# REPORT ON THE PEER REVIEW OF THE HUDSON RIVER PCBs HUMAN HEALTH RISK ASSESSMENT

***—Final Report—***

*Prepared for:*

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EPA Contract No. 68-W6-0022
Work Assignment No. 4-12

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September 2000

**NOTE**

This report was prepared by Eastern Research Group, Inc. (ERG), an EPA contractor, as a general record of discussion for the peer review meeting. This report captures the main points of scheduled presentations and highlights discussions among the reviewers. This report does not contain a verbatim transcript of all issues discussed during the peer review. Additionally, the report does not embellish, interpret, or enlarge upon matters that were incomplete or unclear. EPA will evaluate the recommendations developed by the reviewers and determine what, if any, modifications are necessary to the current risk assessment. Except as specifically noted, no statements in this report represent analyses or positions of EPA or of ERG.

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## LIST OF ABBREVIATIONS

| | |
|---|---|
| CSF | cancer slope factor |
| CTE | central tendency exposure |
| EPA | U.S. Environmental Protection Agency |
| ERG | Eastern Research Group, Inc. |
| GE | General Electric |
| HHRA | Human Health Risk Assessment |
| HI | hazard index |
| IRIS | Integrated Risk Information System |
| NYSDOH | New York State Department of Health |
| PCBs | polychlorinated biphenyls |
| RfD | reference dose |
| RME | reasonable maximum exposure |

## EXECUTIVE SUMMARY

Six independent peer reviewers critiqued the "Human Health Risk Assessment" (HHRA) and its Responsiveness Summary, which were prepared as part of the U.S. Environmental Protection Agency's (EPA's) reassessment of the Hudson River PCBs Superfund site. At the end of the peer review meeting held in May 2000, all six reviewers indicated that the HHRA and its Responsiveness Summary were "acceptable with revisions." Two reviewers indicated that major revisions were required, one indicated the need for minor revisions, and three reviewers did not explicitly state the extent of the revisions needed.

During the 1½-day meeting, the peer reviewers answered nine charge questions that addressed various aspects of the human health risk assessment. These questions asked reviewers to comment on the technical merit of the approaches used in different phases of the risk assessment process, including hazard identification/dose-response assessment, exposure assessment, uncertainty analysis, and risk characterization. Reviewers also evaluated the overall clarity and transparency of the HHRA and its Responsiveness Summary.

Reviewers agreed that the document was consistent with the basic guidelines and guidance set forth for a Superfund human health risk assessment and commended EPA for its efforts. However, the reviewers did identify some weaknesses that they felt lessened the scientific credibility of the risk assessment. Five out of the six reviewers commented that the risk assessment needed to be expanded to provide additional perspective on what the risk estimates mean in the context of the real world. The reviewers encouraged EPA to expand discussions about the uncertainties associated with the toxicity values used and how the consideration of newer toxicity data might change the results of the risk assessment. The majority of the reviewers also indicated the need for an expanded quantitative uncertainty analysis that would generate confidence intervals on the cancer risk estimates and hazard indices. The reviewers also expressed concern that the HHRA focused on anglers and provided only limited analysis of childhood and fetal exposures. Lastly, the group agreed that the HHRA needed to be more transparent when describing and justifying the selection and evaluation of exposure pathways, modeled exposure concentrations, and toxicity values.

A more detailed summary of reviewer comments and recommendations is presented below, by discussion topic. Unless otherwise stated, reviewers voiced general agreement with these summary points.

*Hazard Identification/Dose Response*

- Using the current toxicity values for PCBs from EPA's Integrated Risk Information System (IRIS) is appropriate, but a new section should be added to Chapter 4 (Toxicity Assessment) to provide a quantitative and/or qualitative discussion on the more recent studies on both cancer and non-cancer endpoints to determine what effect these studies might have on risk estimates (e.g., Will risk estimates go up, down, or stay the same?).

- List all sources of uncertainty pertaining to the IRIS toxicity criteria used to calculate the point estimates and qualitatively discuss the effect on risk (high, medium, low) and the extent to which the toxicity data selected for use in the assessment would affect risk estimates (Will the risk estimates go up, down, or stay the same?). For example, factors to consider include the use of animal data, uncertainty factors, modifying factors, and high-to-low dose extrapolation models.

- Some reviewers strongly encouraged a quantitative evaluation of the uncertainty associated with the toxicity data and recommended that this information be incorporated within the overall uncertainty analysis of the Hazard Index (HI) and cancer risk estimates. Other reviewers stated that qualitative discussion of the uncertainty associated with the toxicity data is sufficient.

*Exposure Assessment*

- Fish ingestion rates used in the point estimates are reasonable for adults.

- Data from the New York State Department of Health's (NYSDOH's) recent survey should be incorporated to verify whether the Connelly et al. (1992) study captures the demographics of the exposed population.

- Assuming that all fish consumed originate from the Upper Hudson River seems unreasonable (too conservative).

- Some reviewers commented that evaluating exposures on a location-by-location basis would better characterize exposed subpopulations. Other reviewers felt this issue was minor.

- Justification for scenarios and/or pathways (e.g., soil-related pathways) that were *not* quantified in the risk assessment should be added to Table 2-1.

- All aquatic species that may be consumed (e.g., turtles and eels) may not have been evaluated, which could result in an underestimation of risks. A discussion of this issue should be included in the uncertainty analysis.

- Some reviewers would like information on the size of the exposed population included in the HHRA.

- Because the HHRA assumes that exposure begins in 1999, the text should emphasize that the risks estimated in this assessment are incremental and overlay previous exposures/risks.

- Include a discussion of PCB clearance rates (i.e., half-life of PCBs in the human body) and how these rates relate to exposure duration and the application of the reference dose (RfD).

- The averaging times used are appropriate except for the evaluation of effects to pregnant and nursing women. EPA should evaluate the appropriate exposure duration averaging for this group (i.e., this should be less than the 7 years used in the HHRA [e.g., 1-2 years]). The averaging time for fetuses (pregnant women) should include the range (days to months) for peak exposures. In addition, some reviewers suggested that the exposure duration be 7 years for both the central tendency exposure (CTE) and reasonable maximum exposure (RME).

- Modeling efforts used to calculate fish concentrations and validation of models are not adequately discussed in the HHRA. The text needs to be expanded and clarified to provide information on the uncertainty and temporal and spatial variations in the average concentration in various species of fish.

*Monte Carlo/Uncertainty Analysis*

- Include a table that defines variability and uncertainty (confidence intervals) for all input parameters. For those parameters for which a distribution is defined, the rationale for the selected distribution should be described.

- The uncertainty analysis needs to be enhanced. CTE and RME cancer risk estimates and HI values need to have confidence intervals.

- Because the Monte Carlo presentation was difficult to follow and not always transparent, additional clarification is warranted.

*Risk Characterization*

- Qualitatively acknowledge that background exposures and the fact that the study population has been pre-exposed are likely to increase the HI and cancer risk estimates. Evaluating background and pre-exposures could be important in calculating remediation goals and/or for risk management issues.

- Discuss the conservatism of the cancer slope factor (CSF) and potential non-conservatism of the RfD for PCBs and its effect on the final risk estimates.

- Provide an expanded interpretation of results, clearly explaining that the cancer risk estimates are theoretical and upper-bound and that the true cancer risk is likely to be lower and could even be zero.

*General Recommendations*

- Evaluate exposures of pregnant women (and consequently the developing fetus) and exposures via the ingestion of mother's milk in the HHRA.

- Include a qualitative discussion on the applicability of the IRIS RfD value to pregnant women and nursing neonates, considering the issues related to potential neuro developmental effects of PCBs in children.

- Discuss the potential interactive and cumulative effects that other chemicals, which also may be present in the Upper Hudson River, may have on PCB toxicity.

- Include all the information/data that will be necessary to calculate a range of fish concentrations necessary for risk management objectives.

- Throughout the HHRA, include the necessary and relevant information from other supporting documents to make the risk characterization section more transparent (e.g., calculation of fish concentrations).

## 1.0 INTRODUCTION

This report summarizes an independent peer review by six experts of the following documents the U.S. Environmental Protection Agency (EPA) released as part of its reassessment of the Hudson River PCBs Superfund site:

- Human Health Risk Assessment (HHRA), Upper Hudson River (TAMS Consultants, Inc., Gradient Corporation, 1999).
- Responsiveness Summary for Human Health Risk Assessment, Upper Hudson River (TAMS Consultants, Inc., Gradient Corporation, 2000).

To facilitate their evaluations of these reports, the reviewers also were given copies of several additional reports with relevant background information. Section 1.2.2 lists these additional references.

The reviewers attended two meetings, both of which were open to the public. The first meeting took place in Saratoga Springs, New York, on March 22–23, 2000. This meeting included several presentations and a tour of the Upper Hudson River to familiarize the reviewers with the site and its environmental history. The second meeting took place in Saratoga Springs, New York, on May 30–31, 2000. This meeting was the forum in which the reviewers critiqued the above documents. Eastern Research Group, Inc. (ERG), a contractor to EPA, organized the expert peer review and prepared this summary report.

This introductory section provides background information on the Hudson River PCBs Superfund site, the scope of the peer review of the HHRA, and the organization of this report.

### 1.1 Background

In 1983, EPA classified approximately 200 miles of the Hudson River in the state of New York—from Hudson Falls to New York City—as a Superfund site, because of elevated concentrations of PCBs in the river's sediments. The sediments are believed to have been contaminated by discharges of PCBs over approximately 30 years from two General Electric (GE) capacitor manufacturing plants, one in

Hudson Falls and the other in Fort Edward. After an initial assessment, EPA issued an "interim No Action decision" in 1984 for the contaminated sediments of the Hudson River PCBs site.

Since 1990, EPA has been reassessing its earlier decision to determine whether a different course of action is needed for the contaminated sediments in the Hudson River. EPA is conducting this reassessment in three phases: compiling and analyzing existing data for the site (Phase 1), collecting additional data and using models to evaluate human health and ecological risks (Phase 2), and studying the feasibility of remedial alternatives (Phase 3). EPA has documented its findings from Phase 2 of the reassessment in a series of reports, four of which have already been peer reviewed by independent scientists.

As part of Phase 2, EPA's contractors developed a baseline human health risk assessment (HHRA) for the Upper Hudson River. The HHRA quantitatively evaluated both cancer risks and non-cancer health hazards from exposure to PCBs in the Upper Hudson River, which extends from Hudson Falls, New York, to the Federal Dam at Troy, New York. The HHRA evaluated only those potential health risks associated with exposures to PCBs. The objective of the Phase 2 risk assessment was to update the findings from Phase 1 in light of the following new information: (1) additional PCB data collected in water, sediment, fish and other biota; (2) PCB concentration estimates in environmental media based on extensive modeling efforts; (3) an extensive review of fish ingestion surveys; and (4) an extensive review of the cancer toxicity of PCBs. Another goal of the Phase 2 HHRA was to estimate risk to the average exposed individual as well as to the reasonably maximally exposed individual. Upon its completion, the HHRA was released for public comment. To address comments received during the public comment period, EPA released a Responsiveness Summary, which included EPA's response to comments as well as revisions to the risk assessment. EPA also conducted an ecological risk assessment as part of Phase 2, separate from the HHRA.

To ensure that the assumptions, methods, and conclusions of the HHRA and its Responsiveness Summary are based on sound scientific principles, EPA decided, as per policy, to obtain an expert peer review of the documents. The remainder of this report describes the scope and findings of this independent peer review.

## 1.2 Scope of the Peer Review

ERG managed every aspect of the peer review, including selecting reviewers (see Section 1.2.1), briefing the reviewers on the site (see Section 1.2.2), and organizing the peer review meeting (see Section 1.2.3). The following subsections describe what each of these tasks entailed.

### 1.2.1 Selecting the Reviewers

To organize a comprehensive peer review, ERG selected six independent peer reviewers who have demonstrated expertise in one or more of the following technical fields:[1]

- Exposure assessment
- Risk assessment
- Statistics
- PCB toxicology
- Uncertainty analysis

Appendix A lists the six reviewers ERG selected for the peer review meeting, and Appendix C includes brief bios that summarize most of the reviewers' areas of expertise. Recognizing that few individuals specialize in every technical area listed above, ERG ensured that the collective expertise of the selected peer reviewers sufficiently covers the five technical areas (i.e., at least one reviewer has expertise in exposure assessment, at least one reviewer has experience in risk assessment, etc.).

To ensure the peer review's independence, ERG only considered individuals who could provide an objective and fair critique of EPA's work. As a result, ERG did not consider in the reviewer selection process individuals who were associated in any way with preparing the HHRA or individuals associated with GE or any other specifically identified stakeholder.

[1]ERG initially selected seven peer reviewers. Dr. Arnold Schecter was eliminated as a reviewer prior to the peer review meeting due to the disclosure of a potential conflict of interest.

### 1.2.2 Briefing the Reviewers

Given the large volume of site-specific information in the HHRA and the fact that none of the reviewers had extensive experience with the Hudson River PCBs site, ERG organized a 2-day meeting prior to the actual peer review to provide the reviewers with background information on the HHRA and to tour the Upper Hudson River. The purpose of the meeting was strictly to familiarize the reviewers with the site; the reviewers did not provide technical comments on EPA's reports during this briefing. A copy of the minutes from this briefing can be found in Appendix G.

For additional background information on the site and its history, ERG provided the following other documents to the reviewers. Reviewers were also pointed to additional Reassessment RI/FS documents available on EPA's Web site (www.epa.gov/hudson).

- Human Health Risk Assessment Scope of Work, July 1998.
- Responsiveness Summary For Human Health Risk Assessment Scope of Work, April 1999.
- Executive Summary for the Human Health Risk Assessment, Mid-Hudson River. December 1999.
- Executive Summary for the Baseline Ecological Risk Assessment. August 1999.
- Executive Summary for the Baseline Ecological Risk Assessment for Future Risks in the Lower Hudson River. December 1999.
- Executive Summary for the Revised Baseline Modeling Report. January 2000.
- Suggested charge questions from the public for the HHRA. February and March, 2000.

To focus the reviewers' evaluations of the HHRA, ERG worked with EPA to develop written guidelines for the technical review. These guidelines (the "charge") were presented during the briefing meeting and asked the reviewers to address at least the following topics: the reasonableness of the approaches used in the dose-response assessment, exposure assessment, and uncertainty analysis, and the overall technical soundness, transparency, and clarity of the HHRA. A copy of this charge, which includes many additional topics and questions, is included in this report as Appendix B.

In the weeks following the briefing, ERG requested that the reviewers prepare their initial evaluations of the HHRA and its Responsiveness Summary. ERG compiled these premeeting comments, distributed them to the reviewers, and made copies available to observers during the peer review meeting. These initial comments are included in this report, without modification, as Appendix C. It should be noted that the premeeting comments are preliminary in nature and some reviewers' technical findings might have changed based on discussions during the meeting. As a result, the premeeting comments should not be considered the reviewers' final opinions.

The peer reviewers were asked to base their premeeting comments on the written materials distributed by ERG— mainly the HHRA and its Responsiveness Summary—even though they received many additional documents as background information. Though not required for this review, some reviewers might also have researched site-specific reports they obtained from other sources.

### 1.2.3 The Peer Review Meeting

The six peer reviewers and at least 30 observers attended the peer review meeting, which was held at the Holiday Inn in Saratoga Springs, New York, on May 30–31, 2000. Appendix D lists the observers who confirmed their attendance at the meeting registration desk. The schedule of the peer review meeting generally followed the agenda, presented here as Appendix E. As the agenda indicates, the meeting began with introductory comments both by the designated facilitator and by the designated chair of the peer review meeting. (These and other introductory comments are summarized below.) For the remainder of the meeting, the reviewers provided many comments, observations, and recommendations when answering the questions in the charge. The agenda included two time slots for observer comments, which are summarized in Appendix F of this report. An ERG writer attended the meeting and prepared this summary report.

On the first day of the meeting, Jan Connery of ERG, the designated facilitator of the peer review, welcomed the six reviewers and the observers to the 1½-day meeting. The peer reviewers then introduced themselves, noted their affiliations, identified their areas of expertise, and stated that they had no conflicts of interest in conducting the peer review, after which selected representatives from EPA and EPA's contractors introduced themselves and identified their roles in the site reassessment.

Following the introductions, Ms. Connery stated the purpose of the peer review meeting, identified the documents under review, and described the steps in the peer review process preceding the meeting (the March 2000 briefing and the compilation of pre-meeting comments). Ms. Connery reviewed the agenda, at which time she explained the procedure that observers should follow to make comments and pointed the group to the charge questions that the reviewers would be discussing. Ms. Connery explained how Holly Hattemer-Frey—peer reviewer and the technical chair of the meeting—would summarize premeeting comments and then proceed with question-specific discussions. Lastly, Ms. Connery reminded the reviewers that, at the end of the meeting, each reviewer would be requested to provide individual recommendations.

Ms. Alison Hess, EPA's project manager for the Hudson River PCB reassessment, then provided introductory remarks. She acknowledged several points identified in the reviewers' premeeting comments on the HHRA that required clarification. EPA provided the reviewers with a table that summarized these points. Ms. Hess and David Merrill, Gradient Corporation (EPA's contractor), then briefly reviewed the technical issues presented in the summary table, providing clarification or additional information. The presentation paralleled the issues raised in the charge questions. Specifically, EPA (1) pointed to HHRA and Responsiveness Summary coverage of the newer PCB toxicity studies and its assessment of child and prenatal exposures; (2) reviewed its approach to assessing fish intake rates; (3) justified exposure duration selection; (4) provided additional perspective on the modeled fish concentrations; (5) clarified Monte Carlo analysis methodologies, including justification for not performing a two-dimensional analysis; and (6) provided the rationale for limiting the HHRA to the assessment of potential cancer risks and non-cancer health hazards associated with PCBs in the river sediments (and associated biota).

Following the introductory presentations, Ms. Hattemer-Frey began the technical discussions of the peer review meeting. At the outset, she set the ground rules for the discussions. Specifically, she explained that the reviewers were to discuss technical issues among themselves and were to consult with EPA only for necessary clarifications. Ms. Hattemer-Frey emphasized that the reviewers' primary purpose was to critically review the HHRA and make recommendations that would improve its technical merit. She noted that the meeting would not focus on reaching a consensus on any issue.

Ms. Hattemer-Frey worked with the peer reviewers to discuss and answer the questions in the charge. Ms. Hattemer-Frey noted that common themes identified in the premeeting comments (i.e., issues presented by more than two reviewers or strong comments made by at least one reviewer) would serve as discussion points for the meeting. The remainder of this report summarizes the peer reviewers' discussions and documents their major findings and recommendations.

### 1.3 Report Organization

The structure of this report reflects the order of questions in the charge to the reviewers: Section 2 of this report summarizes the reviewers' discussions on specific questions regarding the technical merit of the primary components of the HHRA (i.e., hazard identification/dose-response, exposure assessment, Monte Carlo analysis/uncertainty analysis, and risk characterization). Section 3 summarizes the discussions on general questions posed to the peer reviewers; and Section 4 highlights the discussions that led to the reviewers' final recommendations. Section 5 lists all references cited in the text. In these sections, the reviewers' initials are used to attribute technical comments and findings to the persons who made them.

As mentioned earlier, the appendices to this report include a list of the peer reviewers (Appendix A), the charge to the reviewers (Appendix B), the premeeting comments organized by the authors (Appendix C), a list of the observers who confirmed their attendance at the meeting registration desk (Appendix D), the meeting agenda (Appendix E), summaries of the observers' comments (Appendix F), and minutes from the March 2000 informational briefing for the reviewers (Appendix G).

## 2.0 RESPONSES TO SPECIFIC QUESTIONS REGARDING THE HHRA

Peer reviewer discussions opened with responses to the seven specific charge questions related to hazard identification/dose response, exposure assessment, uncertainty, and risk characterization issues. The key points communicated during these discussions are summarized below and detailed in the sections that follow.

- *Question 1 (Hazard Identification/Dose-Response).* The reviewers agreed that the use of current IRIS toxicity values for PCBs was appropriate, but strongly recommended that the HHRA include expanded discussions on the uncertainties and the level of conservatism of the CSF and RfD. Also, reviewers recommended that expanded discussions be included on the impact the newer toxicity data (published since the development of the IRIS values) may have on the risk assessment. Mixed opinions were voiced as to whether the toxicity data should be incorporated into the quantitative uncertainty analysis.

- *Question 2 (Fish Consumption Rates).* The reviewers found the consumption rates used in the HHRA to be reasonable for adults, but expressed concern regarding EPA's reliance solely on the Connelly et al. (1992) data. They recommended that the Connelly data be compared to the 1996 NYSDOH data to verify the assumptions made in the HHRA regarding the representativeness of the study population (e.g., demographics).

- *Question 3 (Deriving Exposure Durations).* The reviewers indicated that exposure durations used in the HHRA were appropriate, but several reviewers stressed the importance of clearly stating that the HHRA is a prospective study and evaluates incremental risks only. Some reviewers noted the need to understand and include information on PCB clearance rates and how they may apply to exposure duration.

- *Question 4 (Averaging Times).* The reviewers agreed that the averaging times are appropriate, but that shorter averaging times should be considered for the evaluation of pregnant women (i.e., *in utero* exposures), nursing infants, and young children.

- *Questions 5 and 6 (Monte Carlo Analysis/Uncertainty Analysis).* Everyone agreed that the uncertainty analysis in the HHRA needed to be expanded. Most reviewers recommended that confidence intervals (error bars) be placed on *all* input parameters, and ultimately on CTE and RME risk and HI estimates. The reviewers commented that the Monte Carlo analysis, as presented in the HHRA, requires more explanation and clarification.

- *Question 7 (Risk Characterization).* The overriding message from reviewers was the need for an expanded risk characterization section. Several reviewers emphasized the need to provide more information to enable the decision-makers to put the risk numbers into meaningful perspective and to provide sufficient information to proceed with the feasibility study.

Note: The reviewers' initials used to attribute comments are as follows: HHF (Ms. Holly Hattemer-Frey), OH (Dr. Owen Hoffman), PS (Dr. Pamela Shubat), LS (Dr. Lee Schull), HS (Dr. Harlee Strauss), and RW (Dr. Robert Willes).

## 2.1 Responses to Question 1

The first charge question pertains to the appropriateness of using the *toxicity values* for PCBs currently provided in the Integrated Risk Information System (IRIS) and the adequacy of the discussions of newer toxicity studies published since the development of these toxicity values:

> Consistent with its risk assessment guidance, USEPA considered scientific literature on PCB toxicity, both as to cancer and non-cancer health effects, published since the 1993 and 1994 development of the non-cancer reference doses (RfDs) for Aroclor 1016 and Aroclor 1254, respectively, and since the 1996 reassessment of the cancer slope factors (CSFs). Based on the weight of evidence of PCB toxicity and due to the Agency's ongoing reassessment of the RfDs, USEPA used the most current RfDs and CSFs provided in the Integrated Risk Information System (IRIS), which is the Agency's database of consensus toxicity values. The new toxicity studies published since the development of the RfDs and CSFs in IRIS were addressed in the context of *uncertainty* associated with the use of the IRIS values (see, HHRA, pp. 76-77 and Appendix C). Please comment on the reasonableness of this approach for the Upper Hudson River.

The six peer reviewers agreed that using currently available IRIS values was appropriate for evaluating cancer and non-cancer effects in light of existing EPA risk assessment policy, including EPA's goal for consistency across Superfund risk assessments. However, the reviewers also agreed that newer PCB toxicity data need more in-depth discussion in the HHRA, especially given the magnitude of the decisions that need to be made regarding contamination in the Upper Hudson River. The reviewers recommended including a new section in Chapter 4 (Section 4.5) that discusses the most recent toxicity data. Furthermore, the group agreed that the HHRA needed to include additional discussion on the conservativeness of the CSF and the possible non-conservatism of the RfD. The reviewers indicated that such discussions seemed to fit best into the Risk Characterization section. Several reviewers noted that expanded discussion of these points would provide added perspective when interpreting the findings of the quantitative risk assessment. Mixed views were presented regarding the need to incorporate uncertainties in the toxicity data into the quantitative uncertainty analysis.

A summary of peer reviewer comments related to Question 1 follows, presenting the various points of view on how including expanded discussions on PCB toxicity would improve the risk assessment and to what extent the uncertainty analysis (specific to toxicity data) needs to be enhanced.

- *Using existing values.* All reviewers agreed that EPA's use of currently available IRIS toxicity values in the HHRA was reasonable. Two of the reviewers emphasized that few other choices are available in the context of a Superfund risk assessment and were therefore supportive of using IRIS data (HS,PS). One reviewer pointed out that the use of IRIS values is adequate for screening assessments, but when the HI exceeds 1 or cancer risk estimates exceed $10^{-6}$, then a closer look at other data is necessary (OH).

- *Expanding the text to discuss the level of conservatism associated with the CSF and RfD.* To put cancer risk estimates into a real world context, one reviewer recommended that both the uncertainties and conservativeness of the CSF be described to a greater extent in the HHRA (RW). Two other reviewers agreed that the CSF is very conservative, but noted that, on the other hand, the RfD may not be all that conservative and is probably set close to the levels at which adverse effects might be expected, based on data in various published studies (e.g., Jacobson and Jacobson, 1996; Winneke et al. 1998; Rogan and Gladen, 1991; and Brouwer, 1999) (HS,PS). (See also Question 7)

- *Expanding the text to include more discussion on the newer PCB toxicity data.* Several reviewers commented that using the newer toxicity data would strengthen the scientific credibility of the risk assessment. While it may not make a substantial difference in the risk assessment conclusions, several reviewers agreed that the magnitude of the difference should be estimated and discussed in the risk assessment, especially in light of the high profile nature of the Hudson River site (LS,OH,PS,RW). That is, would use of the newer data result in toxicity values going up, going down, or staying the same? It was recommended that the Kimbrough (1999) data be used to develop a CSF that could provide additional perspective (LS,HHF). Another reviewer questioned whether the same should be done for non-cancer endpoints using the Dutch studies (PS).

  One reviewer suggested that Chapter 4 in the HHRA include a new section that would present the range of available toxicity data (PS). For example, she suggested including data compiled by Tilson (1990, 1998).

- *Documenting uncertainties associated with the toxicity data.* There were differing opinions regarding the need for, or the feasibility of, including a *quantitative* uncertainty analysis of the toxicity values. The group generally felt that, at a minimum, some sort of semi-quantitative/qualitative discussion was needed to clearly identify the sources of uncertainty pertaining to the toxicity criteria. One reviewer stated that discussions in the HHRA need to be expanded to address the uncertainty associated with the use of the IRIS values (LS). For example, this reviewer suggested that decision-makers need more information to understand the significance of the HI of 150 estimated for child exposures.

  One reviewer felt strongly that the limits on the uncertainty of the selected toxicity values need to be quantified, noting that this was one of his greatest concerns regarding the risk assessment

(OH). This reviewer thought that the HHRA should characterize how the uncertainty in the risk estimates is influenced by the various input parameters, including the toxicity values. If the limits of credibility cannot be quantified, then this reviewer feels the assessment is not scientifically defensible even if it is adequate from a policy perspective. This reviewer emphasized the importance of quantifying and understanding the limits of credibility on the risk estimates and encouraged the use of non-classical statistics (e.g., Bayesian methods) to do so. He noted that this type of analysis was performed when addressing PCBs at Oak Ridge National Laboratory (i.e., confidence intervals were put on the CSFs and RfDs). This reviewer also noted that the relative effects of the identified uncertainties needs to be discussed. That is, would the effect be high, medium, or low? Also, to what extent would these uncertainties affect risk estimates? Will the risk estimates go up, down, or stay the same?

Other reviewers agreed in principle (RW,LS,HHF). One reviewer noted that this issue has historically been glossed over and encouraged a quantitative analysis if possible, commenting that this could appropriately set the stage for future risk assessments, especially for PCB issues (LS). Given the state of the art nature of this type of analysis, this reviewer thought that the HHRA should either include a quantitative uncertainty analysis on the toxicity values or justify why such and analysis cannot be done (LS). Another reviewer recommended that, at minimum, EPA perform a comprehensive review of the PCB toxicity data to identify studies that might help reduce uncertainties (PS).

Another reviewer pointed to the fact that the biggest uncertainty in toxicity data sets probably relates to whether the right experiments have been conducted or whether the right endpoints have been captured; she emphasized that these uncertainties cannot be quantified (HS). She cautioned the group about being too quantitative, so that we do not suggest that we know more than we do. This reviewer recommended expanding the toxicological profile included in the HHRA to include more discussion on the derivation of the CSF and non-cancer effects, particularly neurotoxic and immunotoxic effects. She indicated that this type of qualitative discussion on the uncertainties was all that was necessary.

- *Should toxicity data be incorporated into the quantitative uncertainty analysis in the Hudson River HHRA?* One reviewer commented that the time has come for assessors to develop distributions for the toxicity criteria for use in a quantitative uncertainty analysis/baseline risk assessment; this would enable the generation of risk estimates for some percentile (LS). On the basis of scientific merit and the fact that the PCB assessment for the Hudson River will set the standard for other sites, it makes sense to develop toxicity criteria using this approach (LS,OH), although one of the reviewers noted that it may not make a big difference on the outcome and the decisions to be made (LS).

One reviewer reiterated that the limits of credibility should be quantified for the risk estimates, recognizing, in response to an earlier statement, that all the toxicity studies that he thought should have been done might not have been done (OH). He emphasized the importance of clearly stating what is known and not known. Because it is likely that the toxicity criteria will be the driving variable in the uncertainty analysis, this same reviewer stressed that this variable *must* be included in the quantitative uncertainty analysis. Otherwise, it could mislead decision-makers.

Another reviewer emphasized the importance of attempting to quantitatively describe the following: (1) that the CSF represents an upper bound and therefore implies a "low" degree of certainty, and (2) that the RfD will show a greater confidence (although it will be difficult to set a distribution) (RW).

One reviewer (OH) briefly discussed how distributions are generated, pointing to (1) classical statistics where analysts study data and grind them through some fitting routine to identify a particular distribution, and (2) Bayesian methods that generate subjective distributions that come from professional analysis of the state of the knowledge. The Bayesian approach, according to this reviewer, is more appropriate for the uncertainty analysis of the risk estimates; it provides the interval that contains the "true but unknown risk" for the defined population. This reviewer also commented that Monte Carlo procedures are useful because they are robust in propagating distributions, but cautioned that such procedures can be misused when simulating stochastic processes. He encouraged EPA to consider his premeeting comments regarding this issue.

## 2.2 Responses to Question 2

The second question asked the reviewers whether the *fish consumption rates* used in the HHRA are reasonable:

> Since 1976, the New York State Department of Health has issued fish consumption advisories that recommend "eat none" for fish caught in the Upper Hudson River. To generate a fish ingestion rate for anglers consuming fish from the Upper Hudson River under baseline conditions (i.e., in the absence of the fish consumption advisories), USEPA used data on flowing water bodies in New York State (1991 New York Angler survey, Connelly et al., 1992) to derive a fish ingestion rate distribution. The 50$^{th}$ and 90$^{th}$ percentiles were used for the fish ingestion rates for the central tendency (average) and RME individuals (i.e., 4.0 and 31.9 grams per day, equivalent to approximately 6 and 51 half-pound meals per year, respectively) (see HHRA, pp. 24 and 37). Please comment on whether this approach provides reasonable estimates of fish consumption for the central tendency and RME individuals for use in the point estimate calculations.

The six peer reviewers agreed that the central tendency and RME ingestion rates used in the risk assessment were reasonable values for *adults*. Several reviewers commented that the Connelly et al. (1992) study may not be adequate to describe the demographics of the study population and recommended that EPA incorporate the most recent NYSDOH survey to verify if the Connelly study captures the demographics of the exposed population. Specific reviewer comments are summarized below.

- *Adequacy of intake rates.* The fixed intake rates of 6 (CTE) and 51(RME) half-pound meals seemed reasonable and sufficient as voiced by one reviewer (OH). Nobody disagreed, but it was noted that these rates were reasonable for adults only (PS,HHF).

- *Childhood and fetal exposures.* Several reviewers commented that the HHRA did not adequately address child and *in utero* exposures (PS, HS, HHF). Although the Monte Carlo analysis considered child exposures, it did not appear to look at different ingestion rates for children (PS). Reviewers noted that body burdens (in milligrams per kilogram per day) would be greater in children and the fetus (LS,PS). By looking only at anglers and not their offspring, the HHRA excludes a potentially important subpopulation. The reviewers strongly recommended that this subpopulation be considered as part of the baseline HHRA (see also Question 4).

- *Reliance solely on Connelly (1992) data to define the angler population.* All of the reviewers questioned whether using the Connelly data accurately captures the demographics of the current group of anglers on the Upper Hudson River. One reviewer strongly encouraged EPA to include data from the 1996 NYSDOH study, which presents data on the angler population in this area, including information on various subpopulations (PS).

  Several reviewers pointed to Pam Shubat's written comments as clearly expressing pertinent concerns related to this issue and encouraged EPA to review these comments carefully (OH,LS,RW). One reviewer added that Dr. Shubat's comments coupled with GE's comments in the Responsiveness Summary raise some important concerns about the Connelly data (LS). The group recognized that the conclusions of the HHRA may not change, but, as written, the scientific data supporting its conclusions are not completely defensible.

- *Using nonzero data from the Connelly study.* While the exclusion of nonzero data from the Connelly data was raised as an issue in the written premeeting comments, one reviewer commented that this is not problematic (HS). Because of the way in which the data are being used in the HHRA (i.e., looking only at the exposed population, not at the average consumption across the population), the decision to exclude nonzero data is reasonable.

- *Evaluating subreach exposures.* Two reviewers (OH, HHF) encouraged EPA to consider evaluating exposures on a reach-by-reach or location-by-location basis. One reviewer pointed out that some subsets of the populations may be harvesting fish from distinct reaches of the Upper Hudson River; they are not randomly catching fish from the entire 40-mile stretch (OH). A location-by-location analysis, according to this reviewer, also would be more consistent with potential remediation considerations. This reviewer cautioned that "crude" estimates should not be considered acceptable just because the HI was high (OH). The other reviewer thought an evaluation of various subreaches of the Upper Hudson River was covered to some extent in the Monte Carlo analysis but that the findings were buried in the text and graphical presentation of the analysis and, therefore, not easily discernable (HHF). This reviewer noted that analysis on a location-by-location basis would make the HHRA more realistic and technically sound, but she also acknowledged that risk estimates would not likely change significantly. Another reviewer commented that no information was provided suggesting that the various reaches would be largely different (LS).

- *Calculation of fish tissue concentrations.* Two reviewers (PS, HHF) indicated that the derivation of the fish concentrations is not completely transparent in the HHRA. These reviewers acknowledged that supporting documentation for the modeling is presented in other documents, but strongly recommended that the description of the modeling efforts be expanded and clarified in the HHRA.

- *Identification of species harvested.* One reviewer commented that the fish species identified in the Connelly study are not necessarily the same as those found and harvested in the Hudson River (PS). She noted that the NYSDOH study identifies the study area as a bass (smallmouth and largemouth bass) and blue gill (pan fish) fishery for shore anglers; this is not reflected in the HHRA.

- *Possibility of commercial fishery.* One reviewer (OH) questioned whether it was plausible that commercial fisheries may exist under baseline conditions (i.e., with no institutional controls in place). If so, why limit the targeted group to only anglers? Another reviewer (PS) informed the group that in the absence of a specific advisory on the Hudson River, statewide advisories for all fresh water fish would still apply.

- *Consumption of other species.* Two reviewers (OH,HS) commented that it was not clear whether EPA considered other wildlife species (e.g., eels and turtles), noting that the PCB accumulation in turtles is considerably higher than in fish. One of these reviewers, therefore, recommended that EPA consider the extent to which other biota might contribute to risk (OH). One other reviewer suggested that EPA should, at minimum, state in the HHRA that not all wildlife species that may be consumed from the Hudson River (and that may accumulate PCBs) have been evaluated (PS).

- *Developing a conceptual site model.* In light of the types of comments being made regarding the sometimes unclear descriptions of the exposure scenarios evaluated by EPA, two reviewers (HHF,LS) recommended that the HHRA include a conceptual site model that maps out all the key issues and concerns, either in tabular or diagram format. For issues not addressed in the HHRA, it was recommended that the rationale for exclusion be presented. This would improve the transparency/clarity of the document. While the text of the HHRA explains why certain scenarios and exposures were and were not considered, these discussions are not always clear enough and sometimes not comprehensive enough. Others agreed. One reviewer noted, however, that creating a conceptual model would be less critical if Table 2-1 in the HHRA were expanded (see also General Questions, Section 3.0).

## 2.3 Responses to Question 3

The third charge question pertains to the adequacy of the *site-specific exposure durations* for the fish ingestion pathway:

> Superfund risk assessments often assume 30-year exposure duration, based on national data for residence duration. However, because an angler could move from one residence to another and

still continue to fish the 40 mile-long Upper Hudson River, USEPA developed a site-specific exposure duration distribution based on the minimum of residence duration and fishing duration. The residence duration was based on population mobility data from the U.S. Bureau of Census (1990) for the five counties that border the Upper Hudson. The fishing duration was developed from the 1991 New York Angler survey (Connelly et al., 1992). The 50$^{th}$ and 95$^{th}$ percentiles of the distribution were used for the central tendency (average) and RME exposure durations (i.e., 12 and 40 years, respectively). Please comment on the adequacy of this approach in deriving site-specific exposure durations for the fish ingestion pathway (see, HHRA, pp. 23 and 49-57).

Everyone agreed that exposure duration rates are appropriate and changing them would not have a significant effect on risk. Several thought that the HHRA should include a qualitative discussion on PCB clearance rates and how they relate to exposure duration and the application of the RfD. Also, several reviewers recommended that the HHRA clearly recognize that this is strictly a prospective assessment and predicted risks do not account for previous exposure-related risks.

- *Incremental risks.* While the reviewers agreed with the HHRA's assumption that exposure begins in 1999, they also agreed that the text should clearly acknowledge that the current and future risks estimated in HHRA are incremental and layered on to pre-existing risks.

  One reviewer reminded the group that the risk assessment is prospective, not retrospective (LS). He noted that the HHRA appropriately defines risk under baseline conditions, but does not address past exposures where the above-described factors might affect exposure doses. For clarity, EPA should clearly state up front in the HHRA, the purpose of the baseline risk assessment (specifically, what it is and what it is not) (see also Question 7).

- *Exposure duration and PCB half-life.* Several opinions were voiced on the significance of residence duration on the interpretation of exposures. One reviewer commented that if neonates are to be studied, it is important to look at the total uptake of PCBs over time because, in any given year, the mother's breast milk concentrations will be determined by her life PCB-exposure history (OH). He therefore encouraged that PCB clearance rates be considered when examining the adequacy of the residence time assumption in the HHRA. Another reviewer (RW) commented that for each exposure that is occurring, an equilibrium is assumed. Therefore, changing the residence duration from 12 to 40 years does not affect how one interprets exposure relative to the RfD. One reviewer agreed that this is how it is currently assessed, but is not necessarily the best way (OH). Another reviewer commented that the practical reason for choosing these duration times is related to declining PCB concentrations in the fish; the shorter the averaging time, the higher the exposure (PS). Another reviewer (OH) argued that the exposure *rate* (mg/day/weight) will be determined by the length of residence. Another reviewer stated that if you stay within the dose metric of average daily dose, then you are looking at shorter averaging times (HS). It was pointed out that the average daily dose is more practical, but the cumulative dose may provide more accurate information.

  One reviewer (OH) commented that all of the considerations listed above are important for a greater understanding of how close the dose is to the threshold for effects. Another reviewer (PS)

reemphasized the importance of a comprehensive presentation of the toxicologic data, in this case to enable a better understanding of whether people are arriving at steady state and whether site-specific conditions are consistent with conditions in the various toxicity studies. It was therefore recommended (OH,RW) that the HHRA include a qualitative explanation that will make readers aware of PCB clearance rates. One reviewer emphasized that an individual could have a predetermined PCB body burden, which is dependent on the residence time of PCB congeners in the human body, noting that animal studies may not be relevant (OH). Two other reviewers (HS,RW) took this opportunity to stress the importance of communicating congener issues (e.g., uncertainties).

## 2.4 Responses to Question 4

The fourth charge question also relates to the exposure assessment and asked the reviewers whether the *averaging times used to estimate exposure point concentrations* are appropriate to address non-cancer health hazards to both the CTE and RME individuals:

> PCB concentrations in Upper Hudson River fish generally have declined in past decades and the decline is expected to continue into the future. Therefore, to evaluate non-cancer effects for the RME individual, USEPA used exposure point concentration in each medium (water, sediment, and fish) based on the average of the concentrations forecast over the next 7 years (1999 to 2006), which gives the highest chronic dose considered in the HHRA. For the central tendency exposure point concentrations, USEPA used the average of the concentrations forecast over 12 years (1999 to 2011), which is the 50$^{th}$ percentile of the residence duration developed from the population mobility data (U.S. Bureau of Census, 1990). In addition, for completeness, USEPA averaged the exposure concentration over 40 years (1999 to 2039) to evaluate non-cancer hazards for the same time period over which cancer risk was calculated. Please comment on whether this approach adequately addresses non-cancer health hazards to the CTE and RME individuals (see HHRA, pp. 67-68).

The group agreed that the averaging times are generally appropriate, but that shorter averaging times should be considered for evaluating doses to females and children. Specific comments are summarized below.

- *Transparency of the fish concentration estimates.* One reviewer reiterated that information on the modeling efforts used to estimate fish concentrations, including validation information, is not presented sufficiently in the HHRA (LS).
- *Use of a 7-year averaging time for the CTE **and** RME.* Two reviewers stated that the 7-year averaging time is appropriate for the RME, but they were inclined to use 7 years for the CTE as well (HS,RW).

- *Considerations for evaluating effects to children and developing fetuses.* Several reviewers recommended that shorter averaging times be considered when evaluating effects to fetuses and children (HS,OH,HHF,PS). Especially because the HI for PCBs is so high (>100), one reviewer (OH) encouraged EPA to look at the subchronic exposures that may affect such subpopulations. In this case, exposure durations as short as 1 year should be considered.

The reviewers discussed special considerations related to breast milk and *in utero* exposures. One reviewer questioned whether the 7-year averaging time was suitable for breast milk exposure, concerned that this approach may underestimate exposures in cases where higher exposures occur over a shorter period of time (RW). Another reviewer commented that the driving factor for breast milk exposures is maternal body burden and the equilibrium level, therefore she felt that *in utero* exposures would likely be more a concern from this perspective (PS). A third reviewer noted that the underlying assumption is that the mother is at steady state and the pharmacokinetics are available to determine body burdens in the fetus and nursing infant (LS). It was also noted that toxicity criteria are not available for this subpopulation, but the group agreed existing criteria could be used; it was emphasized that justification for the approach used and all assumptions be clearly stated in the risk assessment (PS,HHF).

The group agreed on the following general guidelines for evaluating effects to pregnant and lactating women:

— Evaluate exposures of pregnant women (and consequently the developing fetus) and nursing children. EPA should evaluate the appropriate exposure duration averaging for this group. That is, this should be less than the 7 years used in the HHRA (e.g., 2 years).

— Discuss qualitatively the applicability of the IRIS RfD to pregnant women and nursing neonates, considering the issues related to potential neuro developmental effects of PCBs in children.

— As recommended by one reviewer in her premeeting comments (HS), use a margin of exposure approach to evaluate the potential effects of PCBs on children; include *in utero*, breast milk, and direct consumption exposures. Also, the dose should be calculated using a short averaging time and high end concentrations of PCBs in fish because the critical window of development is likely to be short. Note that this method of calculating dose only applies to *in utero* exposure. (This approach assumes that transient elevations in blood PCBs due to recent PCB-contaminated fish ingestion is important with respect to toxicity, although the maternal body burden is probably the major determinant to *in utero* exposure if averaged throughout gestation). Breast milk exposures should be based on long-term averages because PCB concentrations in breast milk reflect the mother's body burden of PCBs. In addition, it may be appropriate to consider the *in utero* exposure separately as well as in combination, as most (but not all)

of the neuro developmental effects associated with PCBs in the cohort studies cited below appeared to be associated with *in utero* exposures:

Jacobson and Jacobson, 1996.
Rogan and Gladen, 1991.
Winneke et al., 1998.

- *Communicating the degree of conservatism in the analysis.* To aid in risk management decisions, one reviewer felt that the averaging times are reasonable, but thought that the HHRA should clearly state that these numbers are not overly conservative (RW).

- *Should background exposures be considered?* One reviewer questioned whether and how background exposures should be taken into account. The group recognized that this is beyond the scope of the risk assessment, since the assessment focuses on incremental risks. One reviewer (OH) emphasized, however, that background levels may be relevant when assessing threshold effects. Another reviewer (RW) noted that background exposures to PCBs are likely associated with an HI of less than one and are therefore not a big issue. However, this same reviewer added that if PCB congeners are acting like dioxins/furans (on a toxicity equivalence basis), background exposures might be "significant" (e.g., HI ranging from 0.1 to 10). It was stressed that, at minimum, these issues be brought to the attention of the risk manager (see also Question 7).

## 2.5 Responses to Questions 5 and 6

The fifth and sixth charge questions asked the reviewers to comment on the *adequacy of the Monte Carlo/uncertainty analysis*. Regarding the adequacy of the Connelly data, see also the summary of Question 2 discussions (Section 2.2).

*Question 5*

USEPA policy states that probabilistic analysis techniques such as Monte Carlo analysis, given adequate supporting data and credible assumptions, can be viable statistical tools for analyzing variability and uncertainty in risk assessments (USEPA, 1997). Consistent with this policy, USEPA used a tiered approach to progress from a deterministic (i.e., point estimate) analysis to an enhanced one-dimensional Monte Carlo analysis of the fish ingestion pathway (see HHRA, Chapter 3, pp. 33-59). Please discuss whether this Monte Carlo analysis makes appropriate use of the available data, uses credible assumptions, and adequately addresses variability and uncertainty associated with the fish ingestion pathway (e.g., defining the angler population, PCB exposure concentrations, ingestion rates, exposure durations, cooking losses) qualitatively or quantitatively, as appropriate, in the analysis (see HHRA, pp. 72-74).

*Question 6*

For the Monte Carlo analysis, USEPA evaluated a number of angler surveys, but excluded local angler surveys, such as the 1996 and 1991-1992 Hudson Angler surveys (NYSDOH, 1999; Barclay, 1993), due to the fish consumption advisories. The 1991 New York Angler survey (Connelly et al., 1992) was used as the base case and other surveys were used to address sensitivity/uncertainty in fish ingestion rates (see HHRA, pp. 37-46). Please comment on the adequacy of USEPA's evaluation and use of existing angler surveys in the Monte Carlo analysis of the fish ingestion pathway.

Per the reviewers' request, at the outset of discussions pertaining to the HHRA analysis of variability and uncertainty, EPA provided further clarification as to why a one-dimensional sensitivity analysis was performed instead of a two-dimensional Monte Carlo analysis, and why Monte Carlo procedures were not used in the uncertainty analysis. EPA indicated that it chose to perform a sensitivity analysis rather than a two-dimensional Monte Carlo analysis and quantitative analysis on uncertainty because probability distribution data (on variability and uncertainty) were not robust enough.

In response, one reviewer recommended, at minimum, that the reasoning behind the analysis be more explicitly stated in the HHRA (LS). The reviewers generally agreed, however, that the uncertainty analysis in the HHRA needs to be enhanced. Most reviewers recommended that confidence intervals (error bars) be placed on *all* input parameters, and ultimately on CTE and RME cancer risk and HI estimates. It was recommended that the HHRA include a table that defines variability and uncertainty (confidence intervals) and distribution (when available) for all input parameters. Regarding the Monte Carlo analysis presented in the HHRA, several reviewers commented that it was at times difficult to follow and therefore requires more explanation and clarification.

Specific topics discussed by reviewers are summarized below.

- *Interindividual variability analysis.* One reviewer stressed that the Monte Carlo analysis in the HHRA has nothing to do with uncertainty: it is only an expression of interindividual variability of exposure for a defined subgroup of the population (i.e., licensed anglers fishing the reach of the river under study) (OH). This reviewer noted that it did not make sense to perform thousands of simulations when evaluating data from a single angler study with only 221 respondents. This reviewer questioned whether this type of analysis of interindividual variability is truly necessary when exposures to the study population are clearly of regulatory concern. He thought that looking at interindividual variability is only critical when assessing the *total* population exposed,

not just a targeted analysis of anglers. It was noted that in such a case, it would be important to look at the *size* of the total population.

- *Placing confidence intervals on the CTE and RME risk estimates.* Most of the reviewers indicated the need to understand whether the uncertainty at the central tendency or RME causes EPA to understate or overstate risk and commented that this type of analysis is lacking in the HHRA. At minimum, confidence or credibility intervals need to be placed on the CTE and RME risk estimates (HHF,OH,LS,RW). This involves understanding the uncertainty on each of the input parameters. One reviewer stated that addressing *each* of the parameters as subjective probability distributions would have been more appropriate in the Monte Carlo analysis, rather than the sensitivity analysis that was performed (OH). This reviewer stated that instead of using Monte Carlo to simulate interindividual variability, it may be preferable to pick defined reference representative individuals for the high-end, mid-point, and low-end of the distribution and do Monte Carlo to estimate uncertainty at each of these points (OH).

  Two reviewers discussed evaluating the effect of having a high degree of variability (OH,HS). One reviewer stated that in such a case we simply explain why that variability exists and condition the assessment on the CTE or RME. A brief discussion followed as to why the percentiles presented in the HHRA sensitivity analysis were not complete enough. One reviewer stated that the analysis was neither complete nor completely interpretable (OH). To enable a better interpretation, he would like to have seen the following included: a presentation of parameters that expressed stochastic variability, the uncertainties on the mean fish concentrations, the uncertainty associated with fishing at other locations, and the uncertainty of the toxicity values.

  In closing these discussions, the group agreed that uncertainty needs to be better understood to enable an informed decision regarding the extent to which remedial actions, including the existing fishing advisory, are needed. Therefore, the uncertainty analysis in the HHRA needs to be enhanced.

- *Use of Bayesian methods.* Reiterating points made during Question 1 discussions, one reviewer (OH) strongly encouraged the application of Bayesian methods in the uncertainty analysis. Another reviewer (RW) commented that he has successfully used Bayesian methods to generate error bars to see where significant shifts in output are indicated and to identify factors that contribute greatest to these shifts in output. He noted that this type of analysis becomes more important in the next phase of the assessment (selecting remedial alternatives). That is, what parameters might be most sensitive to the remediation efforts. He noted, for example, that the HHRA does not provide information on which parameters are the most critical for "Scenario A" versus "Scenario B." While perhaps not critical to the baseline risk assessment conclusions, this reviewer was concerned whether this information would be available for the remedial alternative selection step.

  These same two reviewers emphasized that data will clearly not be available for all input parameters, but that enough information is available to make some assumptions and initiate a quantitative analysis. This type of quantitative analysis will identify parameters that drive risk estimates and will help identify parameters for which more data may be needed.

- *Input parameter summary table.* One reviewer (LS) commented, and all other reviewers agreed, that a critical first step in evaluating uncertainty is to *clearly identify the uncertainty and variability for all input parameters, and where possible define distributions*. The group recommended that this information be presented within the HHRA in tabular form, possibly following the example provide in Table 2-1 on the following page. One reviewer commented that clearly presenting this information is critical to helping the decision-maker understand why different approaches were taken and how decisions were made in the risk assessment process. For example, why was only a point estimate used and not the probability on a distribution, or how is a particular parameter likely to affect the risk estimate (LS,RW)? One reviewer noted, however, that this is only one step in the process and emphasized that it only looks at one variable at a time (OH). For example, in the case of the HI of 150 for the child, we do not know how the output is being affected by compounding conservative assumptions made in the risk assessment. This reviewer reemphasized that in absence of distribution data, expert judgment can and should be used to quantify the uncertainty. Others (PS) felt less comfortable in advising or directing the risk assessor on *how* to apply this type of judgment.

  One reviewer suggested introducing/describing uncertainty and variability information in individual sections (i.e., in the toxicity and exposure assessment sections) and then carried forward into the uncertainty analysis (PS).

- *Comments specific to the HHRA Monte Carlo analysis.* The meeting chair summarized reviewer premeeting comments on the Monte Carlo analysis as follows:

  — Fish concentrations were not allowed to vary in the analysis.

  — The fraction of fish consumed from the Hudson River was assumed to be 100% and not allowed to vary.

  — Assuming 0% cooking loss is too conservative.

  — Possible changes in fish consumption rates over the exposure period were not evaluated

  — The possibility of consumption of a single species was not evaluated.

The reviewers discussed these issues and others during the meeting. An overview of this discussion follows.

— *General comments.* Several reviewers expressed some confusion regarding the assumptions used and decisions made in the Monte Carlo analysis. In general, the reviewers recommended that the presentation in the HHRA be revised to clarify the approach, both in terms of why and how the analysis was developed. For example, some factors may be kept fixed with justification, but the risk assessment document needs to clearly explain why (LS).

**Table 2-1**
**Sample Uncertainty Table**
**Parameters Used for Fish Ingestion Pathway**

**Risk Endpoint: Reasonable Maximum Exposure Hazard Index**

| Parameter | Units | Point Estimate | Uncertainty | Rationale |
|---|---|---|---|---|
| Fish ingestion | kg/day | 0.032 | fixed | Defined value for RME |
| Fish ingestion | kg/day | 0.032 | 0.015-0.054 (uniform distribution) | Range of plausible values for the RME |
| Cooking loss | -- | 0 | 0.1-0.4 (uniform distribution) | Plausible range from review of literature |
| PCB concentration | mg/kg | 0.3 | 0.5-5.0 (lognormal) | Modeled uncertainty from... |
| Bioaccumulation (sediment/fish) | -- | 1.0 | 1.0-10.0 (log uniform) | Uncertainty in bioaccumulation from sediment to fish |
| Fraction of fish caught in Upper Hudson River | -- | 1.0 | fixed | Defined as part of review |
| Etc. | | | | |

— *Fish concentrations were held constant in the analysis*. Reviewers (PS,HS) expressed concern that the uncertainties in the fish concentration were not clearly described in the HHRA. It was recommended that points relevant to describing the variation in fish concentrations be carried over from the modeling reports to provide greater transparency in the HHRA (HS). Another reviewer (OH) commented that, while not likely a driver in the uncertainty of the assessment, he would like to see the standard error on the mean fish concentrations; it is of particular interest in seeing how PCB concentrations decrease over time and also to understand inter-species differences.

— *Cooking loss*. Although EPA indicated as a point of clarification that error bars were generated with the elements of uncertainty studied in the HHRA (e.g., cooking loss, fish ingestion), one reviewer (OH) did not feel this was easily discernable in the HHRA. Another reviewer (HS) pointed out that cooking loss is fixed in the point estimate, not in the Monte Carlo analysis.

— *Fish ingestion rates*. One reviewer expressed concern that the presentation of fish ingestion *rate* in the HHRA might be misleading and suggest a false sense of certainty (PS). This reviewer noted that in the analysis the *meal size* is fixed and assumed and *frequency of consumption* was the variable studied. While she agreed that the choice in meal size is reasonable, she wondered if treating these two parameters separately would provide a more informed account of health risks.

## 2.6 Responses to Question 7

The last specific question asked the reviewers to comment on the *adequacy of the risk characterization* in estimating the relative cancer risks and non-cancer hazards:

> The risk characterization section of the HHRA (Chapter 5, pp. 67-80) summarizes cancer risks and non-cancer hazards to individuals who may be exposed to PCBs in the Upper Hudson River. Please comment on whether the risk characterization adequately estimates the relative cancer risks and non-cancer hazards for each pathway and exposed population. Have major uncertainties been identified and adequately considered? Have the exposure assumptions been described sufficiently?

The group agreed that the risk characterization section should be expanded and clarified to address several issues. First, the conservatism of the CSFs and the possible non-conservatism of the RfDs should be discussed. Second, to assist decision-makers, the group encouraged EPA to include more information to enable a more extensive interpretation of the risk estimates. Third, the group recommended that the risk characterization section include a brief qualitative discussion on background exposures and the fact that the population may have been pre-exposed to PCBs. Lastly, several reviewers

stressed that enough information needs to be included to enable the back calculation of risk-based remedial goals in the next phase of the assessment.

Many of the points raised during previous discussions were reiterated and discussed in the context of risk characterization during the Question 7 discussions. Highlights of these discussions are presented below.

- *General Comments.* One reviewer (LS) commented that the Risk Characterization section was the most disappointing section in the HHRA. It fails to answer a key question: "What do we make of all of this?" More perspective needs to be provided to support risk management decisions and to better inform the public of what risk estimates mean. This section should explain that the HHRA is a theoretical upper bound prospective study that is designed to ensure that risks are not underestimated; however, an explanation is needed of what the risk estimates mean in the context of the real world. He recommended that Chapter 5 be expanded, especially the uncertainty discussions. Others agreed.

  One reviewer stated that he felt strongly that the Risk Characterization section include "full disclosure" of everything that should be taken into account in understanding and interpreting the risk assessment findings (OH).

- *Evaluation of background and pre-1999 exposures.* The reviewers agreed that the issue of background and past exposures needs to be acknowledged in the HHRA, noting that this evaluation could be important in making risk management decisions and calculating remediation goals. Most reviewers agreed that this could be addressed qualitatively. One reviewer suggested, at a minimum, including a statement that indicates that other sources of PCBs exist (although risks associated with Hudson River exposures likely override background) and that past exposures may have occurred (RW). This, he noted, would help clarify within the HHRA that this is an incremental risk assessment. Another reviewer (OH) reiterated that, wherever feasible, "confounding" factors should be handled quantitatively. Two reviewers emphasized that background concentrations of PCBs will have an influence on remedial decisions, especially during the feasibility study (HHF,RW).

- *Conservatism of the cancer slope factor.* One reviewer (RW) reiterated the importance of recognizing extreme conservatism of the PCB cancer slope factor. In the case of PCBs, where no compelling evidence exists that liver tumors observed in animal studies are predictive of human liver cancer, he strongly recommended enhancing existing text to emphasize the conservatism of the slope factor and to provide additional perspective on interpreting cancer risk estimates. For example, he noted that applying the current slope factor to current PCB background levels would predict liver cancer incidence between 30 and 45 percent. The total liver cancer incidence from all causes reported in the United States is only between 1 and 5 per 100,000. Several other reviewers agreed that this type of reality check is helpful, but recognized that regulators are looking at individual risk not population risk. Furthermore, another reviewer (HS) stressed that it is not the intent of the risk assessment to predict *liver* cancer or cancer at any other site; the CSF

has been developed for regulatory purposes. Another reviewer (LS) replied that it is often interpreted in that way and that is why added perspective needs to be provided in the HHRA.

One reviewer (RW) commented on the importance of considering or explaining how the new cancer guidelines might influence the interpretation of cancer risk estimates, noting that the CSF does not take into account mechanism of action, weight of evidence, etc. EPA indicated that it did address the 1996 cancer reassessment and the new cancer guidelines in the HHRA. Another reviewer (OH) expressed his concern about the credibility of the regulatory approach in estimating cancer "risks" and strongly agreed that information on animal data, mechanism of action, and relevance to humans is needed to be put theoretical risk numbers into perspective ("When are risks real versus artifacts of the regulatory process?").

Lastly, another reviewer cautioned the need to err on the side of conservatism given uncertainties in the mechanism of action (PS). PCBs may not be a liver carcinogen in humans but could still be a promoter. Therefore, she noted that more than the potential for liver cancer should be examined. She, therefore, advised that "reality checks" be carefully presented with a thoughtful review of the state of the science regarding PCB carcinogenicity.

- *Individual versus population risk.* The peer reviewers voiced slightly differing opinions as to whether the size of the exposed population should be factored into the risk analysis. One reviewer (OH) commented, for example, that if a $10^{-4}$ cancer risk is estimated and the exposed population is less than 10,000, then no observable adverse effects are likely; he questioned whether the regulatory process is really increasing quality of life by reducing a number that is near zero to a number that is even closer to zero. In light of this, this reviewer reiterated the need for such reality checks when interpreting risk numbers. He therefore indicated that it was important to give the population size some weight in interpreting the risk numbers. Another reviewer (HHF) commented, even if the population size in the above example is less than 10,000, that does not mean that the risk is zero. A third reviewer (LS) added, however, that knowing the size of the population might help the decision-maker in deciding what to do with the $10^{-4}$ risk estimate.

  As stated earlier, another reviewer (PS) reminded the group that risks *are not* regulated based on the size of the population exposed; instead, regulators identify an "acceptable risk" in the population, not an "acceptable number" in the population that can get cancer. The first reviewer argued, "from a scientific point of view," all different perspectives should be taken into account, not just the regulatory perspective. Another reviewer reemphasized that EPA regulates based on *individual* risk and that this type of discussion moves away from reviewing the technical merit of the HHRA (HS).

- *Including confidence intervals on point estimates.* In light of the issues raised above, the group reemphasized the need to place confidence intervals around the point estimates to provide some added perspective. This is needed to help the risk manager and others understand what the theoretical upper bound estimates mean (HHF, OH, HS, LS, RW). In addition, reviewers pointed to language in EPA's cancer guidelines that indicates that the true risk is likely lower, and may even be zero (HHF,PS).

- *Multiple chemical exposures.* One reviewer raised the issue of potential risks from exposure to other contaminants, questioning whether PCB exposures in the Upper Hudson River are expected to dominate cancer risk and non-cancer hazards (OH). Another reviewer questioned whether the data for other contaminants are available and recommended, at a minimum, that any such data be discussed qualitatively in the HHRA to show the potential for other or additive effects (HHF).

- *Risk-based cleanup goals.* While it was recognized that the HHRA does accomplish the objective of identifying the need for remedial actions for sediment, many of the issues raised during this peer review (e.g., mixtures, bioaccumulation modeling, etc.) will become even more important when back-calculations are performed to establish cleanup goals (LS). It was questioned whether this type of information belongs in the baseline risk assessment. One reviewer indicated that she felt that a baseline risk assessment has the obligation to provide all the information needed to calculate risk-based cleanup levels (HHF). Another reviewer noted that the parameter table recommended by the group (see previous discussions) will be helpful in comparing remedial options (RW). In light of these discussions, two reviewers stated that they felt even more adamant about the need to include the following: a quantitative analysis of uncertainties, population size information, and information on possible co-contaminants (OH,LS).

## 3.0 RESPONSES TO GENERAL QUESTIONS REGARDING THE HHRA

After discussing the seven specific questions in the charge, the reviewers discussed two general questions. These questions generally pertained to how well the HHRA and the Responsiveness Summary met overall risk assessment goals in terms of overall clarity, transparency, and adequacy in characterizing risks to exposed populations, including children. Reviewers were also asked to comment on any strengths and weaknesses in the HHRA not covered in the specific charge questions.

Specifically, the general charge questions asked the reviewers:

> A goal for risk assessments is that they be clear, consistent, reasonable and transparent and adequately characterize cancer risks and non-cancer hazards to the exposed population, including children (USEPA, 1995). Based on your review, how adequate are the HHRA and Responsiveness Summary when measured against these criteria?
>
> Please provide any other comments or concerns, both strengths and weaknesses, with the HHRA not covered by the charge questions, above.

The peer reviewers raised a variety of issues, as summarized below.

- *Flood plain soils and farming exposures.* Soil contamination resulting from flooding is mentioned in the HHRA as a potential exposure pathway but is not quantified. One reviewer noted that this could be a significant pathway (e.g., dairy farm on river's edge) (RW). EPA pointed out that the HHRA and its Responsiveness Summary include a discussion of farms; this pathway was not evaluated quantitatively because the reassessment focused on river sediments and only limited data are available for characterizing PCBs in soils adjacent to the river. Several reviewers commented that direct and indirect exposures to soil need more explicit attention in the HHRA (RW, OH, HHF, LS). No discussion of the soil pathway is included in Table 2-1 in the HHRA.

- *Table 2-1.* At minimum, the reviewers recommended that Table 2-1 be expanded and clarified. Specifically, it should be more comprehensive and include all pathways considered and indicate which pathways were evaluated quantitatively, qualitatively, or not at all (and why).

- *Selection of fish species assessed in the HHRA.* Two reviewers reiterated that the HHRA was not transparent in its discussion regarding fish tissues levels and how species and size were selected (HHF,PS) (see also Question 2). After speaking with a fisheries contact, one reviewer (PS) found the analyses in the HHRA to be generally satisfactory, but felt clarification was needed. The HHRA does not and should list all species present and caught in the Upper Hudson River. Predominant species and sizes fished in this reach of the river should be clearly identified. In addition, more explicit information is needed on the following: Are EPA's modeled

concentrations skin on fillet data? Are the sizes chosen for risk analysis comparable to sizes that anglers keep? What is the effect of "crunching?" Are data available that address the age of the fish consumed and the relationship to PCB concentrations?

- *Consideration of child and in utero exposures.* As identified during exposure assessment discussions (see Questions 2 and 4), the importance of characterizing risks to fetuses, infants, and children was reemphasized (HS).

- *Transparency of decision criteria.* Two reviewers expressed concern that the HHRA did not always clearly explain and justify why various decisions were made (e.g., exposure assessment and Monte Carlo analysis) (PS, HHF). Although EPA noted that Phase 1 and scope of work documents associated with the PCB reassessment contain more detailed information on how decisions were made, several reviewers stressed the need to restate some of this information in the HHRA, especially issues critical to the risk estimates (e.g., fish concentrations). Again, the reviewers emphasized that expanding and clarifying how and why things were done will improve the scientific reasonableness and transparency of the HHRA. Also, it will ultimately aid in risk management decisions (HHF,OH,HS,LS,PS,RW).

## 4.0 REVIEWERS' OVERALL RECOMMENDATIONS

The peer reviewers were asked to provide an overall recommendation, based on their review of the HHRA and the peer review meeting discussions. Specifically, reviewers were asked to select one of the following recommendations and explain why:

The HHRA is

— Acceptable as is.

— Acceptable with minor revision (as indicated).

— Acceptable with major revision (as outlined).

— Not acceptable (under any circumstance).

Prior to presenting individual recommendations, the peer reviewers held open discussions and worked together to prepare conclusion statements and recommendations. The outcome of this effort is presented in Section 4.1. The individual reviewers' final statements are presented in Section 4.2.

### 4.1 Summary of Specific Recommendations

This section presents a summary of reviewer comments and recommendations. These comments were compiled by the peer reviewers throughout the course of the 1½-day meeting and discussed in the final session to ensure that key points were adequately captured. The presentation is organized by charge question.

*Question 1 (Hazard Identification/Dose Response)*

1) The reviewers agree that it is appropriate to use IRIS values, but recommend adding a new section to Chapter 4 (Section 4.5). This section needs to quantitatively and/or qualitatively discuss the more recent studies on both cancer and non-cancer endpoints to determine what effect these studies might have on risk estimates (Will risk estimates go up, down, or stay the same?).

2) Section 5.3.2: List all sources of uncertainty pertaining to the toxicity criteria used to calculate the point estimates (i.e., IRIS data) and qualitatively discuss the effect on risk (high, medium, low) and the extent to which the toxicity data selected for use in the assessment would affect risk estimates (Will the risk estimates go up, down, or stay the same?). Uncertainties include the use

of animal data, uncertainty factors, modifying factors, and the high-to-low dose extrapolation model.

3) Should toxicity data be incorporated into the quantitative uncertainty analysis? Some reviewers strongly encouraged a quantitative evaluation of the uncertainty associated with the toxicity data and that this information be incorporated within the overall uncertainty analysis of HI and risk. Other reviewers believe that qualitative discussion of the uncertainty associated with the toxicity data is sufficient.

*Question 2 (Exposure Assessment)*

1) Fish ingestion rates used in the point estimates are reasonable for adults.

2) Reviewers recommend that EPA incorporate the most recent NYSDOH survey to verify if the Connelly et al. (1992) study captures the demographics of the exposed population (see Pam Shubat's premeeting comments for more details).

3) Risk assessment text is not transparent in describing how fish concentrations were derived. The text needs to be expanded and clarified. The text needs to include information on the uncertainty and variability in the average concentration in fish identified by species, location, and variations in time.

4) Assuming that individuals consume fish only from the Upper Hudson River seems unreasonable (too conservative).

5) Some reviewers believed that evaluating exposures on a location-by-location basis would better characterize exposed subpopulations. Other reviewers felt this issue was minor.

6) Justification for any scenarios and/or pathways (e.g., soil-related pathways) that were not quantified in the risk assessment should be added to Table 2-1.

7) All aquatic species that may be consumed (e.g., turtles and eels) may not have been evaluated, which could result in an underestimation of risks. A discussion of this issue in the uncertainty analysis would be desired.

8) Reviewers would like information on the size of the exposed population.

*Question 3 (Exposure Assessment)*

1) The HHRA assumes that exposure begins in 1999. The text should emphasize that the risks estimated in this assessment are incremental and overlay previous exposures/risks.

2) Recommend including discussion of PCB clearance rates (i.e., half-life of PCB in the human body) and how they relate to exposure duration and the application of the RfD.

*Question 4 (Exposure Assessment)*

1) The averaging times used are appropriate except for evaluating effects to pregnant and nursing women (see recommended guidelines presented in Section 2.4)

2) Modeling efforts used to calculate fish concentrations and validation of models are not adequately discussed in the HHRA (see point 3 under Question 2).

3) For noncancer effects and some receptors, an exposure duration of <7 years may be appropriate (e.g., child exposure of 1 year). In addition, some reviewers suggested that the exposure duration for the CTE and RME scenarios both be 7 years.

*Questions 5 and 6 (Uncertainty Analysis)*

1) Include a table that defines variability and uncertainty (confidence intervals) for all input parameters. For those parameters for which a distribution is defined, the rationale for the distribution should be described (see Table 2-1 presented earlier in this report).

2) The uncertainty analysis needs to be enhanced. CTE and RME risk estimates and HI values need to have confidence intervals.

3) The Monte Carlo presentation was difficult to follow and not transparent. Additional clarification is warranted.

*Question 7 (Risk Characterization)*

1) Qualitatively acknowledge that background exposures and the fact that this population has been pre-exposed is likely to increase the HI and cancer risk estimates. Evaluating background and pre-exposures could be important in calculating remediation goals and/or for risk management issues.

2) Expand/clarify Chapter 5

   - Discuss the conservatism of CSFs and the potential non-conservatism of RfDs and their effects on the final risk estimates.

   - Provide a better interpretation of results, especially a discussion of the fact that the cancer risk estimates are theoretical and upper-bound. The true cancer risk is likely to be lower and could even be zero.

*General Questions 1 and 2*

1) Discuss the potential interactive and cumulative effects that other chemicals, which may also be present in the Upper Hudson River, may have on PCB toxicity.

2) The baseline HHRA should include all information/data necessary to calculate a range of fish concentrations necessary for risk management objectives.

3) The HHRA should bring in the necessary and relevant information from other supporting documents to make the risk characterization section transparent (e.g., calculation of fish concentrations).

## 4.2 Individual Reviewer Recommendations

In summary, all six reviewers found the HHRA to be acceptable, but with minor to major revisions recommended and they commended EPA on the quality and extent of the effort that went into the HHRA. A summary of the peer reviewers' final statements on the HHRA, in the order they were given, follows:

- *Dr. Owen Hoffman.* As a record of disclosing an issue of regulatory concern, Dr. Hoffman stated that the HHRA is acceptable as written. However, he stated *major revision* is needed to make the HHRA more scientifically sound and defensible. Dr. Hoffman indicated that the limits of credibility of the risk estimates should be defined to take the HHRA to its needed next level.

- *Dr. Robert Willes.* Dr. Willes stated that he found the document to be *acceptable with major revision*. He stated that the types of revisions discussed throughout the workshop are critical to making the HHRA more useful and applicable to the feasibility study. He noted that the document is acceptable as written from a regulatory point of view.

- *Dr. Harlee Strauss.* Dr. Strauss also stated that the HHRA was *acceptable with revisions*. Dr. Strauss indicated that the recommendations communicated by the peer reviewers will strengthen the report, but will not change the regulatory conclusion. Dr. Strauss reiterated that reviewers' analyses and discussions have disclosed that the HHRA is too conservative in some respect, but possibly not conservative enough on other fronts. Dr. Strauss noted that she does not believe that, in the end, conclusions will change from a regulatory perspective.

- *Dr. Pamela Shubat.* Dr. Shubat stated that the HHRA was *acceptable with minor revision*. Dr. Shubat commented that the primary deficiency from her point of view was the failure to adequately assess risks associated with fetal, childhood, and maternal exposures. Dr. Shubat indicated that she does not feel as strongly about the need for the HHRA to "push the envelope."

- *Dr. Lee Shull.* Dr. Shull indicated that the HRHA was *acceptable with "minor to major" revision.* Especially in light of the close scrutiny that the Hudson River reassessment has received and will continue to receive, Dr. Shull stated that he felt strongly about taking the science of risk assessment to a higher level. He encouraged EPA to satisfy the special needs of this site and take evolving science into account when revising the risk assessment. He agreed that some of the recommended changes discussed during this peer review workshop will not change the bottom line but again emphasized that the changes will improve the utility of the document and make it as "right" as it can be.

- *Ms. Holly Hattemer-Frey.* Ms. Hattemer-Frey *accepted the document with "revisions" needed.* She stated that she feels strongly that the HHRA needs to be more transparent and complete if it is expected to support the calculation of remediation goals. Dr. Hattemer-Frey indicated that with the implementation of the peer reviewer recommendations, a revised HHRA should be able to serve that purpose. She noted that implementing recommended changes such as further evaluating child and *in utero* exposures and expanding the uncertainty analysis, will afford easier and justifiable back-calculations of acceptable risk levels.

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