplistic and does not account for current knowledge of binding and ligand-transfer interactions of methylmercury and other mercurials.

With respect to toxicity endpoints, the group noted that developmental impacts in the neonatal period should not be dismissed, since neonatal effects of elemental mercury have been reported in mice.

Differential sensitivity to mercurials among human populations is well established, and the fetus is now assumed to be the most sensitive to effects of methylmercury. The basis of such sensitivity includes physiological vulnerability, population variability concerning biotransformations (e.g., demethylation of methylmercury by gut flora), and variable patterns of exposure. Overall, sufficient data are not available to generate a highly resolved summary of differential sensitivity.

Of concern to the reviewers was treatment of the time course of exposure-effect relationships—i.e., are we dealing with latency or a masking phenomenon with long-term exposures?

Some reviewers were critical of the RfD calculation for inorganic ionic mercury (i.e., back-calculating from the drinking water equivalent level [DWEL]). Some also questioned how good a surrogate the Brown Norway rat is for humans sensitive for renal effects in the form of an autoimmune glomerulonephritis. One reviewer thought that the Integrated Risk Information System (IRIS) document

is not convincing in this regard, and recommended that the mercury report at least reproduce the DWEL.

How UF factors were used in the analysis was not clear; the RfDs and RfCs need a closer look. Authors should reexamine the original data to see if they can justify how they used the numbers, and they should better explain their rationales.

The report should indicate that additional studies are under way (other than the Iraqi data set), although it is not known when the data will be available. Basically, the message here was to proceed with caution, but proceed.

Either Chapter 2 of Volume IV should be expanded to provide a concise summary of the integrated exposures to mercury, or an integrating final section should be added in Volume III. The authors should include more information on mercury exposure from dental amalgams and from ground waters that are or will be drinking water sources—particularly when mercury concentrations in these waters approach or exceed the RfC or RfD. Information should be added on how dietary components (other than methylmercury in fish) contribute to human exposure. This should include information, however qualitative, on any linkages of nonfish dietary mercury to atmospheric emissions.

Several comments concerned the mechanisms of mercury toxicology in humans and test animals. Although mechanisms of toxicity are critical to understanding the plausibility of epidemiological relationships reported for different populations and to understanding where thresholds for toxic effects may lie, the report gave them short shrift. The report should expand the discussion of this topic and should address how mercury forms move in and out of cells. However, reviewers recognized that a complete mechanisms sections might require an effort beyond the scope of the report.

Reviewers generally agreed that the health endpoints selected for the assessment and the dose-response relationship for each of the three forms of mercury were appropriate for the risk assessment. However, they thought the authors should strengthen the discussion of the validity of the endpoints and epidemiological data selected. Also, the group recommended that authors scrutinize the numbers employed from modeling, such as the fraction that goes into blood, the half-life, and the elimination parameter. The hair:blood ratio of 250 seems to be a middle-of-the road number and is probably acceptable. Reviewers questioned why the report did not use distributional analysis rather than selecting point values that might result in an unknown bias.

The group's comments on Appendix C of Volume IV mainly concerned model uncertainty and not variability in data-based parameters.

Reviewers considered the issue of selenium-mercury interactions. They felt this issue was complicated because the data sets are isolated and have no mechanistic underpinning. The critical question is how selenium in diet affects long-term exposures and associated chronic toxic endpoints. Was the Iraqi population at risk because of dietary habits (i.e., because they were grain eaters)? On the other hand, the reported selenium content of cereal grains is not vastly different than the selenium content measured in certain fishes. Although the selenium issue may have a bearing on which population exposed to methylmercury is valid for risk characterization, reviewers felt it premature to use selenium intake as a criterion for selection. One problem concerning the selenium-mercury connection is that the clearest associations are seen in gross endpoints, such as high-dose teratogenesis.

Regarding which dose-response data to use in risk characterization, reviewers expressed some sentiment for using at least two RfDs: one for the general adult population and one for pregnant women. Reviewers emphasized that the methylmercury RfD used in the assessment should be reported as an

interim value, and that the assessment should be formulated to facilitate near-term (i.e., within the next several months) modifications to the RfD.

Some comments expressed in the effects breakout group also concerned the risk characterization volume. For example, the values of the NOAELs or LOAELs should be carried forth into the risk assessment instead of transforming them into permissible fish tissue concentrations.

Volume V (Ecological Assessment)

The group generally agreed that the goal was to provide data for a risk assessment and that the appropriate species were identified except for lower trophic levels and wading birds.

There was consensus that methylmercury was the compound of interest in addressing the toxic effects of mercury on piscivores. The consensus was further evidenced by the reported mortality of panthers, which was diagnosed as mercury toxicosis. The group also discussed the fact that the population of wading birds in the Everglades has significantly decreased in the last 5 years. Loss of habitat and exposure to mercury were listed as the suspected causes of these declines. One reviewer reported that loons in Minnesota also were suffering increased mortality from mercury exposure. Analyses showed elevated mercury concentrations in the feathers of juvenile loons. Approximately 2,500 loons died in coastal waters off Florida, in part from mercury exposure.

One reviewer pointed out that ethylmercury was measured in the Everglades, but this compound was not expected to be environmentally or toxicologically important in the overall assessment. Ethylmercury has not been identified in fish, for example. Dimethylmercury also exists in nature, but is quite volatile and, based on known information and the compound's fundamental chemistry, is not expected to represent any significant ecological threat.

Reviewers generally agreed that the report's treatment of methylmercury as a constant fraction of total mercury in the water column was an oversimplification. Additional work might be undertaken to determine the impacts of this assumption on the final estimates of the BAF and wildlife criteria values developed as assessment endpoints.

The group discussed the fact that chronic toxicity tests for methylmercury are extremely limited and that such effects are difficult to demonstrate under field conditions. For example, eggs can be collected from the nests of mercury-contaminated birds; however, it is not easy to detect toxic effects of mercury (e.g., hatching success, survivorship, growth). Different histories of exposure for adult birds may also make it difficult to establish effects in the field. As a result the reviewers suggested that the use of toxic effects measured in the laboratory is justified, particularly developmental effects. In other words, laboratory-to-field extrapolations should be conserved. The group expressed concern about whether frank toxicity is the most appropriate endpoint, but acknowledged that frank effects are the best known.

A couple of reviewers thought that the dose-response relationships were adequately treated, the choice of a NOAEL and LOAEL was acceptable, and the limited toxicity data were used in an appropriate manner to develop the NOAELs and LOAELs used in the assessment. Some discussion ensued concerning the utility of toxicity data from laboratory studies on other animals (e.g., domestic animals and birds); these data might be used to at least help define the range of toxic exposure concentrations. The assessment needs to clarify the use of the wildlife criteria values developed in an approach paralleling human health risks (i.e., protection of individuals) for protecting populations of the selected wildlife species.

There was considerable discussion and concern regarding the validity of the overall conceptual model for the ecological assessment. This relates in part to the consideration of the complex chemistry of mercury in surface waters, where different physicochemical factors might determine exposure. Reviewers noted that lakes located side by side might show very different concentrations of mercury in fish. This multifactor complexity calls into question the linearity implied in the current approach for developing the BAF and wildlife criteria values. The concern is particularly important given the national scope of the intended assessment.

The reviewers noted the need to better articulate the uncertainty regarding the BAFs and the selection of the mean value. They also felt the report needed better discussions of distributions and of the nature of the uncertainty analysis.

Volume VI (Risk Characterization)

The effects breakout group's primary concern regarding Volume VI was its lack of emphasis on risk integration. Volume VI mainly reiterates and summarizes the material presented in the first five volumes. The reviewers were disappointed to find that the wildlife criteria values developed in Volume V were not carried directly through to the risk characterization. Substituting fish tissue mercury concentrations that are consistent with the wildlife criteria values is acceptable as long as the authors can clearly explain in the report why this was done. Nevertheless, the tissue concentrations (or, preferably, the wildlife criteria), should be developed as distributions, not single values. These distributions should be compared with distributions of expected mercury exposures on a regional basis for each of the selected piscivores. Such comparisons, which are more consistent with a probabilistic framework for ecological risk, will quickly identify species and regions of concern. They also will highlight where current information on exposure or toxic endpoints is insufficient to develop distributions that are precise enough for an assessment. Methods such as sensitivity and uncertainty analysis can then be used to examine the variance underlying such imprecision to pinpoint the major factors (e.g., model structure, model parameters) contributing to the overall uncertainty. Identifying the sources of uncertainty is important to promote efficient and effective allocation of limited resources and to improve precision, reduce bias, and refine the overall ecological assessment.

Reviewers felt the risk characterization might also address the risks posed by mercury to production dynamics at lower trophic levels. Clearly, such impacts have a profound effect on fish production that is independent of the direct accumulation and toxic effects on fish. These indirect effects are also relevant for assessing human and piscivore exposure to contaminated fish—fewer, smaller fish translates into reduced exposure, or at least a greater effort to obtain fish and, thus, significant mercury exposure if a larger number of smaller fish are consumed.

The group also expressed concern regarding the report's nearly total reliance on unverified models to produce the risk assessment. Where possible, the models that provided estimates of regional deposition and exposure should be evaluated in relation to known mercury concentrations. Any efforts at "ground-truthing" either the exposure or the toxicity models should be pursued within the resource and time constraints imposed by the overall schedule for delivering the report.

3.4 Overview of Reviewer Discussion in the Plenary Session — Paul Mushak, Ph.D.

Volume VI (Risk Characterization)

Panelists noted that a considerable portion of Volume VI consisted of summaries of Volumes II, III, IV, and V. These summaries covered human and wildlife health effects, overlay maps of sensitive wildlife populations with predicted high mercury depositions, and the uncertainties and assumptions in

modeling emissions. Volume VI then provided a relative exposure ranking, a relative dose-response ranking, and levels of methylmercury in fish tissue that would be of concern for fish eaters.

The panel found the summaries to be confused and lacking; they failed to provide a comprehensive or quantitative discussion of the uncertainties and assumptions, and they did not discuss the extent and magnitude of the harmful exposures. Insufficient attention was given to linkages between anthropogenic emissions and background mercury data with the risk characterization.

One reviewer suggested that an ecological risk assessment be performed by using distributions of the parameters used to develop Tables 4-3 and 4-4 of Volume VI. Reviewers were impressed with the uncertainty analysis for the human RfD value found in Volume IV, Appendix C, and were interested in a discussion of propagated uncertainties.

The methodology and results in the comparative risk chapter of Volume VI were major areas of concern. Reviewers pointed out that the NOAELs and LOAELs are not based on the same set of endpoints and, therefore, are not directly comparable; in fact, the NOAELs and LOAELs may reflect a wide range of adverse responses. Another important concern was that the human NOAEL did not account for uncertainty areas such as different sensitivities. This indicates that use of the RfD would be more appropriate.

Regarding the wildlife criteria, reviewers felt that use of the published rat and monkey dose-response data would potentially capture more subtle effects in the rat. Notwithstanding the problems, information is available to enhance the accuracy of the criteria.

Reviewers offered several caveats regarding the strength of the linkages between point source emissions of mercury and increased levels of methylmercury in fish. Reviewers agreed there is no doubt that fish in certain areas exceed advisory limits. One reviewer claimed that all the conclusions in Volume VI are based on models rather than actual data. The volume would benefit from a discussion of the pathways for which there are claimed to be no data. Reviewers discussed the extent to which the report went beyond actual data, but did not come to a clear consensus.

In terms of fish consumption rates, reviewers felt the estimates of the distribution of such intakes should be improved.

Reviewers agreed that there is a significant need for systematic collection of data on increased levels of methylmercury in exposed wildlife populations.

In the aggregate, the discussion clearly indicated a need to better integrate the exposure and health effects data—for example, by comparing distributions of fish mercury levels with distributions of wildlife criteria. Some reviewers argued that background (baseline) determinations were needed to better determine increases over time. The panel also suggested that the RfD be clearly defined as "interim" and that it be revisited periodically as new data become available. Panelists also questioned the validity of comparing a human NOAEL to overt toxicity-based guidelines in wildlife, and why an RfD was not used.

Several comments concerned specific chapters in Volume VI. Deposition rates drive the overall analysis, and field verification is desirable. With reference to this, the exposure breakout group chair reemphasized that very recent data document the linkage between anthropogenic mercury emissions and deposition (e.g., the existence of a gradient with distance). Also, reviewers agreed that the report should better characterize seafood consumption, since it elevates the baseline for mercury exposure to which freshwater mercury intakes are added for the overall risk characterization. In addition, the panel

recommended that seafood levels not be called "background" because some fraction of mercury in seafood is likely to come from anthropogenic sources.

Volume VII (Risk Management)

Reviewers agreed that Volume VII was generally good, but felt that it emphasized controls and did not adequately examine pollution prevention options. Pollution prevention could include banning products containing mercury (e.g., Minnesota's ban on mercury batteries). Reviewers also expressed concern about the volume's cost estimates for mercury control. For example, could the aggregate cost of reducing mercury emissions by half be calculated?

Reviewers thought it economically inaccurate to allocate all the costs of mercury reduction strictly to mercury, since typical reduction technologies also remove other contaminants. They suggested that the authors lower the cost estimate for mercury reduction by distributing reduction costs over all contaminants controlled by the technologies.

The panel felt that the absence in Volume VII of recommended actions and research needs is a major gap that should be filled. Recommendations could include, for example, market-based approaches, product reformulations, product bans, and recycling. The European experience was suggested as a valuable source for information on market-based approaches.

3.5 Summary of Major Revisions Made in Response to Reviewers Comments

All volumes:

- Executive summaries re-written to be more informative
- Executive summaries written to include conclusions categorized by degree of confidence in the findings, summaries of uncertainties and research to improve the assessment.

Volume II: Inventory of Anthropogenic Mercury Emissions in the United States

- Revised natural emission inventory information to be consistent with Expert Panel Report.
- Added industrial use trends and historical trends
- Updated municipal waste combustor (MWC) inventory to include 50 closures; this resulted in a decrease in the emissions estimate of 10 metric tons/yr to 55 metric tons.
- Added impacts of proposed medial waste incinerator (MWI) and MWC rules.
- Revised inventory to use 1993 instead of 1992 Bureau of Mines data.
- Incorporated maps showing loctions of sources.
- Incorporated industry-specific comments.

Volume III: An Assessment of Exposure from Anthropogenic Mercury Emissions in the United States

- Numerous recent peer-reviewed studies were incorporated.

- Sections added on exposure from anthropogenic , non-ambient sources including dental amalgam, occupational exposure and consumption of marine fish.

- Section added on measured mercury concentrations near multiple local sources

- Additional mercury measurement data from various media added and compared to modeled estimates. These measurements included air concentrations, deposition rates and soil concentrations.

- An assessment of the mercury exposures that result from the input of measured mercury air concentration, deposition rate and soil concentration data to the indirect exposure models was added.

- Modeling assumptions were modified to accommodate new data.

    - Increased percentage of divalent mercury assumed to be particulate bound.

    - Flat terrain only was modeled and effects of complex terrain addressed separately in an uncertainty analysis.

    - The configuration of the watershed was changed and area-averaged deposition rates were utilized.

    - The aquatic trophic levels, which wildlife were assumed to consume, were modified.

    - The assumed quantity of background atmospheric mercury was modified.

    - Deposition velocities for vapor-phase divalent mercury were modified to account for lower dry deposition rates at night.

    - The assumption related to the bioconcentration of atmospheric mercury into green plants was modified to account for lower measured concentrations in edible portions of grains and legumes.

- Exposure models were re-run to accommodate the above assumptions and the revised emissions inventory.

- A section (Appendix H) was added to estimate the size of the fish consuming human population in the U.S., the amounts of fish consumed by the general U.S. population and several high-end-fish-consuming populations, and the amount of mercury measured in surveys of marine and fresh-water fish. These data were used to generate estimates of mercury exposure from fish consumption. These mercury exposure estimates were not attributed to individual sources or source categories.

<u>Volume IV: Health Effects of Mercury and Mercury Compounds</u>

- Section added on pharmacokinetic models. No pharmacokinetic model was chosen for use in the health assessment.

- Germ cell mutagenicity assessment was re-written to remove the numbered classification.

- Additional studies on developmental toxicity of elemental mercury were added raising the overall weight of evidence judgement to "Sufficient Animal Data" for developmental toxicity

- The newly verified RfD for methylmercury was described. A section on input dat and derivation of the benchmark dose was added as was discussion of plausible alternatives to the U.S.EPA RfD.

- Section on interactions of other materials with mercury and section on selenium were re-written.

- A section on mechanism of action of mercury was eliminated.

Volume V: An Ecological Assessment for Anthropogenic Mercury Emissions in the United States

- Discussion of several new studies supplied by the reviewers was added.

- Enhanced discussion of non-mammalian, non-avian life forms

- Obtained original doctoral dissertation describing effects in mink and used as basis for reevaluation of mammalian wildlife criteria.

    - Used revised no observed adverse effect level from dissertation

    - Described uncertainty factor of 10 for subchronic to chronic extrapolation

- Re-evaluated criteria for avian species

    - described available data on loons, but did not calculate a wildlife criterion for this species

    - Described studies form the the National Biological Survey on levels of mercury in eagle feathers.

    - Describe uncertainty in LOAEL to NOAEL extrapolation and species extrapolation

- Analyzed data from laboratory animal studies to bound uncertainty on wildlife criteria

- Clarified assumptions, uncertainties and methods in development of wildlife criteria.

- Described variability and uncertainty in wildlife feeding habits.

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

- Volume was completely re-organized to meet specifications of new U.S.EPA guidance on risk characterization

- Discussion of plausible alternatives to the U.S. EPA RfD on methylmercury included.

- Revised and expanded discussion of uncertainty and variability

- Included estimates of size of "at risk " human and wildlife populations

    - Human estimate based on data from National Center for health Statistics (CDC), U.S. census data, and the Continuous Survey of Food Intake by Individuals. This was combined with measured levels of mercury in marine and fresh-water fish.

    - Wildlife estimates made from literature.

- Highlighted exposure as the major source of variability vs. Species -specific differences in susceptibility to toxic effects.

- Added comparison of mercury exposure estimates with methylmercury RfD or equivalents for humans and wildlife

Volume VII: An Evaluation of Mercury Control Technologies, Costs and Regulatory Issues

- Enhanced discussion of pollution prevention opportunities. These were discussed in qualitative terms and quantified when data were sufficient.

- Integration of control costs with benefits was done, as well as final setion on management alternatives and statutory authorities.

4. SUMMARY OF INTERAGENCY REVIEWERS COMMENTS AND DISPOSITION

Reviews of the External Review Draft of the Mercury Study Report to Congress were obtained from the following U.S. government agencies:

- Agency for Toxic Substances and Disease Registry (ATSDR), Public Health Service, U.S.Department of Health and Human Services.
- National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health
- National Oceanic and Atmospheric Administration (NOAA), Department of Commerce
- U.S. Department of Agriculture (USDA)
- U.S. Department of Energy (DOE)
- U.S. Food and Drug Administration (FDA)
- National Biological Survey.

A meeting of reviewers was held at the U.S. EPA, Washington DC on 1/9/95 to discuss scientific issues concerning the report. Representatives of the above Agencies attended the meeting with the exception of NIEHS; comments from NIEHS were submitted in writing after the meeting. Written comments were requested of all reviewers; responses were received from ATSDR, DOE, NIEHS, USDA and the National Biological Survey. At the meeting and in written reviews point of congruency among Federal risk estimates and methodologies were identified; points of divergent opinion were also noted.

Major critiques are described below as well as U.S. EPA's response (in Italics). It is the Agency's intent to describe in the final Report alternate points of view or risk estimates in those instances wherein U.S. EPA disagrees with another federal agency.

<u>General Comments on the Report.</u>

- Reviewers noted that some references were incomplete or missing.

  These are being completed. To the extent possible within our deadlines papers submitted by the reviewers will be cited in the Report.

- Reviewers felt that the Report would be greatly enhanced in its usefulness if general conclusions on the extent of mercury contamination or degree of hazard could be articulated in plain language.

  This was done for inclusion in Vol. I Executive Summary, which was prepared after the interagency review was completed. In addition, each volume was revised to include a general conclusions summary in its own executive summary.

- Reviewers discussed section 112(n)(1) of the Clean Air Act Amendments of 1990. This specifies the following.

The Administrator shall conduct, and transmit to the Congress not later than 4 years after the date of enactment of the Clean Air Act Amendments of 1990, a study of mercury emissions from electric utility steam generating units, municipal waste combustion units, and other sources, including area sources. Such study shall consider the rate and mass of such emissions, the health and environmental effects of such emissions, technologies which are available to control such emissions, and the cost of such technologies.

- FDA proposed that U.S. EPA was not required to determine or comment upon a threshold for adverse effects of mercury in humans and that it was inappropriate for U.S. EPA to make such a determination in this Report.

  U.S. EPA is obliged to follow consistent methodologies and published Guidelines for Human Health Risk assessment in it evaluation of potential human health impacts of environmental agents. For general systemic non-cancer health endpoints this includes consideration/calculation of reference doses (RfD) or reference concentrations (RfC). The methods used for derivation of RfDs and RfCs are based on the assumption of a population threshold for response in the absence of data which indicates that no threshold exists. It was agreed by both scientific staff and U.S. EPA management that application of state-of-the art methodologies for calculation of RfDs and RfCs was an appropriate part of the Mercury Study. A statement of the FDA critique will be included in the section of the Report summarizing reviewer comments.

- Reviewers noted that the Report did not deal with the impacts of global mercury use or emissions or of "natural" mercury.

  U.S. EPA was directed in the CAAA to deal with emissions from various specified sources and "other sources, including area sources". When data were sought and models constructed, it became obvious that contemporary, reliable emissions data on mercury were not sufficient to support a national survey. Neither the extant data nor modeling technology permitted accurate modeling of emissions from countries other than the U.S. The acknowledged global cycling of mercury was accounted for in the incorporation of a 1.6 ng/m^3 "background level" into the long-range transport modeling (RELMAP). The Report describes the impossibility of determining whether mercury is of "natural" or anthropogenic origin; there is, for example a discussion of hypotheses that mercury soil levels in sites distant from emissions sources can be the consequence of deposition over time of mercury released as a result of human activities. The Executive Summary and Exposure volumes will indicate that any local evaluation of mercury hazard must use local determinations of mercury in media.

<u>Volume II: Inventory of Anthropogenic Mercury Emissions in the United States.</u>

- The emissions inventory was thought generally to be comprehensive and well described. The was general agreement with the conclusions on relative source contributions.

- An explanation should be given in this volume of the use of emissions data in the exposure modeling.

  This was done.

- A description of derivation of emission modifying factors (EMF) was requested; specifically, were these numbers means, representative values, etc.

  This information was added.

- USDA proposed the lack of an estimate of mercury emissions from landfills was a serious deficit.

  Data are not available which permit any sort of generalization about the magnitude of emissions from this source type. There is only one study of mercury emitted from a landfill area; this was done in Minnesota, and there is no indication that this site was representative of other waste sites. Studies on landfills as a potential mercury source have emphasized pathways leading to groundwater contamination rather than release to the air.

- USDA also remarked that mercury from application of sewage sludge to farm land was not considered as a source.
  The Report does include some information on sewage sludge incineration and its potential for mercury release to the atmosphere. Data on consequences of land application of sludge, if provided by the USDA, will be included in Vol II or III as appropriate.

- The National Biological Survey recommended adding more information on the re-emission of deposited mercury of anthropogenic origin.

  This will be discussed in the Report as a source for which data are not available and as a contributor to possible underestimation of over all emissions.

<u>Volume III: An Assessment of Exposure from Anthropogenic Mercury Emissions in the United States.</u>

- There was general agreement that mercury deposition model results were reasonable predictions given available data. There was discussion of impacts of using emission factors from washed coal and from seams most recently used by coal fired utility boilers on the relative ranking of source contributions. There was discussion of the likelihood that methylmercury is released from utility stacks; consensus opinions of U.S. EPA and reviewers were that there were no conclusive data on methylmercury release.

- USDA raised concern that parameters (e.g., amounts of foodstuffs consumed by human populations) used in Vol III modeling were inconsistent with those used in the sludge evaluations.

  The parameters will be compared, and any departures from the sludge methodologies will be described; justifications for departure will be provided.

- USDA identified consumption of wild mushrooms as a source of mercury.
  Description of this source based on material if provided by USDA will included in Vol III.

- ATSDR noted that use of the term "subsistence fisher" in the assessment was inaccurate because the consumption rate used was not sufficient to constitute dietary subsistence.

Use of "high end fish consumer" or some other more descriptive term will be substituted.

- DOE and others cautioned against using "significant" outside a statistical context.

  Another term will be used when statistical significance is not being described.

- There was discussion of the availability and usefulness of mercury total body burden data.

  It was agreed to incorporate such data as were available from ATSDR and on recent reports from Sweden and on a group of Chippewa Native Americans. The Report will describe the limitations on comparison of the modeled predictions with body burden data. Body burden data include cumulative exposure to non-anthropogenic mercury and mercury in marine fish.

- There was discussion on variability in estimates of percent of mercury in food sources as methylmercury.

  The Report describes this variability. Sources of our estimates will be checked to ensure that attribution is clear.

- There was a brief discussion of the impact of dental amalgams on total mercury body burden.

  Discussions in the report on amalgam mercury release will be reiterated in the beginning of Vol III in the section outlining those sources which were modeled, how background is considered, etc.

- Several reviewers pointed to the lack of information on marine fish. It was noted by FDA that one cannot generalize as to whether marine fish or freshwater fish are likely to have higher concentrations of mercury.

  The modeling of mercury deposition employed by U.S. EPA of necessity dealt only with mercury in U.S continental, fresh water lakes and streams. The Report contains one table on measured mercury levels in commercial marine fish. This will be enhanced with data supplied by the reviewers, and the accompanying discussion expanded and moved to the beginning of the report. Conclusion statements of the Report will acknowledge that the majority of fish consumed in the U.S. is marine fish. Marine seafood consumption estimates will be included in discussions in Volume VI.

- The NOAA and the National Biological Survey reviewers said that the mercury species found in fish flesh varies with the type and trophic level of fish.

  Variation reported in the literature will be described in Volume III.

- The reviewer from the National Biological Survey took issue with some assumptions used in the deposition modeling; specifically, he asserted that most precipitated mercury is particulate bound and that methylmercury can be introduced into systems by wet deposition.

The recommended papers (Benoit, Fitzgerald and Damman, 1994., Holtberg et al, Monterey Conference Proceedings) will be evaluated as to inclusion in the Report. Note that Benoit et al is in press and may not be available for evaluation in the time frame of U.S. EPA's Report deadlines.

- The National Biological Survey registered a strong objection to the use of bioaccumulation factors or other means to make generalized statements as to relationship between mercury in water and predicted concentrations of mercury in fish inhabiting the water. The reviewer stated that local biogeochemistry is highly variable with the result that fish taken from water bodies with the same mercury concentration can have very different mercury concentrations in the tissue. Discussion focussed on factors governing this variability; it was acknowledged that there are no data to allow modeling of any one factor or combination of factors. There was discussion of use of the EPRI Mercury Cycling Model (MCM). There was agreement that this is not appropriate as a basis for local or general conclusions as to relationship between water and fish mercury concentrations. The objection to the MCM stems in large part from its basis on data from a water body not considered to be representative of other U.S. freshwater lakes.

  U.S. EPA maintains that some form of estimate of fish tissue mercury level is needed to evaluate the potential impact of anthropogenic mercury emissions on human and wildlife health. The Report will be amended to include local biogeochemistry as a source of substantial variability in fish mercury predictions. Ranges of mercury fish levels provided by the National Biological Survey will be used to describe the extent of variability. This will be added to the discussion of limitations of use of the modeled estimates for any site-specific evaluation.

- USDA described the potential for sheep to consume beet greens which may be a source of mercury.

  Volume III will be reviewed to ensure that sources of mercury contamination not modeled are mentioned.

<u>Volume IV: Health Effects of Mercury and Mercury Compounds.</u>

- There was agreement with the hazard identification categories for carcinogenicity, developmental toxicity and germ cell mutagenicity for elemental, inorganic and methylmercury with the exception noted below. It was agreed that no low dose extrapolation for potential carcinogenicity of inorganic mercury or methyl mercury is supported by existing data. It was agreed that immune-mediated glomerulonephritis is the critical effect for a reference dose for inorganic mercury. It was agreed that a reference concentration for elemental mercury of $3x10^{-4}$ mg/m^3 is reasonable. After much discussion (excerpted below) it was agreed that a reference dose for methylmercury is within an order of magnitude of 10^{-4} mg/kg-day.

- It was recommended that "methylmercury" be substituted for "organic mercury".

  This change has been made in the Report.

- U.S. EPA discussed the pending revisions to the Guidelines for Risk Assessment of Carcinogens.

While the current alphanumeric classification will be maintained in the text, discussion of these classifications will be enhanced to conform to the narrative classifications which U.S. EPA will likely use in the near future. In addition the number classification in the discussion of germ cell mutagenicity will be dropped.

- ATSDR indicated that there are new data on developmental effects resulting from inhalation exposure to elemental mercury.

  These studies will be evaluated and the classification of "insufficient evidence for developmental toxicity" re-examined.

- In its derivation of an intermediate MRL for inorganic mercury ($2x10^{-3}$ mg/kg-day) ATSDR used a NOAEL 0.23 for F344 rats gavaged for six months as part of the subchronic range-finding component of a cancer bioassay (NTP, 1993).

  This study was not available at the time that U.S. EPA convened an expert panel to derive its RfD for inorganic mercury. That panel recommended use of data from short term studies in Brown Norway rats as an animal model appropriate to estimation of potential toxicity in sensitive human subpopulations. The NOAEL and LOAEL from the NTP bioassay are within the range observed in three studies in the Brown Norway rat. U.S. EPA scientists have concluded that the existing RfD, described in the 1988 Drinking Water Criteria Document for Inorganic Mercury is not impacted by the more recent data from NTP. The ATSDR evaluation will be described and compared to U.S. EPA's in the risk assessment chapter of Vol IV.

- The FDA reviewer stated that in deriving an RfD for methylmercury (and other agents) U.S. EPA does not estimate or predict the degree of risk but rather estimates a measure of a "safe" level of exposure. The reviewer felt that the "bright line" approach dose not constitute a risk assessment.

  There was some agreement with the reviewer's position, particularly in the utility of predicting risk above a hypothetical threshold. U.S. EPA, however, has not completed analyses which would support such an estimate of risk. The question of whether the data used (neurologic deficits in children of Iraqi mothers who ingested contaminated grain during gestation, Marsh et al 1987) are suitable to this type of analysis is an open one. At this time U.S. EPA will not include any estimate of risk above the RfD in the Report. Discussion will be continued by U.S. EPA and FDA scientists with the goal of deriving an estimate of methylmercury risk for ingestion levels.

- There was discussion of the impact of current studies of developmental effects in populations which consume high end levels of marine fish and/or mammals (the Faroe Islands and Seychelles Islands studies). Some results these epidemiologic investigations have been presented at recent meetings and have been published in abstract in proceedings. It was the opinion of the FDA reviewer that these studies show no (or little) neurologic impairment in children exposed *in utero* to mercury levels associated with observed effects in the Iraqi population on which U.S. EPA based its RfD. U.S. EPA was encouraged to use these data in their quantitative assessment of non-cancer effects.

  U.S. EPA can only use data which are available to the scientific community and have undergone a process of peer review. The deadlines specified in the CAAA do not permit

delay until the studies have been published in the peer reviewed press or the data submitted to U.S. EPA for a process of expert review. (It was noted that U.S. EPA has missed the submission date (11/94) specified in the CAAA.) The Faroe and Seychelles Islands studies as reported in abstract are described in Volume IV. In response to the critique that there has been no influence of these results in U.S. EPA's risk evaluation, the Report will be amended in the following ways. In both Vol IV and Vol VI (Risk Characterization), the potential for the Faroes and Seychelles results to decrease uncertainty in the RfD will be described. Alternative approaches will be described; specifically, decreasing the uncertainty factor or using the upper bound on the 10% risk level for the benchmark dose (vs the lower bound which U.S. EPA employed). These alternatives will be used to describe the range around the U.S. EPA RfD of $1x10^{-4}$ mg/kg-day.

Volume V: An Ecological Assessment for Anthropogenic Mercury Emissions in the United States.

- There was agreement that data are insufficient for evaluation of mercury impacts on any ecosystem. There was agreement that data were insufficient to calculate a wildlife criterion for Florida panthers. There was no objection to development of wildlife criteria for methylmercury only. It was agreed that lack of data on sensitive indicators of toxic effect in wildlife species is a major contributor to uncertainty in the estimates.

- The National Biological Survey reiterated its concern with use of any method (such as a BAF) which relates water concentrations of mercury to fish concentrations.

  Volume V will repeat discussions of variability in fish concentrations due to local biogeochemistry.

- USDA felt that in derivation of the trophic level 3 and 4 BAFs that a geometric mean was more appropriate than the simple mean used.

  All calculations were performed on the logs of values; arithmetic values presented in tables were converted from logs after derivation of means and percentiles. Geometric means were, thus, used in derivation of the BAFs. Estimates will be included in description of BAF derivation.

- The reviewer from the National Biological Survey objected to the presentation of maps showing overlay of wildlife habitat with mercury deposition and low and normal pH water bodies. The reviewer felt that the maps (with the Florida panther as the example) were misleading and gave a false impression that no problem exists for some species.

  The maps were designed to show only predicted high mercury deposition and do not rule out the likelihood of mercury contamination in areas (particularly wetlands) contiguous to high deposition areas. The purpose of the overlay procedure was to highlight areas and species of concern, not to eliminate areas as of no interest. The extent to which overlap can be quantified is being examined; results will be included in the Report as feasible. The purpose and limitations of the overlay maps will be explicated more completely in Vol V.

- ATSDR indicated in the derivation of wildlife RfDs and criteria that interspecies extrapolation not based on pharmacokinetic data will have an unacceptable degree of uncertainty.

  Thus far, no useful data on pharmacokinetics in the species of interest have been available. Additional literature searches are being conducted in that area. U.S. EPA scientists feel that an adjustment of the NOAEL reported for mink is not need for application to otters. The adjustment of the NOAEL derived in mallards for application to three fish-eating birds will be re-evaluated if data permit.

- Several reviewers queried whether the wildlife criteria were conservative. Questions were raised about the likelihood that wildlife have evolved protective adaptations to mercury toxicity.

  Data are insufficient to answer either question. The endpoints tested in the wildlife species are neither as sensitive nor as subtle as those detected in humans exposed to methylmercury. There is no indication whether individual species or ecosystems are being impacted by mercury such that viability or reproduction is reduced. Discussion of this uncertainty will be expanded and reiterated in Volumes V and VI. Information from the National Biological Survey on correlation between eagle feather mercury levels and reproductive rates will be included.

<u>Volume VI: Characterization of Human Health and Wildlife Risks from Anthropogenic Mercury Emissions in the United States.</u>

- After much discussion there was agreement that data (limited as they are) for wildlife and humans do not show special sensitivity of one species over the others. The range of (adjusted) NOAELs is in within an order of magnitude.

- There was much discussion on the comparisons made at the end of Volume VI: NOAELs and LOAELs for human and wildlife populations, levels of mercury in fish which would result in exposure to NOAELs or LOAELs given assumptions of fish consumption. The utility of this approach was questioned by some reviewers; the soundness of the data and extrapolations were questioned by others.

  U.S. EPA is reconsidering the comparisons made. Our preference at this time is for some form of interspecies comparison; an holistic approach to assessment of risk for human and non-human species is the direction which ORD is taking, based on recent mandates and advice to U.S. EPA. The method of comparison used in the Report is untried. It may be advisable to limit the scientific uncertainty by backing up a few steps; that is to limit comparisons to LOAELs and NOAELs without the additional step of including exposure assumptions to calculate reference levels of mercury in fish. The advantage of the last step is that it makes clear the relationship between measured adverse endpoint in species of concern and guidance levels such as fish advisories.

- Several reviewers found they could not follow the process of wildlife NOAEL estimation from the text or tables in Volume VI.

  The estimation of all NOAELs and LOAEL will be explained more fully in Volume VI. The use of uncertainty adjustments as proposed in the Great Lakes Initiative will be explained.

- Reality checks as to measured levels of mercury in wildlife were requested by reviewers.

  Information from Vol III, Vol V and new information supplied by the National Biological Survey (eg., levels of mercury in feathers) will be carried over to Vol VI.

- There was agreement among all parties that the Report and Volume VI in particular should present conclusions as emphatically and clearly as the science permits.

  Conclusions for all volumes will be articulated and presented in each Executive Summary chapter. These conclusions will be re-stated in Volume VI (for risk assessment) and in Volume I (for all conclusions).

<u>Volume VII: An evaluation of Mercury Control Technologies, Costs and Regulatory Issues.</u>

- There was agreement that the description of control technologies and the costs of controls was comprehensive and as accurate as extant data permit.

- Reviewers discussed the "societal cost" chapter of Vol VII. DOE asked whether a cost/benefit analysis was done. Reviewers asked if impacts on international trade (eg GATT) were considered. FDA inquired specifically if benefits of fish consumption (health and societal) were weighed against costs.

  The CAAA mandate did not specify a cost/benefit analysis for this report. The study included only material which could be used for cost/cost comparisons (e.g., cost of mercury control vs. loss of revenue from recreational fishing). It was agreed after discussion that (unlike the situation for lead exposure) there are insufficient population data or economic impact data for subtle health effects to permit a suitable cost/benefit analysis.