Peer Review Panel Report for the Fox River Human and Ecological Risk Assessments

Mohamed S. Abdel-Rahman, Ph.D., New Jersey Medical School
Halina Brown, Ph.D., Clark University
Barbara G. Callahan, Ph.D., Association for Environmental Health & Sciences
Richard Di Giulio, Ph.D., Duke University
Christopher Metcalfe, Ph.D., Trent University
Christopher Teaf, Ph.D., Florida State University
Raymond S.H. Yang, Ph.D., Colorado State University

Prepared
by

The Association for Environmental Health & Sciences
150 Fearing St.
Amherst, MA
01002

for

The Fox River Group

June 28, 2000

Table of Contents

Peer-Review Panel Report for the Fox River Human and Ecological Risk Assessments

EXECUTIVE SUMMARY

1.0 Introduction

This report provides a critical analysis of two risk assessment reports evaluating the effects of chemical contaminants in the Lower Fox River in Wisconsin. One risk assessment was prepared by ThermoRetec Consulting Corporation (ThermoRetec) on behalf of the Wisconsin Department of Natural Resources and dated February 24, 1999; the other risk assessment was prepared by Exponent on behalf of the Fox River Group and dated January, 2000. The assessments are for potential human health and ecological impacts.

These risk assessments and the reviews focus on the specific impacts of PCBs in the river. Although some comments are directed toward other contaminants, that was not the charge to the review panel. The panel consists of academic experts in the area of chemical effects on health and environment. Three panel members evaluated the human health risk assessments; three panel members evaluated the ecological risk assessments. Panel members visited the site, engaged in meetings regarding the site, met with members of the Wisconsin Department of Natural Resources & the US Environmental Protection Agency, wrote critiques of the Exponent and ThermoRetec assessments, discussed items of concern, and, with this report, provide a written commentary on their views of the assessments.

The review panel found that the consultants used different datasets and different approaches in their calculations. For example, Exponent relied on concentrations from sediment and biota samples collected in 1998 and 1999 for ecological evaluation; ThermoRetec utilized a more extensive dataset collected over the previous ten years. Exponent used a Monte Carlo analysis for human health assessment resulting in a range of risk; ThermoRetec 's assessment resulted in a single point estimate.

Human health risk assessment reviews by the panel are evaluated separately and then compared with each other. The ecological assessments are evaluated separately. Comments provide a critical assessment of strengths and limitations.

Briefly, the panel found both strengths and weaknesses in each risk assessment.

2.0 Overview and Comparison of Evaluations

Human Health Assessment

Some critical panel findings are mentioned below while a complete report is presented in Section B of this document.

1 Panel members agree unanimously that the differences between the risk assessments from the two contractors are sufficiently large to undermine confidence in either the process or the input for risk assessment. For human health Exponent found polychlorinated biphenyl (PCB) cancer risk from eating fish from the river to be between 10^{-5} and 10^{-6} while ThermoRetec calculated 10^{-3} risk for the same scenario. Figure 1 demonstrates the disparity between the risk conclusions from the two assessments.

A comparison of the exposure assumptions for human health used in both contractors' assessments is provided in Table 1.

2. Neither group addressed the potential for prenatal or perinatal effects in their respective risk assessments. The window of opportunity that exists for fetal impacts is sometimes narrow. If, during this short timeframe, fish ingestion occurred, the effects may be greater than that exposure calculated by estimating dose over time (on a per day basis). In addition, although the Reference Dose is low (2×10^{-5} mg/kg.d), cancer and long term effects appeared to be the endpoints of real concern in these risk assessments.

Short term exposure effects could be substantial and in excess of the calculated hazard index, if a large dose was sustained during organogenesis for example or during a susceptible neurodevelopmental timeframe. The Exponent Hazard Indices for fish consumption were 0.2 at the median and 2 at the 95% percentile exposure, indicating that the hazard index for the central tendency exposure is less than one. However, these results also indicate little safety factor if the scenario described above is pertinent.

3 Monte Carlo analysis was undertaken by the Exponent risk assessors. While this approach is acceptable to EPA, the explanation of the process and the *input* parameters were not explained in sufficient detail that the panel was confident of the outcome.

ThermoRetec conducted a point estimate risk assessment with detailed explanation on their methodologies. ThermoRetec also conducted separate risk calculations for different reaches of the river area.

4. Exponent assumed much lower exposure to PCBs because of lower fish ingestion rates and lower concentrations of PCBs in fish. These lower concentrations were calculated based on the assumption that (higher concentration) bottom fish were not eaten by any population in the area and, possibly, by erroneous assumptions in truncating distributions in the dataset.

ThermoRetec assumed higher concentrations by including bottom fish and higher intake because ingestion other than just fillet ingestion was included.

Ecological Risk Assessment

Some critical panel findings are mentioned below while a complete report is presented in Section C of this document.

1. Panel members agree unanimously that disparate conclusions between the two risk assessments appear to negate the relevance of risk assessment. Consistent with the human health risk assessment results, conclusions from the two consultants for ecologic impacts were different.

Exponent concluded that there were no ecological risks to receptors associated with PCB contamination in the area. These results are consistent with Exponent's data but the chosen data were selective. For example, Exponent chose site specific field data to the exclusion of laboratory data as their source of information.

ThermoRetec found that unacceptable risk did occur. ThermoRetec ignored field studies and chose the most conservative values in most cases. Both of these approaches (from Exponent and ThermoRetec) are incomplete.

2. The process for Ecologic evaluation is defined by EPA and shown in Table 2. ThermoRetec addressed predominantly Steps 1 and 2 with little development of other steps while Exponent focused on Steps 3 through 7 and neglected Steps 1 and 2. ***It is the conclusion of the panel that, if these steps were integrated, a more scientifically defensible risk assessment would result.***

3. In handling data, ThermoRetec utilized the 95% upper confidence limit in a normal distribution, calculating this value with data collected over approximately a ten year period. Without appropriate statistical analysis, a normal distribution cannot be assumed. In addition, confidence is low in older data. However, given the persistence of PCBs it may be that an aggregated dataset is reasonable for a medium such as sediment.

Exponent's key driver for exposure was residue data in animal tissue, yet, generally, these data are very limited. Mink and eagle tissue data are limited;

Table 2

Process for ecological risk assessments recommended by the U.S. EPA (1997).

Step 1: Screening level.	**Step 4: Study design & data quality objective process**
Site visit	Lines of evidence
Problem formulation	Measurment endpoints
Toxicity evaluation	Work plan and sampling, and analysis plan
Step 2: Screening level.	**Step 5: Verification of field sampling design**
Exposure estimate	
Risk calculation	**Step 6: Site investigation and data analysis**
Step 3: Problem formulation.	**Step 7: Risk characterization**
Toxicity evaluation	
Assessment endpoints	**Step 8: Risk management**
Conceptual model	
Exposure pathways	
Questions/Hypothesis	

fish data are extensive. No attempt was made to obtain additional data from benthic invertebrates.

4. Toxicity Reference Values (TRVs) from ThermoRetec are very conservative and it is unclear in some cases, the basis of the TRV. For example, two fish TRVs are based upon NOELs for eggs and fish tissue. The egg TRV could not be verified from information provided in the report while the tissue TRV was based upon a very sensitive species.

TRVs from Exponent are questionable in some cases. For example, TRVs for terns and mink appear to be flawed while the fish TRV may be appropriate although the basis for the fish TRV is not clearly defined.

3.0 Summary

While both Exponent and ThermoRetec risk assessments display some scientific rigor, areas for improvement were found in each document. The human health review panel and the ecological review panel were surprised at the lack of concordance between Exponent and ThermoRetec in almost all arenas. This discordance was most obvious in the areas that drive risk results such as concentrations to exposed species, exposure assumptions, and toxicity reference values for non-human species.

Section B

An Evaluation of the Baseline Ecological Risk Assessment Reports Submitted by ThermoRetec and Exponent for the Lower Fox River System

Richard Di Giulio, Ph.D.
Ecotoxicology Laboratory, Duke University,
North Carolina

Chris Metcalfe, Ph.D.
Environmental and Resource Studies,
Trent University, Ontario, Canada

Christopher Teaf, Ph.D.
Center for Biomedical & Toxicological Research
Florida State University
Florida

1.0 Introduction

This report provides a critical analysis of the ecological risk portion of two risk assessment reports evaluating chemical contaminant data of the Lower Fox River in Wisconsin. One risk assessment was prepared by ThermoRetec Consulting Corporation (ThermoRetec) on behalf of the Wisconsin Department of Natural Resources and dated February 24, 1999; the other risk assessment was prepared by Exponent on behalf of the Fox River Group and dated January, 2000. The comments provide a critical assessment of strengths and limitations.

Both Environmental Risk Assessments (ERAs) display a reasonable degree of scientific rigor, but both can be improved. The Exponent report is more selective in terms of the data included in the evaluation of ecological risks. This contributes to a perception of bias in terms of directing the outcome of the evaluation towards a conclusion of no ecological risk associated with PCB contamination in the region. The ThermoRetec report employs a greater array of data, but there is often integration of data from different geographical regions and times, with no clear explanation of the justification for doing this. The consistent selection of highly conservative values for RMEs and Toxicity Reference Values (TRVs) in the ThermoRetec report also contributes to a perception of bias towards the conclusion that there are ecological risks associated with the PCB contamination.

The U.S. Environmental Protection Agency has documented an established process for designing and conducting scientifically defensible ecological risk assessments (U.S. EPA, 1997. Ecological Risk Assessment Fuidance for Superfund: Process for designing and conducting ecological risk assessments. June, 1997). The basic methods for assessing the risks of adverse effects on ecosystems are included in the eight-step process listed below. Neither the Exponent or the ThermoRetec documents include all of these steps. The Exponent report focuses on elements in Steps 3 to 7 and contains little information related to Steps 1 and 2. The ThermoRetec document includes a thorough evaluation of Steps 1 and 2, while the later steps are not developed to any great extent.

Both reports employ site-specific analytical data for estimating exposures. However, the Exponent report emphasizes <u>tissue</u> data collected in the past few years, while the ThermoRetec report places greater emphasis on <u>sediment</u> data and also employs data sets for sediments and tissues collected over a longer period of time. The Exponent Report relies more heavily upon site-specific studies of ecotoxicological effects. While this has advantages, it often emphasizes certain field studies that employ limited data bases and are subject to greater uncertainty. The ThermoRetec report places greater emphasis on laboratory studies to estimate toxicity reference values (TRVs) and associated hazard quotients; often with data from surrogate species. While this approach clearly has uncertainties, it may provide a more valid basis for quantitative ERAs than the Exponent approach of using a small number of site-specific field studies.

The Exponent report is more clearly organized and is presented in a manner that is more understandable to a broad range of readers. The large number of inconsistencies in the presentation and interpretation of data in the ThermoRetec report undermines the credibility of the report and confidence in the conclusions of the risk assessment.

Given that both reports are addressing the same problem, with access to the same data and information, it is startling that there are completely opposite results generated by the Exponent and ThermoRetec reports. These conclusions contribute to skepticism about the value of the ERA process. However, ERA clearly is an inexact process and decisions based on ERA results ultimately come down to the "weight of evidence". Thus, it is incumbent upon those performing ERA's to consider all relevant information. The selection of specific sources of information and omission of others appears to contribute to the disparate conclusions of these two reports. Exponent primarily selected site-specific field studies to the exclusion of laboratory data, which is not appropriate. However, the ThermoRetec report totally ignored field studies, which is also inappropriate. Moreover, when presented with an array of choices for key variables such as TRVs, ThermoRetec consistently chose the more conservative values.

A valid ERA would incorporate all the available information, and would ideally provide a carefully estimated range of risks for each receptor for each sub-region. This range would reflect the major uncertainties in the ERA and would provide decision-makers with a more accurate analysis of the relative risks for various receptors at specific sites. Such information would better inform the decision-making process, including the necessity for site remediation (i.e. risk management).

Table 1
Process for ecological risk assessments recommended by the U.S. EPA (1997).

Step 1: Screening level. Site visit Problem formulation Toxicity evaluation	**Step 4: Study design & data quality objective process** Lines of evidence Measurment endpoints Work plan and sampling, and analysis plan
Step 2: Screening level. Exposure estimate Risk calculation	**Step 5: Verification of field sampling design** **Step 6: Site investigation and data analysis**
Step 3: Problem formulation. Toxicity evaluation Assessment endpoints Conceptual model Exposure pathways Questions/Hypothesis	**Step 7: Risk characterization** **Step 8: Risk management**

2.0 Assessment by Exponent

Chapters 1 and 2

Assessment Area Delineation, Characterization, and Approach to Ecological Evaluation

2.1 Approach to Evaluation:

In this document, only the most recent PCB data for sediments and biota in the assessment area are used; historical data were excluded. Generally, data from 1998-1999 were used, although cormorant egg data were from 1994-1995 and mink data were from 1990 and 1996. Direct measures of PCB concentrations in representative species and life stages of fish and wildlife were used, where these data were available. Chapters 1 and 2 set the stage for the subsequent ERA. Major issues are first raised here, which become important themes throughout the ERA:

2.1.1 "Lines of evidence" (p.1-4 to 1-5). Three of the four lines of evidence focus on site-specific field data that include studies concerning PCBs in the assessment area, population trends in the region, and habitat characterization in the area. The other line of evidence focuses upon an ERA using a traditional approach that includes exposure estimates and toxicity.

2.1.2 Mechanisms of PCB toxicity. The report places great emphasis on aryl hydrocarbon (AhR) receptor-mediated mechanisms of toxicity and hence, the Toxicity Equivalence Quotient (TEQ)
approach for estimating risks. The report concludes that only 12 non-ortho and mono-ortho substituted PCB congeners (i.e. "coplanar" PCBs) bind to the AhR and should be considered in the TEQ approach to risk assessment. The TEQ approach further assumes that:

a) toxicity of individual congeners in mixture is additive.
b) sensitivity to congeners does not vary across species within broad taxonomic groups.
c) dose-response curves for congeners parallel those for 2,3,7,8-TCDD.

It is noted in the report that there are exceptions to all three of these assumptions; in particular, that there is strong evidence that some effects are less than additive and that sensitivity varies among species. The emphasis on Ah- receptor mediated mechanisms of toxicity and the TEQ approach may be misleading. On p.1-5 (last paragraph), it is stated that, "the primary toxicological effects of PCBs that may adversely affect populations of fish and wildlife (i.e., reproductive impairments) are known to be caused by this AhR mode of toxicity." On p. 1-7 (bottom), it is stated that, "The toxicity of PCB mixtures is primarily related to the 12 coplanar congeners (Van den Berg et al., 1998)." Actually, Van den Berg et al. (1998) was referring in this context to the PCB congeners that act as AhR agonists, not total PCB toxicity. Following a similar theme on pp. 2-13 to 2-14, it is stated that "the toxicity of PCBs to fish and wildlife can be measured by determining the affinity of a PCB mixture for binding the AhR". The science in this area is less certain that these statements would indicate, both in terms of Ah-independent effects and the linkage between AhR agonism and the toxicity of coplanar PCBs. For instance, estrogen agonism/antagonism and the neurotoxicity of PCBs are not AhR-mediated.

The report acknowledges that other PCB congeners may exhibit effects that are not AhR-mediated (e.g, pp. 1-8 to 1-9) and contends that this is taken into account to the extent possible; in part by using some of the data available on concentrations of "total Aroclors". However, in the actual risk assessment that follows, the TEQ approach is either emphasized or relied upon entirely. The

TEQ approach is a conservative procedure that is commonly used in ERAs to calculate total dioxin-like equivalents in complex environmental matrices that are contaminated with PCBs and other halogenated aromatic compounds (e.g. PCDD/DFs). However, given the current state of scientific understanding, especially for toxic responses such as reproductive impairment and developmental effects, risk assessments should use both total PCBs and TEQs.

2.1.3 Emphasis on trophic relationships: The report introduces the concept of emphasizing trophic relationships in the ERA, and subsequently discusses trophic interactions among fish, birds and mammals. However, benthic invertebrates were eliminated from the ERA; ostensibly because sediment triad assessments reported in an earlier study (WDNR, 1995) with 10 sediment deposits known to contain PCBs showed no positive association between PCB concentrations and toxicity. Other agents, including several metals and pentachlorophenol were positively correlated with invertebrate toxicity in the WDNR study. Apart from those conclusions, for which we do not have the underlying study, it would have been appropriate in the Exponent document to include a discussion of literature which addresses the responses of benthic macroinvertebrate populations to PCB exposure. This discussion would present a more persuasive case that sediment quality, at least in terms of PCBs, was not of environmental significance. Eliminating invertebrates from the ERA introduces substantial uncertainty. Given the relative wealth of sediment PCB data available for this study and the direct linkage between this source of PCBs and exposure of benthic invertebrates, the exclusion of macroinvertebrates from the ERA is puzzling and inappropriate.

3.0 Ecosystem Characterization:

The assessment area described for the lower Fox River region appears reasonable and is in agreement with the ThermoRetec report. The habitat characterization represents a field-directed, rather than desktop approach to analysis, and spatial analysis is provided by the application of Geographic Information System (GIS) techniques. However, the species evaluated were vertebrates only, with no invertebrates. These included fish, piscivorous birds, passerine birds, and piscivorous mammals. On p. 2-3, the use of wildlife habitat maps to "identify important food web interactions" is again raised.

3.1 Interaction Between PCBs and Other Stressors

It is appropriate and important to explicitly recognize other physical and chemical stressors (p. 2-8), many of which may have as much or more of an effect than PCBs. Each stressor is addressed in a summary paragraph to better define the issue. This section raises the obvious question, should ERAs such as this one be performed with or without regard to other natural and anthropogenic stressors? The assumption implied in this section of the report is clearly that other stressors should be considered. While a great deal more discussion of natural stressors would be possible, this represents a reasonable summary.

The report points out that the lower Fox River ecosystem is reportedly impacted by the presence of over 360 toxic substances, in addition to the PCBs that are highlighted in this report (p. 2-11). The point presumably is raised to illustrate that PCBs may be only one contributor to the overall poor quality of the ecological system. This observation places pressure on the risk assessor to accurately evaluate a highly complex chemical milieu. It also will present a thorny risk management issue in terms of site remediation. This point is especially germane to a particular issue raised later in the Exponent report with regard to the possible role of metabolites of DDT in reducing the reproductive success of cormorants.

3.2 Overview of PCB Ecotoxicology to Vertebrates (Section 2.3):

In general, this section is too sparse to be of much value. While the emphasis is, and should be, the literature related to the Fox River, a huge body of literature has been generated over the past several decades regarding the ecotoxicology of PCBs in other systems such as the Hudson River, other areas of the lower Great Lakes and regions in northern Europe. A reasonable overview should include some treatment of that information. If this section is to be retained, it should be expanded to provide a more comprehensive view of the literature. As noted previously, there is no discussion of the ecotoxicology of invertebrates in this document.

3.3 Specific Comments

3.3.1 On p. 2-14, the text makes a passing reference to the TEQ approach for 12 coplanar PCBs for fish, with no details of the application of this method.

3.3.2 On p. 2-15, the authors note the sometimes large differences in sensitivity to PCBs among bird species, but do not discuss whether highly sensitive birds (e.g. ospreys) are found in the Lower Fox River area.

3.3.3 The toxicology of PCBs for amphibians is raised, though amphibians are excluded as key receptors in the report based on citation of studies which show no apparent effects of PCBs on amphibians (p. 2-19). However, the qualifications placed on these studies in the report limits the reader's confidence in that conclusion.

4.0 Problem Formulation (Chapter 3)

The conceptual site model appears reasonable; though simplistic, as discussed below. The assessment endpoints and questions related to associated risk appear generally reasonable. There is an emphasis placed on fish, birds and mammals, based on the assumption that mid to high trophic levels are at greatest risk from the toxic effects of bioaccumulative substances such as PCBs. As in previous sections, the discussion on p. 3-1 and the Conceptual Model (Figure 3-1) both include macroinvertebrates as part of the exposure pathway. It would be useful to clarify in the report that invertebrates are only considered as sources of PCBs to higher predators, and there is no consideration of direct toxicity to invertebrates beyond the minor mention on p. 2-7. The omission of invertebrates as receptors is questionable, as discussed above.

The choice of fish receptors is also questionable. The report makes it clear that walleye and northern pike were selected because they are fish from an upper trophic level. While pike and walleye are piscivorous fish species at the top of the aquatic food chain, contaminants have never been implicated in reproductive impairment of these species; as has been done for salmonids in the Great Lakes. This may indicate low sensitivity of these species to contaminant-related effects or alternatively, contaminant concentrations may be relatively low in these species because of the low lipid content of pike and walleye tissues. Benthic fish species such as carp and bullhead are likely to be highly exposed to PCBs in the Fox River/Green Bay area. This is born out for carp by an examination of the PCB concentration data provided in this report (Table C-1). The ERA relies heavily on field studies performed in the region on one of the fish receptors (i.e. walleye). The TRV-HQ approach is applied to walleye and pike, but only with TEQs and not total PCBs.

Analysis of the risks to passerine birds (red-winged blackbirds and tree swallows), double-crested cormorants and bald eagles only employ field studies. TRVs are developed for terns, but again, these are TEQ-based. The analysis plan for mink appears reasonable, although again, only TEQs are considered.

Questions related to impacts on receptor species (pp. 3-2 and 3-3) all reduce to effects on reproduction, which are identified as the most sensitive measure of adverse effects. This focus on reproductive responses brings into question the validity of using the TEQ approach almost exclusively for risk characterization. As mentioned previously, there are many biological responses to contaminants that impact on reproduction (e.g. estrogen agonism/antagonism, androgen antagonism, disruption of endocrine hormones, neurological effects, egg-shell thinning) that are not mediated by binding to AhR. There is no explanation whether the WDNR (1995) study on sediment toxicity to macroinvertebrates, which was used to eliminate invertebrates for consideration, evaluated reproductive endpoints in its suite of investigations.

4.1 Other Specific Comments:

4.1.1 On p. 3-8, in Section 3.2.1, the text inadvertently lists mink in the section under avian receptors. Clearly, there should be a Section 3.2.1.3 (Mammals), and mink should be listed in that section.

4.1.2 Assessment endpoints are shown in Table 3-1, which are all related to population health and reproductive success. It is not clear in the text or on Table 3-1 why population issues are addressed for all species except the Bald Eagle, where individual eagles are the assessment endpoint.

4.1.3 Data sources are discussed briefly here, but more fully later in Chapter 4. It isn't clear why some studies that are relied upon heavily are presented explicitly, while in other cases, the text says "other supporting studies" were used. This distinction of presenting some but not all references seems arbitrary.

5.0 Exposure Assessment (Chapter 4)

On p. 4-1, Section 4.1, an explanation of the Assessment Zone was given that divides the geographical area into five assessment zones. This approach is appropriate, since the watershed is impounded by dams along its length that delineate many of these zones. Based upon 186 sediment samples, PCB concentrations were mapped within these sub-regions. This seems to be a limited data set for delineating the distribution of PCBs along a 70 km stretch of the Fox River and the southern end of Green Bay. There may well be "hotspots" of PCB contamination that were not detected in this sampling scheme. For sediment data, PCB TEQs were not calculated; presumably because no analytical data were available for coplanar congeners.

In the section beginning on p. 4-8, Section 4.3.3, it is explained that the actual distribution of mink throughout the assessment area is not known and therefore, the distribution and foraging range of mink are estimated. GIS was used to map the habitat for many of the receptors, including mink. This provides useful information, but must be employed with care in performing risk assessments. For example, it may be inappropriate to conclude that there are areas with high human population densities and high PCB contamination that pose no risk to receptors solely because there is no suitable habitat. These conditions may change, as human communities may decide to create habitat, or birds and mammals may move into areas with high human population densities over time.

As noted previously, the exposure assessment employed may be flawed with respect to the choice of receptors, (e.g., omission of invertebrates and benthic fishes) and its focus on TEQ-based evaluations. A very strong concern is the limited data base of tissue residues used for exposure assessments; especially for bald eagles and mink. This problem appears to be exacerbated by the focus on TEQs, which requires more sophisticated and expensive analytical techniques for coplanar PCBs. For instance, there are PCB data presented for only 6 mink, of which 4 samples were rejected from the exposure assessment because the animals were judged to have been captured outside of the assessment area. In addition, no other relevant data are presented for the mink samples, such as the estimated age and the sex of the animals.

For bald eagles, there are PCB data for only 6 eggs, of which data for 4 eggs from Marinette County were rejected because they were judged to be outside of the assessment area. Two of these eggs contained very high levels of PCBs (>100 ppm) and a decision to include them in the assessment area would have significantly affected the risk assessment outcome. In addition, these contaminant levels should be compared to concentrations in other geographical areas. For instance, the data on mink from Lake Erie reported by Proulx et al. (1987) indicate that PCB concentrations in mink from the lower Fox River were similar to those observed in the mid-1980s in mink from the western Lake Erie area, but higher than mink from the central Lake Erie region.

In the case of birds and fish, the TEF values recommended by the WHO (Table 1-1) were used. However, for assessments with mink, the TEF values from Safe (1990, 1994) were used, even though TEFs for humans/mammals are presented in the WHO table. The reason for this departure is not explained beyond the authors' statement that the Safe TEFs gave the best dose-response curve fit. However, on balance, it must be stated that the Safe data typically give a more conservative estimate, since most of the Safe TEF values are equal to or more restrictive than the TEF estimates recommended by WHO.

5.1 Other Specific Comments:

5.1.1 On p. 4-10, Section 4.4.3, regarding Bald Eagle exposure, the report discusses that researchers analyzed eggs for organochlorine pesticides, PCBs and lipid content. It is worth noting that there could be other persistent, lipophilic contaminants in the eggs that could be detrimental, but which were not analyzed (e.g. PCDD/DFs).

5.1.2 In Appendix H, related to the section on Bald Eagles, a model was employed to predict concentrations and risks. There appear to be quite a few layers of uncertainty in the model, including the methods for estimating PCB concentrations in eggs and other factors that may generate overestimates of exposure (e.g. time spent in the area). Therefore, this seems to be a highly conservative model.

6.0 Ecological Effects Characterization (Chapter 5)

The first part of this chapter (Section 5.1) presents an analysis of population estimates of avian receptor species, and a putative linkage is made to the ecological evaluation. It would appear from this discussion that all populations of selected bird species are increasing. These data are presented as evidence that PCBs are having no effect upon the reproductive success of the bird species. The population trend analyses provide useful information, but are limited in what they bring to a risk assessment.

6.1 Effects on Fish

The section on ecological effects analysis (section 5.2) is perhaps the most critical part of this ERA, and requires considerable attention. In Section 5.2.1.1, assessments are made for PCB impacts on walleye, based upon survey data for 1996 and 1997. The authors concluded that any tumors and lesions found in fish were not caused by PCBs. However, assays for other chemicals in sediments (e.g. PAHs) were apparently not conducted, and thus one cannot postulate alternative causative agents. There are no data in the literature indicating that neoplasms or other lesions observed in walleye are related to exposure to PCBs, or any other class of chemical contaminants. Indeed, there is more evidence that there is a viral etiology for neoplasms in walleye. Earlier, it was stated that the most ecologically relevant endpoints of PCB toxicity are reproduction and development. It is well known that for some fish species (e.g. lake trout), these are very sensitive endpoints. The fish health indices examined do not provide information concerning potential PCB effects on reproduction and development.

Two other points merit mention. The lowest tissue concentrations illustrated on the x-axes of figures 5-9, 5-11, and 5-13 are greater than 2 mg/kg, which seems high, and higher than many of the values reported in fish tissue (Table C-1). The lack of association between PCB residues and EROD activities is presented as evidence for lack of biological response in these walleye. However, it should be noted that a lack of CYP1A induction has been noted in populations of fish that have been exposed to PCBs and other Ah agonists for multiple generations (Hahn, 1998). Laboratory studies of these fish demonstrate reduced inducibility, which may represent an adaptation to chronic exposure to Ah agonists.

6.2 Effects on Birds

In Section 5.2.2, data were evaluated for red-winged blackbirds and tree swallows. The report concluded that no adverse effects on reproduction could be attributed to exposure to PCBs, and therefore, passerine birds were eliminated from further analysis. Although the results of the two investigations cited are consistent with that conclusion, they are both small studies and are not very persuasive. In addition, the site of the assessment for the blackbird study (Rothstein et al., 1989) was in marshlands in lower Green Bay, a region which appears to have low levels of PCB contamination (based upon sediment data) relative to other regions in the assessment area.

6.2.1 Effects on Terns

The analysis presented for the tern species is not helpful. The data presented for Forster's tern populations in the assessment area (Figure 5.1) show no trend between 1970 and 1986, and the data end in 1986. Except for Kidney Island, the same is true for common tern populations (Figure 5.3). The lack of data after 1986, except for the state-wide breeding bird survey illustrated in Figure 5.2 which is not very relevant, should be explained.

In Section 5.2.3, assessments are made for the effects of PCBs on Forster's and Common Terns. The authors conclude that there were no adverse effects due to exposure to PCBs. First of all, in focusing on the field studies, the report does not deal with some very convincing experimental evidence that PCBs, and coplanar PCBs in particular, affect reproductive success and cause deformities in terns. On pages 5-17 to 5-19, a great deal of attention is paid to refuting the conclusions of Kubiak et al. (1989) that there was evidence during a 1983 survey of impaired reproductive success of Forster's terns at a site in Green Bay (i.e. Long Tail Point) relative to a reference site (Lake Poygan). The report cites another population assessment of the reference site conducted during the same season by Mossman et al. and contends that Kubiak et al. (1989) overestimated the reproductive success of terns at the reference site. However, it appears that Mossman et al. did not replicate the study of Kubiak et al. (1989) by conducting simultaneous assessments of the reproductive success of terns at both the Green Bay and reference sites. Bearing in mind the variability related to estimates of reproductive success in birds by two independent researchers, it is difficult to see how the authors of the Exponent report can state that, "this (sic) more comprehensive data indicate that there were no adverse reproductive effects due to PCBs for birds breeding at Green Bay in 1983" (page 5-17, last line), or "there is no evidence of reduced productivity for birds breeding in the assessment area.." (Page 5-18, line 10). The report also ignores data presented by Kubiak et al. (1989) of reduced egg hatchability, and reduced weight at hatch and increased HSI in hatchlings from the Green Bay tern eggs raised in laboratory incubators

In the section on Common terns (Section 5.2.3.2), the report draws conclusions that are the opposite of those presented in the original paper. In discussing the paper on common tern eggs by Hoffman et al., 1993, the report states (top of p. 5-20) that "Abnormality rates were also significantly higher (in Green Bay eggs) ..... than at the two Saginaw Bay colonies, although PCB residues in these sites were not significantly different from Green Bay eggs". This is a misinterpretation of the data in Table 3 from Hoffman et al (1993). That table indicates that abnormality prevalences in Green Bay eggs (11%) were significantly different from the prevalences at the one reference site that was statistically tested (i.e. Cut River - 0%). Eggs from the two Saginaw Bay sites, that like eggs from Green Bay contained significantly greater concentrations of PCBs versus reference sites, had abnormality rates of 5% and 8%. The prevalences of abnormalities in Saginaw Bay eggs were not significantly greater than the 0% rate from Cut River. Abnormality prevalences in Green Bay eggs were not statistically tested against eggs from the Saginaw Bay sites.

6.2.2 Effects on Cormorants

In Section 5.2.4, there is an assessment of the effects of PCBs on double-crested cormorants. The report reviews the literature on this subject in a rather cursory fashion, and concentrates on studies that appear to show no association between PCB exposure and either reproductive success or developmental deformities in cormorants. A closer evaluation of these two studies introduces doubt as to the validity of the conclusion that PCBs do not affect reproductive success in cormorants.

The study by Larson et al. (1996) is reviewed in section 5.2.4.1 of the report. A first-hand evaluation of this publication shows that Larson et al. (1996) demonstrated a reduced proportion of eggs hatching and increased prevalence of hatchlings with deformed bills in a colony in Lake Michigan (Spider Island) relative to a reference colony, and this was consistent with elevated PCB concentrations and bioassay- derived TEQs in eggs from the Lake Michigan site. However, <u>within</u> the Lake Michigan site, PCB concentrations and TEQs in sibling eggs were not correlated with hatching success and the prevalence of deformities. This latter observation is the only one highlighted in the Exponent report (Page 5-22). The actual conclusions of Larson et al. (1996) were that, "we were unable to either accept or reject the hypothesis that environmental chemicals caused the observed embryo mortality and hatching deformities in cormorants at the Spider Island site.... Our results are consistent with the interpretation that PCBs reduced reproduction at this site...". The Exponent report goes on to interpret these data as representing an unbounded NOAEL for hatching success of 134.3 pg/g TEQ (Page 5-22), but this NOAEL was never suggested by the authors of the original study.

In the study reported by Kuiken et al (1999) reviewed in section 5.2.4.2, it is reported that 8 of 20 hatchlings from cormorant eggs collected at an uncontaminated site in Saskatchewan, Canada developed bill deformities. These deformities were first noted at 2-3 weeks after hatch, and were not congenital deformities. This very high rate of deformities, compared to the prevalence of bill deformities in wild cormorant populations of approximately 50/10,000 and the development of the deformities <u>after</u> hatch led the authors of this study to conclude that, " the factor or factors that caused such malformation were associated with, or exacerbated by, their captive state. The captive chicks may have been deficient in vitamin D3...". The authors of the Exponent report take the statements of the authors of this study out of context on Page 5-23 (line 12) when they contend that they stated that bill malformations are not caused by PCBs. Instead, the authors of the paper said that, "It is unlikely that PCBs or other contaminants in the egg caused bill malformations of these captive cormorants, because their bills became malformed only 2 weeks after hatching, and their free-living siblings......had a significantly lower prevalence of bill malformations". A hypothesis which is consistent with this mechanism is one in which the levels of vitamins (e.g. vitamin D and A) in eggs from contaminated regions are reduced as a result of PCB-induced alterations to vitamin homeostasis in adults; resulting in congenital malformations in chick embryos.

In section 5.2.4.3, the Exponent report also concentrates on a site-specific study by Custer et al. (1999), in which the study authors concluded that hatching success was associated with concentrations of DDE in eggs, but not with concentrations of PCBs. The studies in the literature which have demonstrated an association between exposure to PCBs or PCB-related TEQs and developmental and reproductive effects in cormorants have all been studies involving surveys of two or more cormorant colonies, varying in the degree of contamination (e.g. Larsen et al., 1996; Yamashita et al., 1993; Tillett et al., 1992). It is also interesting to note that a study by Henshel et al. (1997, J. Great Lakes Res. 23:11) demonstrated a relationship between TEQs and brain abnormalities in cormorant chicks sampled from 5 different colonies varying in the degree of contamination. In the study by Custer et al. (1999), eggs were collected from a <u>single</u> cormorant colony on Cat Island in Green Bay and the data were evaluated by relating the reproductive success (and embryo abnormalities) in the eggs to the contaminant concentrations in sibling eggs removed from the same nest. The validity of this approach may be questioned since there may be variations in contaminant concentrations among siblings. In addition, TEQs were not calculated for these eggs since only PCBs as total

Aroclors were determined. "Logistic regression analysis" showed an association between DDE concentrations and reproductive success in this study, but this relationship is not visually convincing and appears to be driven by 5-6 samples with very high DDE concentrations.

7.0 Derivation of Toxicity Reference Values (TRVs)

In this section, TRVs are developed for use in risk assessments regarding fish, tern and mink. In contrast, risk characterizations are developed in Chapter 6 for passerine birds, cormorants and bald eagles, based on the results of site-specific field studies. The section on development of TRVs for fish (5-30) begins with a statement regarding effects of 2,3,7,8-TCDD. The linkage to PCBs is never made clear, except insofar as they both exhibit AhR-mediated effects. The EPA-determined value of 50 pg/g for whole fish is recommended by Exponent for use as a TRV for PCBs. However, the citation provided in support of this value is U.S. EPA (1993b), which is a paper regarding TCDD. [It is worth noting that this value 50 pg/g value is quite close to the LD50 reported by the authors for lake trout sac fry (65 pg/g).

Further, the expression of whole body tissue concentrations as LD50s is, from a strict terminology perspective, inaccurate]. The studies cited that appear to provide a solid basis for the selection of fish TRVs are all derived from data on TEQs in eggs, not in adult fish tissue. It is not clarified how adult tissue residue values were extrapolated from egg concentrations. The point at which this becomes a significant issue is in Section 6 and in Appendix C, where the line between the whole body PCB concentrations and the TEQ for PCBs becomes blurred. If one accepts that the TCDD/PCB nexus is reasonable, the real question then becomes whether the 50 pg/g TRV is a "whole body" value, or whether it represents a value to be compared with TEQ values. At the least, this section and Section 6 need to be more explicitly constructed for clarification. If the 50 pg/g was intended to be compared with "whole body" concentrations, then there is a different problem.

7.1 Tern TRVs

In the section on pp. 5-30 and 5-31, a TRV of 521 pg/g is developed for Forster's and common terns using TEQs based on analytical data for four congeners only (i.e. 77, 105, 126, 169) and the results of one field study (Harris et al., 1993). This TRV is highly suspect. No justification is provided for using the

Harris study as the sole basis for No Observed Effect Levels (NOELs), to the exclusion of data from other relevant field studies and better controlled laboratory studies, many of which are reviewed by Bosveld and Van den Berg (1994). While the 4 coplanar congeners may be the only usable data, some explanation of this approach would be useful. For instance, the TEFs recommended by WHO for risk assessments with birds include a value for congener 81 that is equal to the TEF for congener 126. (i.e. 0.1) Therefore, the absence of data on congener 81 may greatly underestimate the TEQ.

7.2 Mink TRVs

On page 5-31, the TRVs derived for mink were 1.2 □g/g total PCBs in adult tissue and 100 pg TEQ/g food for mink diet. These values appear to be very non-conservative. The total PCB TRV (1.2 ug/g) corresponds to the EC50 value for litter size (Figure 5-16) developed by Leonards et al. (1995); that is, the value resulting in an average reduction of litter size by 50%. This is higher than a TRV based upon observed or predicted NOELs and LOELs, which would be more appropriate. The basis for the TEQ-based TRV for PCBs in mink food (100 pg/g food) is confusing. In the graph referred to (Figure 5-16), the x-axis is labeled as whole body concentrations, not the dietary concentrations. Like the adjacent graph for total PCBs, it appears that the 100 pg/g value coincides with the EC50 value, not a threshold concentration. Also, this value is far higher than other TRVs suggested for mink diets, including a very recent one of 1.4 - 1.9 pg/g for aquatic and marine mammals (Kannan et al., 2000, Human and Ecological Risk Assessment 6:181-201).

7.3 Other Specific Comments

7.3.1 Figure 5-2, which is cited in the text on p. 5-32, presents data for Forsters Terns, not mink as the text suggests. It may be that the authors meant to cite Figure 5-16, which is embedded in the text on p. 5-33.

8.0 Risk Characterization (Chapter 6)

Based upon the field studies examined and the HQs for fish, terns and mink, it is concluded in the report that PCBs pose no adverse risks to any of the ecological receptors examined. There are three general reasons why these conclusions can be questioned:

1. This ERA places undue emphasis on field studies performed in the assessment region. The inclusion of these field studies is appropriate. However, these studies oftentimes do not provide a firm basis for conclusions regarding specific cause-effect relationships since many confounding factors are present (natural stressors, other contaminants, inherent variability), or in some cases, there may be poor experimental design. In several cases, the studies cited involve small sample sizes, so the power to detect significant differences is reduced.

2. PCB residue data in animal tissue, the key driver for exposure assessments in this ERA, is very limited, considering the geographical area encompassed, spatial patterns of PCB residues in sediments, and the number of receptors potentially at risk.

3. The TRVs employed are questionable in some cases. TRVs were, except for mink, only calculated for TEQs, not total PCBs. When possible, both should be employed, for two reasons: a) it is not clear to what extent non co-planar congeners can contribute to toxicity and, b) the inclusion of total PCBs will greatly expand the data base available for estimating exposures and TRVs.

As described above, TRVs for terns and mink appear to be flawed. The TRV for fish may be appropriate, but its derivation is not clear (see comments above). In regard to the risks for Forster's and Common Terns, the text states that "more than 80 percent of the USFWS tern egg samples contained PCB concentrations that were less than the TRV for hatching success ...". We can interpret this to mean that 20% of the eggs exceeded that value; indicating potential risk to the population.

In section 6.6.2 of the report it is stated that the model used to predict PCB TEQs in mink diet gave values below the TRV of 100 pg/g in food and the data on mink whole body samples collected in the vicinity of Green Bay indicated that mink had tissue concentrations below the TRV for reproductive effects (i.e. 1.2 ppm). However, it is interesting to note that one mink collected at Potter Creek, which was considered outside of the assessment area had a total PCB concentration of 1.8 ppm (Table C-10); above the TRV of 1.2 ppm. It is also not clear how sensitive the mink model is to changes in the relative contribution of fish (with higher PCB concentrations) and crayfish (with lower PCB concentrations) to the mink diet. There is some discussion of this point on page 7-7 in the section on Uncertainty Analysis, but it is not clear from the wording in this section how this issue was resolved. The present population of mink is likely to be only 20 mink, though available habitat suggests that the region could support over 900 animals. There is no speculation regarding explanations for the low population numbers.

The following comments apply to the risk characterizations derived from field studies. With regards to risks to passerine birds, the report conclusions are based on two studies that show no adverse effects of PCBs on populations of red-winged blackbirds or tree swallows. As noted previously, the small sample sizes of the studies and the location of one of the studies in a relatively uncontaminated area limits the strength of these conclusions. The authors of the report conclude that PCBs do not pose a risk to populations of cormorants in the assessment area. As pointed out in the comments above, the focus on one site-specific field study (Custer et al., 1999) to the exclusion of other experimental and field studies is a major weakness of this risk characterization process. In the risk characterization for eagles, recent population trends and field studies suggest no risk, although a screening model shows some potential for risks, since calculated HQs were above 1 but less than 7. One would assume that the risk of toxic effects would be very high in the 2 eagle eggs collected from a nest in Marinette County with PCB concentrations >100 ppm; although these eggs were rejected from the study because they were judged to be outside the study area.

8.1 Other Specific Comments:

On p. 6-2, the HQ equation is presented and said to be applied in this document to mink and to terns. As a point of clarification, it seems also to have been applied to fish.

9.0 Uncertainty Analysis (Chapter 7)

The characterization of uncertainty analysis on p. 7-1, while brief, is accurate. Several instances were identified in previous comments where assumptions may not have been as conservative as reflected by the text on p. 7-1. Nevertheless, these are nominal items that typically would not have a large effect on the results of the analysis. Mink and eagle tissue data were limited, as was noted on p. 7-2, while data for fish were extensive. This is not surprising, and reflects the relative difficulty of data collection. The same argument does not necessarily apply to data for crayfish and benthic macroinvertebrates, which apparently were limited by availability, but could have easily been collected on short notice. However, because invertebrate data were not used to any degree in the assessment, it is of little consequence. The decision to exclude invertebrates from consideration may represent a significant gap in the analysis. If that decision was made prior to the scoping of the assessment, that should be noted in the Introduction to the report.

One wonders about the wisdom of collecting 2 mink for study out of an estimated population of 20 (page 7-6). As noted above, there is mention of the uncertainty associated with developing a model that estimates the relative contribution of crayfish and fish to the mink diet. However, it is unclear from the wording on page 7-7, how this uncertainty was addressed in the development of mink TRVs.

10.0 Summary and Conclusions

The conclusions in the Exponent report are consistent with the data presented in the ERA, but as noted above, the authors of the Exponent report were very selective of the data included in the evaluation of ecological risks. This contributed to the outcome of the evaluation which concluded that there were no ecological risks to receptors associated with PCB contamination in the region. It is interesting that the report does not include any recommendations; especially in relation to possible remedial activities in the lower Fox River.

10.1 Additional Specific Comments:

1. On p. 8-1, northern pike are included in the bullet regarding upper trophic level fish. While they certainly are representative of that category, pike do not appear in any significant way in the ERA. The reason for inclusion of pike in this section is not clear.

2. Supplementary Notes on Tables:

Table 4-1: Surface sediment PCB Results for the Lower Fox River and Green Bay. What is the source of the data with no dates for Zones 1, 2, 3,4, and 5? What is the significance of PCB data normalized to Total Organic Carbon (TOC)? As noted in the text, the normalized data were not used for any purpose in the report.

Table 4-2: Explanation of c footnote is missing. It is not appropriate to present a mean or max when there is only one sample, and this may have been what footnote c was directed toward.

Table 5-1: Mink Density. Questionable reliability of population density data based on studies in Sweden and on data from either 1936 or 1949.
Table C-1 (6th page): Missing results for samples F10027 through F10046; later in Table, missing data for WB0054-WB0057, WB0066, and F10027-F10046.

3. Supplementary Notes on Appendices:
Appendix I
Mink Exposure Model. Values are correct, but units for Dose avg (Daily Adult intake) should be pg/g-day, as follows:
= [(pg/g)x unitless) + (pg/g x unitless)]x g/g-d
= (pg/g)x g/g-d = pg/g-day
Appendix K
• Data are from 1996, data in Appendix (presented Walleye data also, apparently much lower values).
• Make sure units are right, as shown in mg/kg. The 1996 data presented on this table are shown for several Fox River areas, with a mean for the Lower Fox River of 6 mg/kg. That is not the mean that one calculates from the 1996 WDNR walleye samples presented on Table C-3 If another data set was used, or if the data in Appendix K and Appendix C were handled differently, that should be defined and presented in the text. It could make a substantial difference in the results.

11.0 Assessment by ThermoRetec

It is important to note that the evaluation of the ERA document prepared by ThermoRetec was based upon an analysis of the ecological risks associated with exposure of receptors to PCBs only. No assessment was made of the risks associated with exposure to the range of other contaminants identified and discussed in the ThermoRetec document. While this evaluation approach is consistent with the terms of reference provided to the evaluation panel, there are fundamental questions related to the advisability of considering PCB data alone and excluding factors related to other anthropogenic stressors in the ecosystem.

11.1 Problem Formulation

The Problem Formulation focuses on the site conceptual model (Figure 6.1) that "establishes complete exposure pathways, and relates assessment and measurement endpoints for the Characterization of Exposure (Section 6.4) and Rick Characterization (Section 6.6) for this site." Unfortunately, no figures for

Chapter 6, including the conceptual model (Figure 6.1), were included in the copy of the report provided. This model comprises a critical medium for conveying the problem; hence its exclusion is very unfortunate. However, based upon the subsequent descriptions of assessment endpoints, measurement endpoints, ecological receptors, exposure pathways, etc., the Problem Formulation appears reasonable.

An issue of significant concern is the adequacy and suitability of data bases available and/or employed for ERA's for the lower Fox River/Green Bay region. Adequate data appears available for mapping sediment PCB concentrations in the region to identify hotspots, prioritize potential clean-up efforts, etc. However, tissue residue data is far spottier for most fish, bird and mammal species identified as ecological receptors.

The issue of suitability is more complex. For water, sediment and tissue matrices, it appears that data collected over about a 10 year period by various investigators were aggregated (though still segregated by site and species). Actually, there appear to be data from 1979, over 20 years old, that may have been used (see p. 2-2-, paragraph 4). Given the data limitations described above, this less than ideal approach may be justified. However, the uncertainties this introduces should be acknowledged; particularly for tissue PCB concentrations that may be more temporally dynamic than sediment levels. The authors justify this aggregation by stating that while tissue concentrations declined from about 1975 until the mid 1980's, they have subsequently stabilized over the 10 years that were aggregated. This conclusion appears to be generally supported by the data for fish tissues illustrated in Figures 2-1 to 2-20. However, data points are too sparse for making such a conclusion with confidence. Ultimately, the approach taken here appears justified. However, the uncertainties inherent in this approach should be acknowledged.

Another aspect of this ERA that bears upon the issue of data aggregation etc. concerns the overall goals of the ERA with respect to the ongoing RI//FS process. On p. 7-1, it is stated that "The overall objective of the Fox River RI/FS is to determine risk-based corrective action that may be applied to contaminated sediments within the Lower Fox River." Given that, it would seem that the greatest emphasis should be placed on sediment PCB concentrations (the subject of chapter 7, discussed later). Given the persistence of PCBs, the assumption appears to be that sediment concentrations are likely to remain reasonably stable over a period of several years, thus justifying data aggregation.

It appears that for some sites, sufficient data are available to test this assumption, and if so, this should have been done. Given that these data are critical drivers for decisions concerning remedial action, an accurate assessment of "current" conditions is critical.

11.2 Fundamental Approach to the Risk Assessment

The choice and description of "assessment endpoints", "measurement endpoints" and "ecological receptors" appear reasonable. The overall approach for this ERA was to derive exposure information from site-derived residue data (in water, sediment, and tissue) and compare these with laboratory derived effects criteria (TRVs). For the water column and benthic invertebrate communities, the detected concentrations over the last decade were compared with ecological benchmark criteria. Several different source values were used, including NOAELs, LOELs, TECs and LD values. Apparently, the report used EPA (1995) as a reference, per Table 6-5, but this reference is not included in the reference list. For invertebrates, the authors used national AWQC Continuous Concentrations, defined as the highest concentration of a pollutant to which aquatic life can be exposed for an extended period of time (4 days) without deleterious effects.

Potential limitations of the comparison approach used in this document were articulated in a U.S. Dept of Energy document (U.S. DOE, 1997), which indicated that "To evaluate ecological effects of contaminated sediments for a baseline ERA, it is recommended that sediment be collected for toxicity testing and the benthic macroinvertebrate community be surveyed". This is important because chemical concentrations are not always accurate predictors of biological and ecological effects. This is because the percentage of the chemical that is bioavailable may range from 0-100%" (U.S. DOE, 1997). It does not appear that bioavailability was addressed in the calculations or comparisons.

The dominant value used for exposure analysis was the Reasonable Maximum Exposure value (RME), based upon the 95% upper confidence interval in a normal distribution (or the maximum value with very small (n<5) or non-normal data sets. Dominant TRVs employed were NOELs and LOELs for "functional communities" (pelagic and benthic invertebrates) or reproduction and survival (fish, birds, mink). These TRVs were based largely on data from laboratory studies available in the literature. For fishes and birds, these studies were usually based upon species other than the receptors identified for this ERA.

This overall approach is a reasonable one and appears consistent with current approaches promulgated by the US EPA, for example. The reliance upon TRVs for species other than those of interest is not unusual, and is necessitated by the few species for which TRVs are available versus the large number of potential receptor organisms. However, the strict reliance on this approach is questionable. On p. 6-25, it is stated, "While the population status of many of the receptor species are discussed below, evaluation of the receptor's current population, as a measure of risk, will not be evaluated." While the caveats concerning such studies that are discussed in the text immediately below this statement are valid, such studies can provide useful information for an ERA. As is made abundantly clear from this overall review of PCB risks in the Lower Fox River, ERA is a very imprecise process. All relevant information should be included in the ERA for this system.

It should be noted that the food chain model for mink described on pp. 6-21 to 6-22 was not used for PCBs. Rather, a simple exposure model comparing contaminant concentrations in fish with NOELs and LOELs for mink reproduction was used for PCBs. This approach also seems reasonable. Selection of the mink as the ecological receptor representing mammals was based on their known sensitivity to PCBs (hence, protection of mink will very likely protect other mammals) and their historic range in the study region. However, the report states that the presence of mink populations in the area has not been confirmed; placing into doubt the selection of mink as an appropriate receptor.

11.2 Other Specific Comments

11.2.1 No reference is provided for ARCS TEC values that are cited in Table 6-5, but it may be U.S. EPA (1996).

11.2.2 p. 6-25 to 6-26: Invertebrates may be an assemblage worthy of future study, since some relatively insensitive species were reportedly dominant in the samples. It would be worth determining whether this is because of chemical influences, or whether these invertebrates are not present in uncontaminated areas either.

11.3 Effects Criteria (TRVs)

While the approach for developing TRVs is reasonable, the derivation of the TRVs for ecological receptors from NOAELs, LOAELs, etc. is generally performed with limited explanation in the text of the report. In conjunction with intake rates, these TRVs essentially control the outcome of the risk assessment. Therefore, a discussion more explanatory than that presented on p. 6-39 would be appropriate to define the technical foundation for the methodology.

An additional point of confusion occurs in Table 6.5 (i.e. Selected Values as Criteria of TRVs). Based upon the definition of LOEL vs. NOEL, the NOEL should be a lower concentration. However, the NOEL for total PCBs listed in this table for bald eagle, cormorant, and terns is higher (4 mg/kg) than the LOEL (0.8 mg/kg). This anomaly is not explained, but may reflect the fact that the numerical values are for different endpoints (i.e. reproduction vs deformities).

Following are comments for specific TRVs:

11.3.1 Pelagic invertebrates: The selection of the TRV seems reasonable.

11.3.2 Sediment invertebrates: The TRV is primarily derived from the ARCS SEC (EPA, 1996) value of 31.6 µg/kg. Apparently, this is an accepted sediment PCB threshold, but this merits additional scrutiny.

11.3.3 Fish: For TRVs based on total PCBs, the authors of the report arrived at two TRVs based upon NOELs of 0.5 mg/kg for eggs an
d 0.75 mg/kg for fish tissue. In the case of the egg TRV, it is not clear how the value was arrived at, though it appears to be based upon a NOEL from Niimi (1996). The fish tissue TRV (0.75) was selected as the lowest NOEL for lake trout mortality. This may be overly conservative because it is based upon a very sensitive receptor (i.e. lake trout) and more importantly, because it is based on the "lowest NOEL." There is no indication of the gap between the LOEL and NOEL, but theoretically, a NOEL can be far below the threshold for effects.

In discussing TRVs for PCBs in fish (p. 6-47), the authors correctly acknowledged that it is difficult in the field studies to separate effects of PCBs alone from the effects of other contaminants (e.g. DDT). This assumption renders the PCB numbers very conservative and makes conclusions based on these values also conservative. The TRVs derived from PCB-TEQs are perhaps better justified. They are based upon several studies from well-recognized laboratories that are in reasonable agreement. Also, these TRVs are based upon a mean value of the NOEL and LOEL. It is not clear why this same approach was not used for total PCBs. As pointed out in the review of the Exponent report, the TEQ approach is specific for AhR-mediated toxicity and there are several assumptions associated with use of this risk assessment model, including:

i) toxicity of individual congeners in mixture is additive.

ii) sensitivity to congeners does not vary across species within broad taxonomic groups.

iii) dose-response curves for congeners parallel those for 2,3,7,8-TCDD.

While much of the toxicity associated with PCBs may be related to AhR interactions, this association does not apply to several toxic effects (e.g. estrogenicity, neurotoxicity). Thus, the use of both approaches is appropriate.

11.3.4 Birds: Again, TRVs were developed for both total PCBs and coplanar congeners (i.e. TEQ approach), which is appropriate. However, TRVs were developed for eggs only. These TRVs are again based upon NOELs, which brings up similar issues as stated above for fish. Also, TRVs were developed for both lethality and deformities, with the latter endpoint having a lower TRV, as expected. It is not clear how these two TRVs will be used in decision-making about risks; that is, will decisions be made ultimately on the criteria of the risk of deformities? Again, the TRVs based on PCB-TEQs have a more sound basis in field situations where there are many contaminants potentially affecting the birds, but again, it is not clear how the three different values obtained (i.e. for 20% and 30% mortality, and the NOEL) are employed in the risk assessment.

11.3.5 Mammals (mink): The TRVs were again developed for both total PCBs and coplanar congeners (TEQs). In this case, the values are for concentrations in diet, using carp as the model prey item. For total PCBs, a NOEL (0.015 mg/kg prey) and a LOEL (0.72 mg/kg prey) were developed, and it is not clear from the text how these two values are to be ultimately used in the risk assessment. This is very important, considering the 48-fold difference between the two. Moreover, this difference further calls into question the emphasis on NOELs for fish and birds.

The TEQ-based TRV (1.9 ng/kg prey) appears to be once again based upon a more sound scientific foundation, and represents the midpoint between the NOEL and the LOEL. Also, this value is very similar to a more recent analysis of the toxic risks of coplanar PCBs to aquatic mammals (Kannan et al., 2000, Human and Ecological Risk Assessment 6:181-201).

However, there are several factors which make this risk assessment process very conservative for the mink receptor. The TEQ-based TRVs were the most conservative values available (pp. 6-43 and 6-44). This assumption certainly affects the results since even the authors acknowledge (p. 6-43) that "Use of different TEF values can result in widely different TCDD-Eq estimates, even though each are well correlated with actual TCDD-Eq levels measured." In addition, the authors chose the lowest value reported of several dietary exposure values (p. 6-53 and p. 6-54), in the absence of residue-based values, which typically would be preferable.

11.4 Other Specific Comments:

11.4.1 p. 6-37: The terms NOEL and LOEL were used, but the terminology should accurately be NOAEL and LOAEL, because both are described as levels at which "adverse" ("A") effects were observed.

11.5 Characterization of Exposure:

In this report, various zones of the Fox River are evaluated individually with regard to potential adverse effects on ecological receptors. That is a reasonable approach for species with a limited range, but may be inaccurate for birds or mammals which have the ability to access multiple areas of the river. The "forward" method of calculating risks as a function of potential exposure and toxicity endpoints is a conventional approach, but is different than the approach taken by Exponent which sought to determine whether effects were observed or anticipated based on existing knowledge.

For exposure characterization, the Reasonable Maximum Exposure value (RME) was used, which is the 95% upper confidence interval in a normal distribution, or the maximum value with very small (n<5) or non-normal data sets. This approach is widely employed in ERAs and is reasonable for conservative estimates of risk. In this study, concerns arise over the aggregation of data collected over an approximately 10-year period (discussed previously) and the oftentimes very limited tissue data sets, which are in contrast to the more abundant sediment data.

An additional concern is that of data distribution. The 95% upper confidence interval that is the primary basis of RMEs assumes normal data distributions. According to the text on p. 6-75, the authors did not test for normality, although this assumption is complicated by a brief mention on p. 6-76 of testing the data sets for normality. Typically, according to standard practice and experience, environmental data sets are not assumed a priori to have a normal distribution. Rather, one of several tests is applied to determine the issue. In the event that the data are not normally distributed, it is common practice to conduct a log-normal transformation, as outlined by the U.S. EPA in the Risk Assessment for Superfund (RAGS) document released in 1989. Alternatively, non-parametric statistical procedures may accomplish a similar goal in non-normal data sets. Without the appropriate analysis, it is not reasonable to assume normality.

The following section addresses the issue of the adequacy and accuracy of analytical data for PCBs. To some extent, a document such as the ThermoRetec report must be judged in the context of the care that was exercised in its preparation. The document presents a large amount of information, and presents many tables of summary calculations which themselves are not available for review. The number of discrepancies and inconsistencies identified in the analytical data (see below) does not engender full confidence in the calculations and, in turn, the conclusions of this section. Because of the complexity of the report, the number of receptors considered, and the inter-related data and calculations, a much more careful effort should be undertaken by the authors to verify and correct this section.

11.6 Discrepancies and Inconsistencies

11.6.1 Water

i) The text on p. 6-79 (Section 6.4.3, Water) indicates that total PCBs were detected at a mean of 18.5 mg/L. Table 6-9 indicates that all values reported are in ng/L. The text also indicates that, "This is roughly double the concentrations detected in the Little Lake Butte des Morts reach." However, Table 6-9 indicates that the mean concentration for total PCBs (unfiltered) in Little Lake Butte des Morts reach is 18.86 ng/L ,which is equivalent to the concentration of 18.48 ng/L in the unfiltered samples for Appleton to Little Rapids reach.

11.6.2 The text on p. 6-81 (Section 6.4.4) indicates that approximately 50% of total PCBs was in the filtered fraction. On Table 6-9, however, PCB concentrations (ng/L) are presented for filtered and unfiltered water, respectively, as maximums of 27.6 and 96.3, means of 11.1 and 31.28 and RME of 12.27 and 35.31, which correspnds approximately to 29%, 35% and 35% for maximum, mean and RME values; not 50% for any case.

11.6.3 Sediments

11.6.3.1 In Table 6-8, the background sediment concentration for PCBs (total) in the RME case is listed as 36 mg/kg, while the maximum is 35 mg/kg. Clearly there is an error here. All other RMEs are maximum values.

11.6.3.2 In Table 6-10, the detected minimum for total PCBs should not be listed as 0, but as "not detected" or "<LOD". Typically, the reported detection limit or one half of the reported detection limit would be used in statistical analysis of analytical data for concentrations below detection limits.

11.6.3.3 On pp. 6-81 to 6-82 (Sediment), the text indicates that PCB congener concentrations in this reach were less than one-third of the congener concentrations measured in the Little Lake Butte des Morts reach. A review of other sections and tables suggests that this statement is not accurate. A comparison of Table 6-20, Little Rapids to De Pere Reach and Table 6-11, Little Lake Butte des Morts Reach, shows that all concentrations on Table 6-20 are greater than concentrations in Table 6-11; most by at least two-fold or more. This apparent discrepancy could affect conclusions for one or more of the reaches under consideration.

11.6.3.4 On p. 6-83, the greatest concentrations of coplanar PCBs were listed in order of congeners 118>77>105. This is surprising since mono-ortho congener 105 is usually found in environmental samples at concentrations well above those of non-ortho congener 77.

11.6.4 Biota

11.6.4.1 In the text on p. 6-79, it was stated that coplanar PCB concentrations in whole body samples of birds were generally less than egg concentrations. However, on Table 6-15, for PCB congener 105, both the minimum and maximum concentrations were greater in whole body tissues than in egg, and the maximum for PCB congener 118/106 was greater in whole body than in egg (e.g., 150 vs. 120).

11.6.4.1 In Table 6-13, for coplanar PCB congener 126 in carp and walleye, the mean concentration is greater than the highest detected concentration. That is, of course, not possible.

11.6.4.2 On the text on p. 6-79 and in Table 6-15, it is stated that coplanar PCB congener 77 was not detected in whole body samples of birds, but other non-ortho congeners were detected. This seems odd since congener 77 is generally one of the more prevalent non-ortho congeners in biological samples.
11.6.4.3 In the text, on p. 6-80 (Section 6.4.3), for Fish, the text indicates that total PCB concentrations in perch were slightly greater in Appleton to Little Rivers reach. In actuality, on Table 6-12 and Table 6-17, maximum concentrations in perch are identical. Also, it would seem difficult to compare PCB data for walleye, since it appears that only a single fish was sampled in the Appleton to Little River reach.**11.6.4.4** In the text on p. 6-82, in the last statement in this section, it is indicated that at Little Lake Butte des Morts, concentrations of coplanar PCBs were lower in carp than walleye. This is not an accurate statement based on a review of the accompanying tables. Maximum and RME concentrations for three of the five congeners are higher for carp but not for the other two congeners, where walleye concentrations were higher. For mean concentrations (Table 6-13) values for carp and walleye were essentially equivalent for four of five congeners.
11.6.4.5 On p. 6-85 (Section 6.4.5), in the last sentence under Fish, the text indicates that PCB congener 169 was detected in 100% of walleye. However, Table 6-26 indicates that this congener was detected in 10 of 11 walleye.
11.6.4.6 On p. 6-85, in the section on birds, the text indicates that data for tree swallows in Little Lake Butte des Morts reach is located in Table 6-11. This table contains data on surface sediments, so the correct table is Table 6-14.
11.6.4.7 On p. 6-86 (Section 6.4.5) and Table 6-29, regarding Fish, the text indicates that PCB concentrations are highest in De Pere to Green Bay reach. However, total PCBs in yellow perch are highest in Green Bay Zone 2 (Table 6-29, p. 6-160).

12.0 Risk Characterization

Risks are characterized with Hazard Quotients (HQs), which are simple ratios of TRVs/RMEs. This is a standard approach in ERAs and appears reasonable for this study. The uncertainty of the risk characterization is related to the uncertainties going into these ratios (i.e., the values used for TRVs and RMEs) which have been discussed earlier. Key issues include:

- validity of the ARCS SEC value for sediments
- emphasis on NOELs for TRVs derived from total PCB for fish, birds and mammals (mink)

- lack of clarity about how different TRVs within a receptor were used
- aggregation of data underlying RMEs
- adequacy of fish and bird tissue data for certain reaches

This risk characterization places heavy emphasis on laboratory-derived TRVs, which may be appropriate. However, the exclusion of potentially useful population studies in the Lower Fox River/Green Bay region is questionable. This approach to risk characterization employing largely laboratory TRVs for effects, RMEs for exposure, and assuming risk if the HQs exceeded 1 is very conservative. Little distinction appears to be made between HQs just above 1 versus HQs that are much higher. In addition, there seem to be inconsistencies in the decisions that are made regarding the significance of the risk when the HQ is between 1 and 10. Such distinctions may be important when decisions are ultimately made concerning subsequent allocations of major resources. Relatedly, most HQs are provided as point estimates. This approach seems to not take full advantage of the data available, which could provide estimates of a range of risks based upon the range of exposure data (e.g., sediment and tissue concentrations) and toxicities (TRVs).

As noted in the comments related to the section on exposure, there are also many inconsistencies in the risk characterization section between the text and the tables. These inconsistencies make one wary of any conclusions drawn from these results. Examples of these inconsistencies are included below:

13.0 Inconsistencies

13.1 p. 6-91, Section 6.5.1, sediment, and Table 6-16. Indicates that the value for RME HQ for total PCBs was 907. According to Table 6-16, the value is 971.
13.2 p. 6-95, Section 6.5.1, De Pere to Green Bay Reach, Sediment. Indicates that "Only the HQs for PCBs exceeded 10 and were 100 times those observed for the other COPCs." However, if you look at Table 6-23, this is not an accurate statement, since the HQs for PCBs vary from 14 to 285 times greater than those observed for the other COPCs.
13.3 p. 6-96, Section 6.5.1 and Table 6-50, mink. Text indicates for total PCBs, the LOEL HQ was 27. However, Table 6-50 indicates that the LOEL HQ was 21.18.
13.4 p. 6-98, Section 6.5.1 and Table 6-54, birds. Green Bay. Sentence states that, "Presently, the RMEs of total PCBs are 7.3 and 7.1 respectively ....." These

values are apparently are concentration data and should be expressed as 7.3 and 7.1 mg/kg, respectively.

14.0 Risk Summary

The Risk Summary is a succinct recapitulation of the Risk Characterization section, put in the context of the eight assessment endpoints stated on pp. 6-13 to 6-16, and provided for each of the five sub-regions comprising the study area. Thus, many of the issues here are essentially the same as those stated in the Risk Characterization section. As in the Risk Characterization section, the conclusions seem to vary when considering the significance of HQ of 1 versus HQ of.10 This is a recurring comment, and highlights the lack of clear assessment guidelines in the range of HQ=1 to HQ=10. The use of data which span a 10 year period increases the uncertainty of the risk assessment by a wide margin. Conclusions that are based on a more relevant (i.e., newer, recent) data set would be more defensible.

A shortcoming of this section is the lack if any attempt to synthesize the data. What do these data tell us about relative risks to different receptors? What do these data tell us about relative risks in different parts of the study area? How does one reconcile different spatial patterns of risk for one receptor versus another, given that sediments are the critical repository for PCBs in all area? Is there a temporal pattern to risks? That is, if exposure data were segregated by year of collection, would there be differences in HQs as a function of time? Such unreconciled differences and unanswered questions underscore the uncertain nature of ERAs, including this one.

Once again in this section, there are many inconsistencies between the text and the data presented in the tables. Again, these inconsistencies make any conclusions tentative until the apparent problems can be resolved. If the problem turns out to be a case where the tables are correct but the text is incorrect, the issue may be somewhat superficial. If, on the other hand, the text is accurate and some or all of the inconsistencies in the tables are substantive, then the conclusions may require re-evaluation.

As a general comment, the oddities inherent in this type of analysis are illustrated by the fact that the risks posed by Aroclor 1242 often exceed the risks presented for total PCBs. This may be an "analytical" peculiarity related to how the substances are aggregated, but this anomaly should be explained in the accompanying text.

Inconsistencies between the text and tables include:

i) p. 6-101, Section 6.5.2 and Table 6-60, Little Lake Butte des Morts. The report indicates that "Sediment HQs for total PCBs were 100 to 1,000 times greater than any other COPC." This appears not to be an accurate statement in all cases. For example, on Table 6-60, the HQ for Aroclor 1242 is three times greater than the HQ for total PCBs and the HQ for total PCBs ranges from 21 to about 12,000 times greater than other COPCs. Once the calculations are reviewed and corrected as necessary, they stand on their own and text summaries should be reconciled.

14.1 p. 6-105, Section 6.5.2 and Table 6-62. Appleton to Little Rapids. In the first paragraph, the text indicates that sediment HQs for total PCBs were up to 30 times greater than any other COPC. This is a somewhat misleading statement, since the HQ for Aroclor 1242 of 1108 is 69 times greater than the total PCB HQ of 16. HQs for other COPCs vary from anHQ for mercury which is 1.06 times greater then the HQ for total PCBs, to an HQ for arsenic which is 32 times less than the HQ for total PCBs.

14.2 p. 6-107, Section 6.5.2. In the text (line 12) where the impacts on receptors are summarized, no reference is made to the conclusion that impacts are predicted for fish. It should also be pointed out that there were no data on piscivorous birds that could be used to estimate risks.

14.3 p. 6-108, Section 6.5.2 and Table 6-64, Little Rapids to De Pere Reach. The text indicates that the HQ for total PCBs was 147 while Table 6-64 indicates a value of 93. Again, HQs for total PCBs were not 10-100 times greater than any other COPCs. Aroclor 1242 was about 1.5 times higher than total PCBs and the HQs for other COPCs ranged from 3.9 times lower for mercury to 189 times lower for arsenic.

14.4 p. 6-109, Section 6.5.2 and Table 6-64. The text indicates that coplanar congeners were not present in sufficient concentration to cause adverse effects to survival of pelagic fish fry, even though there was an HQ of 2 (Table 6-64) for the NOEL RME. Here and elsewhere in the document, the gray zone of "acceptable vs unacceptable" in the range of HQ=1 to HQ=10 is uncertain, and seemingly arbitrary.

14.5 p. 6-110, Section 6.5.2 and Table 6-64. The authors did not discuss the Total TEQ and the significance to mink, even though the NOEL RME for reproduction showed an HQ of 47 (Table 6-64). In the text on p. 6-111 where the impacts on receptors are summarized, no reference is made to the conclusion that impacts are predicted for fish. It should also be pointed out that there were no data on birds that could be used to estimate risks.

14.6 p. 6-111, Section 6.5.2, De Pere to Green Bay. The report indicates that "Sediment HQs for total PCBs were 10 to 100 times greater than any other COPC." This appears not to be an accurate statement in all cases. The Aroclor 1242 HQ was almost twice as high as the total PCB HQs and others ranged from 12 (mercury) to 157 times (DDE) less than the HQ for total PCBs.

14.7 p. 6-114, Section 6.5.2 and Table 6-66 and Table 6-67. The text indicates that the NOEL HQ for Aroclor 1242 in carp was 219. The value is shown as 218 both in Table 6-66 and Table 6-67. In the text where the impacts on receptors are summarized, it should be pointed out that there were no data on birds that could be used to estimate risks.

14.8 p. 6-115, Section 6.5.2 and Tables 6-68 through 6-72. This section is very confusing because the text does not agree with tables and the tables are incorrectly identified in several instances. The text indicates that Tables 6-67 through 6-70 provide summaries of RME HQs and that risks are presented for Zone 2 and combined for Zones 3A and 3B. However, the correct citation for the Tables should be Tables 6-68 through 6-70, and the risks do not appear to be combined. Table 6-68 is for Zone 2; Table 6-69 is for Zone 3A; and Table 6-70 is for Zone 3B. Table 6-71 lists the RME HQs for birds. The Table 6-72 title indicates that it is a summary of the results for Zones 3A and 3B, yet the data presented in Table 6-72 are for Zone 2 and the data for birds in Green Bay are listed in Table 6-71.

14.9 Table 6-72. There are several zero values presented for the HQs. It is not clear how that would be achieved.

14.10 Throughout Section 6.5.2, the term "water quality invertebrate communities" should be corrected to "water column invertebrate communities".

15.0 Uncertainties and Major Data Gaps

In general, the report demonstrates an appropriate understanding of the major uncertainties associated with this ERA. In terms of data gaps, the most important problem is the spotty availability of tissue residue data. This is particularly true for mammals (i.e., mink) and birds, but also is true for fish in many sub-regions. Even with apparent aggregation of different data sets, many sample sizes are very small (n<10) and provide a limited basis upon which to calculate RME's with high confidence. A temporal analysis of RME's based upon tissue residues appears impossible. The text on p. 6-121 (Section 6.6.3) indicates that there may have been a lack of adequate quality control of the data on PCBs in sediments and water in Green Bay. This fact is critical since many of the risks to receptors are attributed to exposure to either sediment and/or water. Thus, the exposure side of this risk assessment exhibits great uncertainties.

While the effects side of the risk assessment appears to have a more solid foundation, important gaps exist here as well. A significant data base exists upon which to make calculations for a variety of TRVs for PCBs in ecological receptors, and this study appears to have performed a good job of identifying them. As noted, most TRVs used in this assessment were developed from data for species other than those occurring in the lower Fox River/Green Bay region. However, given the vast array of potential receptors available for study, this situation is typical, and the use of carefully selected "surrogates" is a generally accepted and reasonable approach for deriving TRVs.

The discussion of the selection of TEFs suggests a generally thoughtful selection of these values. The TEFs for fish were based on salmonids that are known to be sensitive to AhR-mediated toxicity, which may not be appropriate for the fish receptors in this region. However, the availability of these values drives the selection of these more conservative TEFs. On the other hand, the selection of avian TEFs based on bioassay data using H4IIE rodent cells provides for less conservative estimates in comparison to TEFs derived from bird models. An additional problem related to the selection of TEFs for birds is the high value for coplanar congener 81 (i.e. TEF=0.1) recommended by WHO (1997). This compound was not included in the risk assessment, which may lead to underestimates of risk for bird receptors.

However, for mammals, the most conservative TEFs by Safe (1992) were selected of the three TEF data bases available (the others being Ahlborg et al., 1994 and WHO, 1997). The only basis for the selection of Safe (1992) appears to be that it is the most conservative (p. 6-44). This is an important consideration that merits more attention, particularly in light of the HQs ultimately derived, which indicate far greater risks for mink than for fish or birds. For example, TEQs for the 5 major coplanar PCBs considered by Safe (1992) and WHO (1997) varied in potencies by factors ranging from 20x to 1000x, with the Safe (1992) TEQ always higher (indicating greater potency). It may have been appropriate to also calculate risks to mink using TEQs based on values proposed by WHO (1997). This exercise might provide useful information concerning the range of risks associated with mink exposures to TEQs in this region.

16.0 Sediment Quality Thresholds (Chapter 7)

Since a critical outcome of the overall RI/FS is to determine potential corrective actions regarding contaminated sediments in the Lower Fox River region, the development of sediment quality thresholds appears to be perhaps the most important aspect of this process. And in contrast to tissue residues, the data base for PCB concentrations in sediments appears to be extensive. Thus, the development of models based upon sediment concentrations that can accurately predict risks to humans and ecological receptors is very appealing.

For this analysis, a model was developed that used the model of Gobas (1993) as a starting point. This model was modified as described in the report to allow, for example, for inputs of site-specific parameters and reversible probabilistic predictions. As described, it is difficult to ascertain how appropriate this model is for the purposes described. Several concerns exist concerning the development and application of this model, many of which are repeats of concerns for the ERA. These include:

- use of a ratio of PCB in sediment to PCB in water of 1×10^5, rather than the value published for the Great Lakes of 1×10^6 (Burkhard, 1998). This appears to be a critical parameter that will directly affect subsequent bioaccumulation factors by an order of magnitude. This adjustment is based upon data (see table 7.1) largely from 1989-1990, and the precise nature of the water concentrations are not clear (i.e., dissolved vs. suspended PCBs).

- it appears that in this model, fish are treated as static entities that do not grow, change with respect to diet, body composition, spatial distribution, etc.

- the model appears to assume that PCB accumulation is a function of lipid composition, which remains controversial.

- previously described limitations of tissue data that reduce confidence in model verification.

- previously-discussed concerns for TRVs and HQs.

- an analysis of how the thresholds derived here compare to thresholds from other areas where PCBs are of concern, i.e., the Hudson River, NY.

Despite these potential shortcomings, the development of a model to predict sediment thresholds is potentially very valuable. The model described herein may be fundamentally sound, but other approaches (e.g. bioenergetics models) should also be considered. In any event, great care must be paid to input variables.

16.1 Other Specific Comments:

16.1.1 p. 7-5, Section 7.1.1. Model Description. Equation 1, the term ffd is not defined. This may be a typographical error and perhaps should be fd, not ffd.

16.1.2 p. 7-5, Section 7.1.1. Equation 2, the units do not agree, since the text indicates that fd is dimensionless. The way the formula is written gives units of kg/L for fd.

16.1.3 p. 7-5, Section 7.1.1. In Equation 2, the value kow actually should be koc, with units of L/kg.

Section C

An Evaluation of Baseline
Human Risk Assessment Reports
Submitted by ThermoRetec and Exponent
for the Lower Fox River System

Prepared by

Halina Brown, Ph.D.
Clark University
Massachusetts

Raymond S.H. Yang, Ph.D.
Colorado State University
Colorado

Mohamed S. Abdel-Rahman, Ph.D.
New Jersey Medical School
New Jersey

1.0 Introduction

This report provides a critical analysis of the human health risk portion of two risk assessment reports evaluating chemical contaminant data of the Lower Fox River in Wisconsin. One risk assessment was prepared by ThermoRetec Consulting Corporation (ThermoRetec) on behalf of the Wisconsin Department of Natural Resources and dated February 24, 1999; the other risk assessment was prepared by Exponent on behalf of the Fox River Group and dated January, 2000. Each risk assessment is evaluated separately and then compared with each other. The comments provide a critical assessment of strengths and limitations, particularly in the areas requested in the scope of work.

The two risk assessments reviewed were conducted by very different methodologies. ThermoRetec provided a point estimate exposure calculation while Exponent utilized Monte Carlo probabilistic assessment yielding a range of exposure. While both these methods are acceptable to US EPA, it is interesting and disturbing to note that the ThermoRetec human health risk from ingestion of PCB contaminated fish is 10^{-3}; the Exponent risk from the same scenario is between 10^{-5} and 10^{-6}. Such a differential suggests that one of the methods is inappropriate or that inaccurate parameter values were utilized in exposure equations. For neither of the assessments was it obvious that such was the case.

Both risk assessments display scientific rigor but each could be improved. Exponent utilizes more site specific data, generally a demonstration of sophistication in the risk assessment. ThermoRetec used EPA suggested values for its exposure equations thus providing confidence in the health protective quality of the work.

The panel was impressed with the probabilistic risk assessment undertaken by Exponent but could not find adequate explanations of the method. Mention of the software used did not seem enough to explain or validate use of such a model. No equations were provided by the risk assessors to describe the method, and input was also lacking. Therefore, review was hampered.

Before the discussion of the two reports, it is worth noting the structure of polychlorinated biphenyls (PCB_s) and their fate in the environment as well as the concentration of PCB_s in fish and their fate in the human body.

2.0 Polychlorinated Biphenyls

Polychlorinated biphenyls (PCB_s) are a class of chemical compounds in which 1-10 chlorine atoms are attached to the biphenyl molecule. This group of synthetic organic chemicals include the possibility of 209 chlorinated biphenyl compounds known as congeners. In addition, various configurations are possible because there can be free rotation between the benzene rings. PCB_s can also be categorized by degree of chlorination. The two extreme configurations are planar (the two benzene rings in the same plane) and nonplanar (the benzene rings are at a 90^o angle to each other). The number of substitutions in the ortho positions determined the degree of planarity, resulting in steric hindrance to rotation. Thus, non-ortho substituted PCB_s are considered to be planar or coplanar. The most toxic congeners are coplanar.

PCB_s are persistent in the environment. The production of PCB_s stopped in 1977 because of their build up in the environment that increased harmful health effects. In water, photolysis appears to be the only viable chemical degradation process and the estimated photolysis half-lives ranged from 17 to 210 days. Highly chlorinated PCB_s bind strongly to soil and sediment. The half-lives of the various PCB congeners in soil and sediment are on the order of months to years (Gan and Berthouex, 1994). In water, PCB_s build up in fish and marine mammals and the concentrations of PCB_s are hundreds of thousand times higher than the levels in water. In a 1980-1981 survey conducted by the U.S. Fish and Wildlife Service, PCB_s were detected at a geometric mean concentration of 0.5 μg/g (ppm) in whole freshwater fish (Schmitt *et al.,* 1985). In the 1986-1989 National Study of Chemical Residues in Fish by the EPA, the mean concentration of PCB_s was found to be 1.9 μg/g in bottom-feeding fish and game fish collected from 91% of 362 sites surveyed (EPA, 1992; Kuehl *et al.,* 1994). Total PCB concentrations were 2.4, 4.3 and 5.0 μg/g wet weight in muscle of young, middle-aged, and old carp, respectively, from the Buffalo River in New York (Loganathan *et al.,* 1995). PCB contamination in sediment of the lower Passaic River is biomagnified in the food chain through fish and shellfish, which presents a total risk to humans of up to 6.6×10^{-4} (i.e., 6.6 cases in 10,000 people) (Finley *et al.,* 1997).

2.1 Health Effects

Oral exposure

Serum PCB levels were significantly associated with increased systolic and diastolic blood pressure and serum levels of both alanine aminotransferase (ALT) and cholesterol in the residents of Triana, Alabama (Kreiss *et al.,* 1981). The residents were exposed to PCB_s via consumption of contaminated fish. Loss of appetite and gastrointestinal symptoms such as anorexia, weight loss, nausea, vomiting and abdominal pain were reported in capacitor workers exposed to Aroclors (Fischbein *et al.,* 1979). In a study of 89 women with repeated miscarriages, Gerhard *et al.* (1998) found that blood concentrations of PCB congeners 101-180 were significantly increased when compared to the general population. The decreased blood level of β_2-microglobulin in workers at a PCB_s-producing plant may be related to immunotoxic effects (Langer *et al.,* 1997). Neurotoxic effects have been shown in Native Americans and Eskimos who eat fish from waters contaminated with PCB_s (Schantz *et al.,* 1996).

2.2 Toxicokinetics

PCB_s are absorbed by the inhalation, oral and dermal routes. PCB_s are well absorbed when administered orally, but they are absorbed less efficiently following dermal exposure. In humans, PCB_s are found in highest concentration in adipose tissue due to their lipophilic nature. Because of its high fat content, human milk has a high concentration of PCB_s which is then transferred to children through breast-feeding (Jacobson *et al.,* 1984; McLachlan, 1993). Offspring can also be exposed to PCB_s through transplacental transfer (Jacobson *et al.,* 1984).

2.3 Prenatal Effects

Initial evidence of PCB teratogenicity came from studies of pregnant women in Japan and Taiwan who consumed cooking oil accidentally contaminated with PCBs. These effects, however, may have been due to a mixture containing dibenzofurans. In addition to having reduced birth size and dermatologic anomalies (Higuchi, 1976; Wong and Hwang, 1981), children born to these women have shown poorer performance on standardized intelligence tests in follow-up studies (Harada, 1976; Rogan *et al.,* 1988). Neurodevelopmental deficits have also been found in infants born to women who consumed relatively large quantities of Lake Michigan fish (Fein *et al.,* 1984). Prenatal PCB exposure was associated with poorer performance on the Brazelton Neonatal Behavioral Assessment Scale (Jacobson *et al.,* 1984b) and on the psychomotor index of the Bayley Scales of Infant Development (Gladen *et al.,* 1988). Higher cord serum PCB and maternal fish consumption levels were associated with poorer performance in the Fagan Visual Recognition Memory Test (Jacobson *et al.,* 1985), one of the best-validated assessments of infant cognitive function (Bornstein and Sigman, 1986). The children who were previously evaluated for PCB-related deficits in infancy were assessed again at 4 years of age. Prenatal exposure predicted poorer short-term memory function on both verbal and quantitative tests in a dose-dependent manner (Jacobson *et al.,* 1990a). Another study showed that prenatal exposure was also associated with lower weight, (Jacobson *et al.,* 1990b), an effect consistent with reports of growth retardation in children exposed at high levels in Taiwan and at general population levels in Japan. Contemporary body burden (assessed by 4-year serum PCB level) was associated with reduced activity. This effect, attributable to lactation exposure, was strongest among the offspring of women with above average milk PCB levels who breastfed for at least 1 year. Cognitive development was tested in 118 Taiwanese children born to mothers who consumed contaminated rice oil (Chen *et al.,* 1992). Children prenatally exposed to high levels of heat-degraded PCBs had poorer cognitive development than their matched controls. The effect persisted in the children up to the age of 7 years, and children born long after the exposure were still affected. Since *in utero* exposure to PCBs has been linked to adverse effects on neurologic and intellectual function in infants and young children, Jacobson and Jacobson (1996) conducted the study to determine whether these effects persist through school age and examine the importance in the acquisition of reading and arithmetic skills. The study showed that prenatal exposure to PCBs was associated with lower full-scale and verbal IQ scores after controlling for potential confounding variables such as socioeconomic status.

2.4 Susceptible Populations

Populations who are at greater risk due to their unusually high exposure to PCB_s are recreational and subsistence fishermen who typically consume larger amounts of locally caught fish; native American populations such as the Inuit of Alaska or other subsistence hunters/fishers; breast-fed infants of mothers who consume large amounts of contaminated fish or wild game (ATSDR, 1999).

Breast fed infants could be exposed to higher PCB levels than formula fed infants in the general population. Infants and young children may be more susceptible than adults to PCB_s since they consume a greater amount of food per kilogram of body weight and, therefore, have a proportionately greater exposure to PCB_s than adults (Cordle *et al.,* 1982). The studies conducted by Jacobson and Jacobson (1996) suggest that PCB_s are several-fold more harmful when the fetus is exposed *in utero* than when an infant is exposed through breast milk.

3.0 General Comments on the Two Reports

a. It is disturbing that two Baseline Human Health Risk Assessments focusing on the same scenario of fish ingestion in the same problem area (i.e., Lower Fox River, Wisconsin), presumably using most of the same data, came to completely different conclusions. The perpetuation and propagation of this kind of “conflict” would denigrate the science-base of risk assessment.

b. The ThermoRetec Report was issued first (February 1999) and it was sponsored by the Wisconsin Department of Natural Resources. The Exponent Report, issued in January, 2000, was apparently the result of a study commissioned by the Fox River Group, an industry consortium, following the release of the ThermoRetec Report. While the ThermoRetec Report concluded that there is substantial risk of cancer and other noncancer health concerns for the Recreational and Subsistence Anglers, the Exponent Report concluded that there are no bases for such risks.

c. Both reports have strengths and weaknesses. The specifics may be found in the individual sections that follow:

3.1 Exponent

Exponent conducted a probabilistic human health risk assessment using Monte Carlo methodology. The assessment relied on the recently analyzed fish tissue data for PCB_s. It incorporated site-specific information regarding fish consumption and preparation from angler's surveys that included the assessment area. The Lower Fox River and areas of Green Bay were all included together as the assessment area.

The risk analysis was limited to the risk of ingesting fish contaminated with PCB_s. Other exposure pathways and chemical contaminants were considered negligible compared to this contaminant/pathway pair and not evaluated. Recreational anglers and their friends and families who consumed certain fish from the assessment area were the only receptor population evaluated. Cancer and non-cancer effects from chronic (long term) exposure were considered. Short term effects were not considered. EPA dose-response standard risk factors for both cancer and non-cancer effects were incorporated into the risk characterization.

Exponent did not conduct a point estimate risk assessment to compare with the probabilistic range and to see where the point estimates fall on the probabilistic scale. The strength of a probabilistic assessment is that it gives a wider range of risk values and assigns a likelihood to those values. While still somewhat controversial, probabilistic risk assessments are often considered more state-of-the-art than point estimate risk assessment.

Risk assessments that incorporate site specific data are also generally considered more scientifically vigorous. Unfortunately, while Exponent incorporated these state of the art techniques into its analysis, it did not do so successfully. As discussed in detail in subsequent sections, the scientific rigor of the risk assessment is compromised by its over-interpretation of site specific data and other inappropriate assumptions, all of which collectively serve to underestimate the predicated health risks associated with the assessment area.

The Exponent Report provides very little explanation of the methodologies used in their risk assessment. For instance, Probabilistic Risk Assessment is the central theme and yet there were only four lines of explanation of Probabilistic Calculations (Section 2.3.4 on Page 2-11) and no explanation was given on Monte Carlo simulation. A sentence such as “The probabilistic calculations were completed using Crystal Ball (v.4) (Desioneering, Inc.) and Microsoft® Excel (Microsoft 1997).” doesn’t explain properly to the risk assessor. In a December 1989 publication on Probabilistic Risk Assessment (PRA), (www.epa.gov/superfund/programs-/risk/rags3adt/index.htm), EPA stated "If a PRA is conducted, the assumptions and inputs of the probablistic model should be sufficiently documented so that the results can be independently reproduced...”. Exponent failed to provide the PRA model, assumptions, and inputs.

3.2 ThermoRetec

ThermoRetec conducted a point estimate risk assessment that closely adheres to the guidelines for conducting risk assessment under the Comprehensive Environmental Response, Compensation and Liability Act of 1980 (CERCLA). The ThermoRetec Report has detailed explanation on the methodologies and calculations in their risk assessment; thus, it is much easier for peer-reviewers to evaluate what has been done. ThermoRetec conducted separate risk calculations for different reaches of the Lower Fox River and several sections of Green Bay. The calculations were based on fish tissue and other environmental samples from the identified sub-regions.

ThermoRetec included multiple exposure scenarios and all identified chemical contaminants in all media tested, but focused most of their attention on ingestion of fish from various reaches of the Lower Fox River and Green Bay. PCB exposure received the most attention, as ingestion of PCB_s via contaminated fish is <u>clearly the risk driver</u>. Cancer and non-cancer effects from chronic (long term) exposure were considered. Short term exposure effects were not considered. EPA standard dose-response risk factors for both cancer and non-cancer effects were incorporated into the risk characterization.

ThermoRetec included point estimates for receptors under reasonable maximum exposure (RME) and central tendency exposure (CTE) conditions. They further evaluated the RME exposure using two different exposure point concentrations in the fish: upper bound and mean concentrations. They evaluated the toxicity of PCB_s using three different methods (total PCB_s, Aroclors, and congener specific) in order to get a range of estimates. RME and CTE calculations were conducted for both recreational anglers and a subpopulation evaluated as subsistence anglers.

The problem with the ThermoRetec Report is that it lacks proper style and format. The authors used abbreviations/acronyms to such a point that readers from the general public (and even scientists not closely associated with risk assessment) would find this difficult to read. A statement in the ThermoRetec Report that polycyclic hydrocarbons (PAHs) detected in sediments were not expected to bioaccumulate in food chains is questioned by the reviewers. There is no need for PAH analysis data in fish to determine that an accumulation of such lipid soluble chemicals would occur (but will not drive the risk when PCBs are present in the concentrations defined at this site).

4.0 Key Factors Contributing to the Different Risk Estimates in the Two Reports

Many of the major assumptions that contribute to the risk estimates provided in Exponent and ThermoRetec reports are provided in Table 1.

There are large differences in several of the basic assumptions used in the exposure assessment of the two risk assessments. These differences in assumptions are unrelated to the differences in risk assessment approaches, namely point estimate versus probabilistic risk assessment.

Briefly, the Exponent risk assessment assumed much lower exposure to PCB_s because of its lower, site-specific fish ingestion rates, and more importantly, lower concentrations of PCB_s in fish. These lower concentrations of PCB_s in fish arise from: (1) the use of fillet only data (compared to skin fillets); (2) omission of carp and other bottom feeders from the anglers diet. (Carp consistently had the highest concentration of PCB_s compared to perch, walleye and white bass in each reach where data were available as described in the ThermoRetec Report); and (3) erroneous assumptions in truncations and sample distributions in Monte Carlo methodology. Also, incorporation of degradation rates of PCB_s from fish was lacking.

The ThermoRetec Report follows Superfund Risk Assessment Guidelines using the point estimate approach. The Report provided detailed stepwise procedures and explanations and it appeared to be of high scientific rigor for the approach taken. The Exponent Report, on the other hand, provided little explanation of the procedures used nor evidence for the verification of the assumptions employed in the Monte Carlo simulations of exposure levels. Thus, it is of questionable scientific rigor.

5.0 Consistency with CERCLA, NCP, USEPA Guidance

5.1 Exponent

The Exponent report is well written and describes the basis for many of its available assumptions. Presumably, it utilized Monte Carlo methodology to incorporate variability and uncertainty directly into the risk assessment, as permitted under recent EPA guidance. Also as permitted under Superfund guidance, the assessment departs from the standardized exposed population (RME) (recreational anglers) and average population (CTE). It attempts to use site-specific recent data on fish contamination, an appropriate departure from default values. On the other hand, the report's compliance with the regulatory requirements falls short on several other counts. These include:

- Consideration of sensitive subpopulations

- Adequate justification for departures from standardized assumptions
- The definition of RME and assumptions used to evaluate risks to RME
- Model, assumptions and inputs for Monte Carlo methodology

CERCLA requires that sensitive subpopulations be considered in the risk assessment. This includes groups who are particularly sensitive to the effects of the contamination and groups who are more highly exposed to the contaminants. Three potential sensitive subpopulations at this Site are: pregnant women and nursing infants, possibly subsistence anglers, and fish consumers with particularly risky behavior (those who eat bottom feeders and/or whole fish).

Exponent did not separately consider pregnant women and nursing infants as susceptible populations. These populations are particularly sensitive to the adverse effects of PCB_s in terms of neurodevelopment and behavioral changes. Transplacental exposure (i.e., exposure of the fetus via the pregnant mother) and ingestion of mother's milk through nursing are known to be key exposure pathways for developing humans as described above under prenatal effects. Tilden *et al.* (1997) reported that 60% of women and 80% of ethnic minorities who had eaten sport fish were unaware of fish consumption advisories. With respect to a subsistence fishing population, Exponent examined data from multiple surveys of anglers in Wisconsin, some of which included the assessment area. Exponent concluded there was no evidence of a subsistence fishing population, and thus such a population did not need to be explicitly included in the risk assessment. This is a reasonable assumption.

The risk assessment for the high end exposure population (RME) is not adequate because of the assumptions about the way the exposed populations prepare and consume the contaminated fish. The same angler surveys used to assess subsistence fishing demonstrated that anglers used a range of food preparation methods, some (notably the Hmong, a Southeast Asian population who have immigrated to this area) ingested parts of fish other than fillets. Others (including the Hmong) targeted bottom feeding fish when angling. These behaviors lead to a more highly exposed population than was considered even for the most highly exposed angler in the recreational angler exposure assessment (see exposure assumptions below). For example, the population that consumes bottom fish was neglected when the carp data were dropped out of the dataset used to calculate exposures.

The issue of assumptions regarding the culinary habits of high risk populations for the species of fish consumed is discussed at greater length further in this document.

5.2 ThermoRetec

ThermoRetec conducted a standard Superfund risk assessment based on the 1989 Risk Assessment Guidance for Superfund (RAGS) Manual published by US EPA and subsequent guidance on exposure and risk characterization. ThermoRetec did not incorporate any new methodology and primarily relied on EPA standard assumptions.

ThermoRetec evaluated all likely chronic exposure scenarios and exposure pathways, used RME and CTE exposure scenarios, included data on all contaminants and calculated cumulative risk estimates (both cancer and non-cancer) based on all chemicals and all exposure pathways. ThermoRetec evaluated uncertainty qualitatively by discussing various assumptions and selecting those that tend to overestimate risk. ThermoRetec also evaluated uncertainty in a partially quantitative way by conducting a sensitivity analysis of fish ingestion rates and several methods of expressing PCB concentrations. The risk assessment considered subsistence anglers as a sensitive subpopulation. These are all the report's strengths. Unfortunately, like Exponent, ThermoRetec did not consider pregnant women and nursing infants as sensitive populations. Similarly, ThermoRetec did not separate out anglers who consume fish using different preparation methods or whole fish as a more highly exposed population. On the other hand, the ThermoRetec exposure assessment included consideration of more fish species and fattier parts of fish than the Exponent assessment.

6.0 Support of the Findings by Technical Analysis and State of the Art Scientific Methods

This section provides details regarding the assumptions of the two risk assessments and a critique of those assumptions. The assumptions are primarily included in the exposure assessment section, but also pertain to hazard identification and dose-response assessment.

6.1 Exponent Risk Assessment

The Exponent exposure assessment contains a variety of assumptions regarding fish contamination concentrations, degradation rates of PCB_s in fish over time, fish preparation methods, and fish consumption. In general, Exponent attempts to use site specific information rather than more commonly used EPA default methods and values. The adequacy of these site specific assumptions are examined below. Most are inadequately justified. They also all tend to reduce the calculated exposures, primarily by excluding the higher exposure end of the distribution. The influence of fish advisories on fishing habits and consumption patterns is not considered. Therefore, the review panel could not determine if more fishing would occur if advisories were not in place. People were observed fishing from banks of the river during a site visit by the panel.

Exponent used Monte Carlo simulation for PCB concentration in edible fish. However, they did not present the equations for Monte Carlo simulations so the readers may know exactly where the variabilities are incorporated, given an assumed distribution. Since PCB concentration in fish is pivotal to the outcome of the risk assessment, it is important to look into the calculations and their related assumptions critically. Concentration in fish which was calculated with the assumptions of "Truncated Normal" with "Min. = 0 ng/kg" and "Max. = mean + 3 (Standard Error) ng/kg" may be incorrect. The reasons are as follows:

- In Appendix A, data on total PCB_s in fish fillet samples from the Lower Fox River System (pages A-1 to A-4) were presented. According to our summary of these data, there are 202 samples in total. None was zero µg/kg (this was the unit used in Appendix A which is 1000-fold higher than ng/kg, the unit used in Exponent Min. and Max.). The number of samples with concentrations greater than 1,000 µg/kg was 112. The PCB concentrations range from 34 to 7,500 µg/kg. Thus, it is clearly a log normal distribution skewed toward higher concentrations. This point is particularly prominent in examining the data on page A-4 where 36 out of 38 samples are over 1,000 µg/kg with a high of 7,500µg/kg.

- Since there was no zero value in any of the samples analyzed, the setting of "Min. = 0 ng/kg" artificially lowered the values of "Concentration in fish (C_{fish})" in the Monte Carlo simulations.

- In Table 2-4, the arithmetic means and standard errors for walleye and brown trout are, respectively 975 $\pm$ 89.5 and 2,633 $\pm$ 146.3 ng/g (or µg/kg). Thus, the setting of "Max. = mean + 3 (Standard Error) ng/kg" would be at artificially low levels of 1,243.5 µg/kg for walleye and 3,071.9 µg/kg for brown trout. If one surveys the analytical results in Appendix A, one would find that the true Max. is 4,000 µg/kg for walleye and 7,500 µg/kg for brown trout with many values over the artificially low Max. values Exponent used in their calculations. An inconsistency exists when Exponent uses ng/kg in their assumptions in Table 2-1 whereas they used ng/g (equivalent to µg/kg) in their summary in Table 2-4 and µg/kg in Appendix A. If the calculated values from Table 2-4 for Min. and Max. were used directly in Table 2-1 for Monte Carlo simulations, there could have been a 1,000-fold error in values of fish concentration of PCB_s.

- If these potential problems were taken cumulatively, it would mean that Exponent derived very low values for the PCB concentrations in fish in their Monte Carlo simulations. As these values were used further in cancer and non-cancer risk assessment, the risk concluded could be artificially low. For any sort of modeling such as Monte Carlo methodology to be credible, the model simulation results should be compared with the observed data as a form of verification of the adequacy of the modeling methodology. The review panel would have liked to examine Exponent's Monte Carlo simulation results of PCB concentrations in fish as compared to the actual analytical data presented in Appendix A, to be sure that the Monte Carlo simulations were in agreement with the values and distributions of the analytical data presented in Appendix A for various species of fish.

One of the Exponent's three main arguments for the superiority of their report is their use of site-specific data (page 5-6). Exponent stated "...Specifically, a site-specific angler survey was used to derive highly accurate and site-specific fish consumption rates for the assessment area. Previous assessments, however, derived fish consumption rates from the published literature, which may or not be relevant to the assessment..". However, if one examines the data in Tables C-3, C-6, and C-8, one finds that the data base for "site-specific data" is small. For example, in Table C-6, the "Number of Successful Trips to the Assessment Area" is 61 which is 0.87% of the 7,026 total trips. In Table C-8, the Hmong Anglers with Successful Trips to the Assessment Area is 0%; The reviewers question as to how "highly accurate" information could be derived from such a seemingly small dataset?

Even if the use of such a small database of site-specific data is considered adequate, the inputs into the risk assessment assumed that the fishermen consume only fish fillets, and not other parts of the fish. (Data are available on the concentration of PCB_s in other parts of the fish.) The use of fillet only data prevents the representation of the full range (specifically the higher end) of the exposure point concentrations to recreational anglers. Exposure to fillet only is not fully justified in the risk assessment.

Exponent included the following assumptions in its determination of PCB concentrations in fish consumed by anglers at the current time:

- Anglers ingest fish fillets only
- Anglers ingest primarily yellow perch and walleye (93% of fish consumed)
- Anglers do not consume any bottom feeders (carp, catfish) in the assessment area

These assumptions are only partly supported by the results of a survey of Wisconsin anglers (TER, 1999) and described in Appendix C of the Exponent report. This survey was mailed to Wisconsin anglers who had agreed to participate; after a telephone interview. This limited the survey to those who had a telephone, could read, write and speak in English, and would fill out monthly surveys. Surveys were conducted over a four month period (June through September) in 1998. Surveys were mailed to 1275 anglers who had agreed to participate, fishing summary data were obtained from 841. Three of these anglers identified themselves as Hmong, the subpopulation that had been, at the outset of site assessment, identified as a group of potential concern. Data from additional surveys (Hutchinson and Kraft, 1994) that included Hmong anglers (that were conducted by Native Hmong speakers) were also cited and discussed below.

Exponent cites the TER (1999) angler survey as the basis for using fillet only data. However, this survey actually showed that while 57% of anglers only eat the fillet, the remainder of the population also eat other parts of fish, usually by frying skin-on fillets (p. C-10).

Exponent also assumed that of the fish actually consumed from the assessment area, 67% were yellow perch, 26% walleye, 3% smallmouth bass and the remainder were brown trout, white perch and other panfish. They used these data in the calculation of the exposure point concentrations by including them as weighting factors on the PCB contamination levels of these fish species. The weights of all bottom feeding fish (carp, catfish) were set to zero. This distribution of consumption was justified on the basis of the TER (1999). However, as discussed on page C-2, bottom fish (carp, catfish, and white sucker) were not included in the TER survey because they are "not a popular species," although one question in the survey found that catfish were targeted by 4% of the anglers. Moreover, according to Exponent, only 30 anglers (of the 841 survey respondents) successfully fished in the assessment area, 29 of whom were Caucasian and one was Native American. However, all the fish consumption and preparation data are based on this small subsample.

Exponent reported data on one Hmong angler who fished the assessment area, albeit unsuccessfully, for catfish. This was not included in the assessment because this person was not successful in catching catfish during the reporting period. Exponent also reported that other Hmong participants in the survey utilized the internal organs of the fish. Thus, while the cited Hmong anglers may have been unsuccessful at fishing during the four month survey period, it is clear that other Hmong fish in the area, fish for bottom feeders, and consume the entire fish, not just the fillets. The importance of Hmong fishing activity is reinforced by the Hutchinson and Kraft (1994) survey and 1997 Hutchinson survey of Hmong that were conducted by researchers at UW-Green Bay and discussed on page C-15 of the Exponent report. More than half the households reported fishing at least once per month, and approximately 10 households (of 118 included in the survey) stated they consume fish from local waters 2-3 times/week. Two Hmong households reported targeting carp and catfish, although the frequency is not clear.

The use of data on fillets-only likely represents a substantial underestimate of the PCB exposure to populations that consume other parts of the fish, either as fried skin-on fillets, whole fish, or fish boiled in soup. According to Exponent (p. C-10), the TER (1999) angler survey indicated that 57% of the survey respondents ate only fillets or steaks, 39% ate skin-on fillets and 4% (1 person) ate only skin. Thus, the use of fillet only fish data as the basis for the risk assessment will underestimate the intake of PCB_s <u>for nearly half</u> the consuming population, based on this limited set of data.

The data used by Exponent did not include the fish species with the highest PCB concentrations, namely the bottom feeders, by setting bottom fish consumption weight to zero. This is an incorrect assumption that is contradicted by the data in the TER (1999) survey. Again, use of data in this way serves to underestimate exposure to an identified, fish consuming population.

As discussed previously, PCB concentrations in yellow perch were given the largest weight in determining the fish contaminant concentration. However, a review of of the data summary in Table 2-4 shows that there were only nine samples of yellow perch, too few samples on which to base a major premise (exposure point concentration) of this risk assessment. However a wealth of fish concentration data are available. For example, even in the Exponent recent, fillet-only data, there were 73 samples of walleye, 63 samples of carp and 26 samples of white suckers.

In summary, Exponent makes inappropriate assumptions about the parts of fish ingested and the species of fish ingested. These assumptions are, in the opinion of the review board, based on the overinterpretation of limited data, and may lead to substantial underestimates of PCB exposure to portions of the likely exposed population. This problem of underestimating exposure is exacerbated by the use of inappropriate cooking retention factors and PCB degradation rates that are discussed in the next two subsections. Moreover, the risk assessment is ultimately based largely (67% of the weighted average of the exposure point concentration) on nine samples of yellow perch fillets, and inappropriate winnowing down of a very large set of data on PCB concentrations in fish.

6.1.1 Assumptions Regarding PCB Degradation Rate

Exponent assumed that PCB_s in fish populations decrease over time, and assigned degradation rates for each fish species considered. The loss rate from perch, the fish species assumed to be consumed with the highest frequency, was fixed at 0.116 yr^{-1}. This translates into a half-life of 5 years, assuming first order kinetics. However, the data provided in the ThermoRetec report, which spans a longer period of time, do not support this assumption. From the more complete data, it appears that the loss rate from fish may be biphasic, and the current loss rate is quite slow if not negligible (see below). Thus the Exponent assumption of degradation may incorrectly reduce the estimate of PCB exposure over time and hence may underestimate potential risk.

A number of studies have measured the loss of PCB_s due to cooking of fish. These factors are expressed in numerical form as either cooking loss factors or fractional retention after cooking. Exponent used a summary of studies published by Wilson *et al.* (1998) to select a retention value after cooking. Based on the Wilson *et al.* summary, Exponent assumed a range of values with a 50th percentile fractional retention rate of 0.68. However, the study on perch, the fish assumed by Exponent to be most frequently consumed from the Fox River, showed no loss of PCB_s upon cooking, based on the discussion in Wilson *et al.* Thus, for the major fish species considered in this study, the data suggest that 100% retention should be assumed. Therefore, Exponent's assumption of cooking loss rate will reduce the estimate of PCB exposure and hence further underestimate potential risk.

6.1.2 Data for Ingestion Rates/Fish Preparation Methods (Surveys)

Exponent developed its distribution for site specific fish ingestion rates (7 g/day to 26 g/day) based on the TER (1999) survey described in Subsection a. above. Thus, the fish ingestion rates suffer limitations from the small and possible skewed sample distribution. It is also noted that Exponent used a fish meal size based on the national rate for freshwater sportsfish consumption recommended by USEPA in the 1997 Exposure Factors Handbook, rather than the higher rate utilized by ThermoRetec based on MI and WI data only.

6.1.3 Endpoints Considered/Averaging Times

As is common in many hazardous waste site risk assessments, Exponent only considered chronic exposure scenarios in the risk assessment. This is appropriate for assessing cancer risk and non-cancer risks due to long term exposures. However, for PCB_s, the exclusion of short term effects may be a serious weakness, since PCB_s have adverse effects during prenatal and perinatal development, particularly on the nervous system. Immunological impairment is also a concern in regard to PCB_s. Both of these effects require evaluation of short term exposures. In other words, peak exposure during the height of the fishing season, not averaged out over a year or a lifetime, is necessary. This is particularly important for pregnant women and nursing infants, populations of particular concern for the developmental and neurotoxicity of PCB_s. These sensitive populations should have been evaluated, and short term averaging times should have been used to calculate dose. (See also discussion under Issues Related to Uncertainty in Item No. 7).

6.1.4 Dose-Response Assessment

The Exponent cancer risk assessment incorporates the most recent cancer slope factors and methodology recommended by EPA for total PCB_s. In addition, Exponent calculated a PCB cancer potency factor using epidemiologic data. For the non-cancer risk, Exponent used the EPA published reference dose for Aroclor 1254, which is based on exposures to adult rhesus monkeys. It was stated that this reference dose is also protective of *in utero* exposures and exposures of nursing infants. The use of EPA default values for the dose-response assessment is appropriate in this regulatory context.

6.1.5 Risk Characterization

Exponent used EPA published standard methods for risk characterization of cancer and non-cancer effects. The main deficiency here is the absence of an evaluation using an appropriate averaging time for *in utero* and nursing infant exposures, i.e., a short-term average based on upper end exposure point concentrations and appropriate weights.

6.2 ThermoRetec Risk Assessment

6.2.1 Exposure Assessment

ThermoRetec used a different dataset for fish contamination. .It assembled fish contamination data from multiple studies which had been conducted over the course of approximately 20 years. While there is some value in using historical trends (for example, environmental degradation rates can be estimated), for the purpose of assessing the risks from consumption of contaminated fish, a problem may exist with the data consistency and quality, especially since the quantification of PCB_s is technically a difficult task (hence, old analytical results may be subject to considerable error). In addition to performing a multi-pathway, multi-contaminant risk assessment, ThermoRetec conducted a focused risk assessment for PCB_s through fish ingestion. The fish contamination data for the focused risk assessment were based on the fish sampling data from the 1990's. This more recent focus may have circumvented some of the consistency problems associated with the up-to-20 year old analytical data used for the more general risk assessment.

ThermoRetec based its exposure point concentrations on fish samples comprised of skin-on fillets, meaning that both the fillet and the fattier skin were tested. Based on the results from the TER (1999) survey discussed above, this is a reasonable approach. However, even this approach may not be sufficient. Using this assumption for all population receptors will still lead to exposure underestimates for individuals who eat whole fish, including the entrails.

ThermoRetec included multiple fish species, including bottom feeders, in its exposure point concentration calculation. According to ThermoRetec (p.5-50) "the species selected include those fish species that a person would reasonable eat, regardless of restrictions proposed in consumption advisories." Apparently, all the available data on edible species were evaluated by sample type (e.g., skin-on fillet or whole body), and statistics such as the mean and 95% upper confidence limit of the arithmetic mean were generated. These statistics were generated for each of the Fox River species evaluated in the report. This is a reasonable approach and the appropriate statistics used *if* the data are normally distributed.

Thus, unlike the Exponent risk assessment, there was no weighting of the data according to species of fish apparently preferred by anglers. One benefit of the use of this extensive set of data is that the risk assessment can be subdivided into different reaches of the River in order to determine if potential risk areas were localized.

6.2.2 Assumptions about PCB Environmental Degradation Rates

ThermoRetec assumed that the PCB concentrations observed in the 1990's would remain steady for the foreseeable future. This assumption was based on an examination of PCB concentrations in various fish species over time and the observation that the curve was biphasic. There was a substantial decrease in PCB_s in the 1980's, but the concentrations appeared to have reached an asymptotic value in the late 1990's. The graphs in the report somewhat support this interpretation, although the differences in the quality of the fit of the one and two exponential loss curves (Section 5.9.1) is not very different, especially considering the extra parameter in the two exponential models. The history of the area does support the notion of a decrease in the rate of loss of PCB_s in fish tissues. In the early years of measurement, PCB_s were still entering the River at various points, but controls were put in place to decrease the influx. In recent years, the influx of PCB_s into the Fox River has decreased to negligible amounts (according to ThermoRetec), but the loss of PCBs is primarily due to the redistribution of PCB contaminated sediments downstream. PCB concentrations in fish tissues would also decrease from the covering of contaminated sediments with newly deposited sediments that are not contaminated with PCB_s. This is a reasonable approach. Also, the rate of PCB desorption from the sediment which will be available to the fish will be decreased.

6.2.3 Data for Ingestion Rates/Fish Preparation and Effect of Cooking Methods (Surveys)

ThermoRetec assumed mean and high end fish ingestion rates of 15 and 59 g/day respectively for recreational anglers In part, these rates were based on meal sizes of 227 g (0.5 lb of fish). It is noted that these values are higher than EPA recommendations (EPA Exposure Factors Handbook, 1997) based on data from throughout the U.S. However, the data used by ThermoRetec to calculate ingestion rates were from the Wisconsin and Michigan angler surveys that were included in the EPA review. The final, lower EPA recommendations were derived by including data from other areas of the country. Based on the somewhat site specific nature of the angler studies utilized (i.e., Midwest), the higher consumption rates may be justified. This is a reasonable approach.

ThermoRetec used fish data in which samples were skin-on fillets of various species in the different reaches of the Lower Fox River and Green Bay. They accounted for the anglers who eat only the fillet (without the skin) by using a reduction factor of 50%. This included a 20% loss from trimming and a 30%

reduction from cooking. However, ThermoRetec used this reduction value universally, even though they cited survey data by West *et al.* (1993) that reported 44% of anglers did not trim fat and 36% of the anglers didn't remove the skin. The cooking reduction factor appears to be too high.

ThermoRetec also applied the 50% loss factor to the Hmong anglers considered in the subsistence population. However, the survey data from Hutchinson and Kraft (1994), which is represented in ThermoRetec Table 5-14, show that the largest number of people answered "other" regarding the size of fillets used. Based on Asian cooking, this could mean that the entire fish (not fillets) was used in cooking, as soup, fish paste, or cooking the whole fish. This interpretation is further supported by other information in the Hutchinson and Kraft (1994) report and subsequent Hutchinson surveys of Hmong in Wisconsin, as discussed in both the ThermoRetec and Exponent reports. These fish preparation methods would make the 50% cooking reduction value inappropriate to use. The use of the 50% reduction factor would lead to an underestimate of PCB intake for certain fish preparation methods.

In short, a more conservative approach would be to assume that 100% of PCB_s found in fish during chemical analysis are consumed, both because of negligible loss during food preparation, and because some populations are likely to consume all parts of the fish body.

6.2.4 Endpoints Considered/Averaging Times

As discussed previously, the risk assessment considered only endpoints from long-term (chronic) exposures. This is a critical defect as fetuses are exposed *in utero* when PCB_s cross the placenta, and nursing infants are exposed via breast milk. As discussed in the toxicity section of the ThermoRetec report, a significant fraction of lifetime exposure occurs during this period. Thus, explicit consideration of this population, along with a short term averaging time (blood PCB_s are elevated after eating PCB containing fish, and this is the basis of the maternal/placental diffussion coefficient) should be included in the risk assessment.

6.2.5 Dose-Response Assessment

The ThermoRetec cancer risk assessment incorporates the most recent cancer slope factors and methodology recommended by the EPA for total PCB_s. In addition, ThermoRetec calculated PCB related risk using Aroclor specific exposures and dose response and congener specific TEFs. However, the fish contaminant database is inadequate to support the congener specific analysis because of too few datapoints. The use of PCB data tabulated as Aroclor is questionable as the environmental distribution of individual PCB_s may substantially differ from the original Aroclors (although the Exponent analysis indicates that the environmental PCB_s are similar to Aroclor 1242 and 1254).

For non-cancer risk, ThermoRetec used the EPA published reference dose for Aroclor 1254, which is based on exposures to adult rhesus monkeys. No attempt was made to assess the appropriate reference dose for acute, *in utero* exposures and exposures to nursing infants. However, the approach to dose response assessment is appropriate.

6.2.6 Risk Characterization

ThermoRetec used EPA published standard methods for risk characterization. The inadequacy with respect to acute and subchronic effects (*in utero* exposures and nursing infants) has been addressed elsewhere. ThermoRetec determined cumulative risk by combining appropriate exposure pathways and exposure scenarios.

7.0 Appropriate Site Specific Use of Site Specific Data

7.1 Exponent

Although the Exponent report utilized site specific data, the concern here is that, because of the limitations of site specific data including the comprehensiveness of the anglers surveys, the data may not be adequately inclusive of the full population. This is particularly the case for species of fish consumed, as described in the previous section. Furthermore, a particular concern is that site specific data were consistently incorporated into the risk assessment in a manner that resulted in an underestimate of exposure, especially at the high end.

7.2 ThermoRetec

The ThermoRetec risk assessment uses a much larger data base rather than site specific factors in the exposure assessment. The possible exception to this is the discussion of survey data regarding fish consumption for the general angling population in Michigan and Wisconsin. While these data are not site specific, they are most likely more representative of the population living in this area than standard EPA default values. However, the risk assessment assumes that all recreationally caught fish were caught in the Lower Fox River and Green Bay. This assumption is not supported by the more site specific surveys conducted by Hutchinson and Kraft (1994). The total recreationally caught fish consumption values used in the risk assessment (15 g/d for the CTE, 59 g/d for the RME scenarios) seem consistent with the MI and WI data, although they are higher than the US EPA recommended default values (8 g/d for the mean (CTE) and 25 g/d for the upper 95th percentile (RME)).

The report also incorporates information about Hmong anglers from reasonable local surveys, but again, not specific to the Lower Fox River. The report makes inferences about fish ingestion frequency of the Native American populations in the area based on information published elsewhere, but the appropriateness of these data is uncertain.

8.0 Communication of Basis and Findings

8.1 ThermoRetec

. The ThermoRetec Report has a detailed description of the procedures used. However, the presentation of the risk assessment is muddied by its wordiness and the large amount of boilerplate language and as mentioned previously, the problem of excessive use of abbreviations/acronyms. The discussion of the basis of key assumptions, such as the selection of the fish ingestion rates and the surveys on which they were based, was superficial. More details about the surveys and their interpretation are needed.

The focused analysis of risks due to ingestion of PCB_s in fish, provided in section 5.9, is quite helpful. This analysis uses the more recent fish sampling data (1990s) and calculates the risks due to consumption of different fish species in addition to a basket of all fish types sampled.

Some internal contradictions are not explained. For example, the toxicity section highlights developmental neurotoxicity and the importance of *in utero* and breast milk exposures but the risk assessment completely disregards these endpoints. The question of how the fish advisories that have been in place throughout the region since 1976 affect fish ingestion rates and food preparation methods is also not explained.

The summary of the uncertainty in the report is superficial, and mainly points out the conservativeness usually associated with using EPA default assumptions. There is some analysis of the differences in risk estimates based on the rate of fish intake, but this is the only uncertainty really considered. Virtually no attention is paid to data gaps, including the lack of site specific information such as site specific consumption and preparation information. There is no discussion of the uncertainty and variability associated with the fish contamination data base, which is likely to be large and important. The focused fish ingestion risk assessment evaluated separately the bottom feeders (carp) from the more commonly ingested sportfish. This is useful, and might be relevant for the risk management plan. However, the assessment was buried in the report and its summary section.

ThermoRetec provided estimates of the duration of the problem of fish contamination in the absence of remedial action. These estimates are helpful for risk mangers. Unfortunately, this information was buried in the report and was not included in the executive summary or the major summary sections.

8.2 Exponent

The Exponent Report is well written. It provides clear descriptions of the bases of its available assumptions and allows the reader to follow the calculation. However, other important and critical assumptions and supporting information are missing.

The results of the analysis are also clearly presented, although a thorough description of the Site and its history would have been extremely helpful in evaluating the selection of exposure scenarios and contaminants. Exponent did not conduct a point estimate risk assessment to compare with the probabilistic risk assessment and to see where the point estimates fall on the probabilistic scale. This would have been helpful not only as a check on the probabilistic approach, but also to help risk managers evaluate the results in the context of more familiar methodology. It should be noted that the risk assessment report on PCB_s in the Upper Hudson River that Exponent cites as a good precedent for their assessment included a point estimate calculation along with its Monte Carlo assessment.

Why does the report appear unfinished? This is especially the case for a reviewer familiar with some of the reports discussed. For example, the introduction (p. 1-1) states that for a recently completed human health risk assessment on PCB contamination in the Upper Hudson River:

> "The EPA contractor that prepared this risk assessment focused exclusively on fish consumption, adding further support to the presumption that other exposure pathways are likely trivial by comparison at the Fox River."

This is incorrect. The Upper Hudson River report evaluated contact with sediments and water, and inhalation of volatilized PCB_s as well as fish ingestion in its point estimate evaluation. The fish ingestion pathway (but not the others) was also evaluated using a Monte Carlo approach. In fact, stating the broader approach of the Hudson River assessment, and the findings of risk below the levels of concern, would have strengthened the argument for neglecting these pathways (the full text of this risk assessment is available at www.epa.gov/region02/superfnd/hudson). Acknowledging the ThermoRetec findings in the Lower Fox River regarding these pathways (generally risks below levels of concerns, and far less than fish ingestion) would also be useful.

The Exponent Report lacks any explanation of the history of the Fox River area, and how the PCB_s came to be in the Fox River. This is important to understanding potential risks from the Site, and what types of PCB_s may have been released to the River. For example, the report states that the PCB_s detected in the Fox River are appropriately characterized as Aroclor 1242 and Aroclor 1254. While this is likely correct, it would have been helpful to know that Aroclor 1242 was used in carbonless copy paper, and this type of material was manufactured in the paper plants along the River (according to the ThermoRetec report). In other words, knowing the Site history would strengthen the reader's confidence in the report's assertions. On the other hand, ThermoRetec did very well in explaining the history of the Fox River contamination.

9.0 Scientific Rigor

9.1 Exponent

While Exponent attempted to use state of the art methodology and highly site specific data in its risk assessment, it failed to use these methods in a scientifically rigorous way. The Exponent report raises concern about its scientific rigor, because of the apparent lack of understanding of the limits of epidemiology, for example, the following statement appeared on page 1-1:

> "Thus, if doses experienced by fish consumers in the assessment area were sufficient to induce cancer, it is reasonable to expect that there would be an elevated cancer rate in the counties and town surrounding the Lower Fox River and Green Bay".

The basis for this statement appears to be county-wide statistics of total cancer incidence and death rates for two years. This is a <u>very insensitive</u> measure of health impacts in a population. Only a small proportion of the county population is expected to be exposed, and that risk is one in a thousand at the high end of the ThermoRetec estimates. Thus, any elevation in cancer at a specific site (organ) of the highly exposed population would be diluted out by the combination of data for exposed and unexposed populations, and the consideration of total cancers rather than a PCB specific cancer.

The Exponent Report used the following two points as arguments for their conclusion that the PCB_s in the Lower Fox River System should have no impact on cancer incidence rate:

(I) The Wisconsin Cancer Reporting System maintained by the Wisconsin Center for Health Statistics of the Division of Health showed that both the cancer death rate and cancer incidence rate for Brown and Outagamie Counties (two of the most populous counties surrounding the Lower Fox River, upstream and adjacent to the city of Green Bay) are well below that of the state average (WDH 1999), (Page 1-1, last paragraph).

(II) In the most recent and comprehensive PCB epidemiological study, performed on highly exposed workers from former General Electric capacitor manufacturing facilities, Kimbrough *et al.* (1999) demonstrated that despite having high blood levels of PCB_s, there were no statistically significant relationships between PCB exposures and deaths due to cancer or any other diseases... (Page 1-2, paragraph 1). If the American Cancer Society in 1999 claimed that one man out of two and one woman out of three will have cancer (page 5-2, second paragraph, Exponent Report), how can the relatively small cancer incidence rates due to PCB ingestion from fish be detected against such large background incidence of 0.5 to 0.3? Thus, shouldn't we be more careful to draw conclusions when an epidemiological study turned out to be negative? It is interesting to note that the scientist(s) at Exponent argued that because of such high background cancer incidence rate, it is impossible to detect a small increase (e.g. an incremental risk of 10^{-5}), namely from 0.3 to 0.30001 (page 5-2, second paragraph). However, these same scientists didn't seem to think about the similar line of argument presented above for cancer risks for the Lower Fox River Anglers!

The Exponent Report emphasizes that there is no evidence that PCB_s are human carcinogens. The report continues to make reference to epidemiological studies to show a lack of cancer risk from PCB_s (p. 1-2) by citing a study by Kimbrough *et al.* (1999) on workers at two General Electric capacitor manufacturing plants. However, the EPA review of this study found many limitations and will likely not use it to reevaluate the carcinogenicity of PCB_s, as stated in the Human Health Risk Assessment of the Upper Hudson River. None of these critiques are provided in the Exponent Report. Again, the lack of balance in the presentation of information in this report can only be construed as a lack of scientific rigor.

Several key assumptions in the Exponent Report, such as fish ingestion rates (fishing frequency and harvest rates), species consumed and fish preparation methods are based on Site specific surveys. However, the interpretation of the Site specific data assumes that they have captured all relevant variability in their surveys. As discussed above, these assumptions are unjustified. The impact of the assumption is that they have not captured the entire variability and have truncated out the high end tails of the distributions, leading to an underestimation of the high end exposure and risk.

9.2 ThermoRetec

The ThermoRetec report provided some information that is useful for risk management decisions. The full report shows that the "risk driver" is the fish ingestion pathway, and PCB_s represent the primary contaminant of concern.

While the focused fish ingestion risk assessment did evaluate separately the bottom feeders (carp) from the more commonly ingested sportfish, this assessment was buried in the report and its summary section. The differences in risk from these different species are likely to be important to risk managers.

ThermoRetec provided estimates of the duration of the problem of fish contamination in the absence of remedial action, a useful exercise. Unfortunately, this estimate was buried in the report and its summary sections. ThermoRetec conducted a risk assessment that closely adhered to established Superfund regulatory guidance. However, it did not include any of the attractive newer techniques of risk assessment, such as probabilistic risk assessment to understand the range of variability and uncertainty.

The implication of this approach relative to the questions of scientific rigor is a matter of judgment. If we believe that EPA has derived its default values by applying as much scientific rigor as possible to limit variable and uncertain data, then the ThermoRetec Report benefits from that view.

10.0 Utility for Risk Management Decisions and Issues Related to Uncertainty

Several principal issues of the risk assessment of the Lower Fox River System exist:

A. The amount of contaminated fish consumed by Anglers is a pivotal factor to the calculated risk level. Depending on the values used from different studies (Tables 5-10 and 5-11, ThermoRetec Report), the risk levels calculated might change. Therein lies the first level of uncertainty. Further, in both Reports, calculations were done based on fish consumption "normalized" over 365 days. If an individual has 2 fish meals per week, the pharmacokinetics of such episodic intake of PCB_s are totally different from those when the annual consumption is "normalized" over 365 days with a smaller amount of daily intake. This difference is similar to comparing 20 boluses per year vs. constant daily infusion over a whole year. Here we are talking about another level of uncertainty which may have rather profound effects on PCB toxicities, particularly fetal impacts occurring during a narrow window of opportunity.

B. Both Reports indicated that the cooking process, principally frying, would reduce the amount of PCB_s in the fish. However, no one knows if during such a cooking process, a possible high temperature oxidation, that other more toxic chemicals (e.g., dioxins) might have been formed. Dioxins are known to form when chlorinated organic compounds are burnt, a more vigorous oxidation process. If such a possibility exists, a new level of risk will exist.

C. Even though the Expert Panel was asked to address only the issues related to PCB_s, the reality of chemical mixture exposure cannot be overlooked. The existence of other contaminants in the lower Fox River system added a problem to the entire risk assessment process. The body burden of multichemical exposure such as DDE, dieldrin and dioxin (all of them have very long half lives) will increase the health risk even in the presence of a small concentration of PCB_s for human and sensitive human populations. This could be a particularly important toxicologic issues in nursing mothers where fat mobilization would add whatever stored lipoplilic contaminants into the milk. Thus, it is possible that additional PCBs (those originally stored in the mother's fat) and other xenobiotics may complement the PCBs taken in through consumption of fish.

D. For very low exposures resulting from environmental contamination, most practicing toxicologists would probably consider that toxicologic interactions are unlikely. This is due to the common belief that these concentrations, usually at part per billion (ppb) levels, are far below the saturation levels for most biological processes, particularly for the detoxifying enzyme systems. Are these common beliefs true? To answer this question, Yang (1994) calculated possible impacts of 1 ppb chloroform in drinking water due to the chlorination disinfection process. He indicated that this level of chloroform means there are more than 5 quadrillion molecules in 1 liter of water. Using a series of illustrations and arguments, Yang (1994) concluded that:

(1) even at 1 ppb level, there are a huge number of molecules in our body;
(2) these molecules are not present "alone" in the sense of chemical species, they are present along with other xenobiotics;
(3) there is a very narrow range (probably less than three orders of magnitude) between "no effects" and "effects" in the various toxicity studies;
(4) toxicologic interaction(s) seems possible, at least theoretically, at low exposure concentrations; however, the sensitivity of detection may pose a problem. His contention was, in part, supported by some experimental findings particularly the clear dose-related *in vivo* cytogenetic toxicity in rats treated with an "ultra low" concentration (*i.e.,* ppb levels) of pesticide/fertilizer mixture (Kligerman *et al.*, 1993) and marked carcinogenic activities in a mixture of very low doses (1/50 of TD_{50}) of 40 known carcinogens (Takayama *et al.,* 1989).

Considering carcinogenicity as an endpoint in toxicologic interactions, a number of studies were published in the literature on multiple chemical exposures. In one series of studies (Elashoff *et al.,* 1987; Fears *et al.,* 1988, 1989), binary mixtures of 12 known or suspected carcinogens were evaluated for tumorigenicity. These investigators observed synergism, antagonism, and lack of interactions. In a review by Arcos *et al.* (1988) on binary-combination effects of carcinogens, a total of 976 interactions involving almost 200 carcinogens in ten chemical classes were uncovered. The predominant target organ was the skin, accounting for nearly 50% of all synergistic combinations. Similarly, Rao *et al.* (1989) examined the literature on 600 tumor promoters or co-carcinogens and found 1,250 interactions involving chemicals from 21classes.

If environmental pollutants are active in any process which involves cascading **amplification** such as hormonal effects or carcinogenic processes, they may cause toxicologic interactions even at very low concentrations. For example, the concentration of epinephrine needed in the blood to stimulate glycogenolysis and release glucose from the liver and muscles can be as low as 10^{-10} M, a stimulus that generates a concentration of more than 10^{-6} M cAMP in the cell. Because three more catalytic steps precede the release of glucose, another 10^4 amplification can occur, so that blood glucose levels ultimately increase by as much as 50 percent (Lodish *et al.*, 1995). If certain environmental pollutants can interfere with this process at the epinephrine level or similar processes with cascading and amplification effects, it is conceivable that disproportional toxicologic interactions may result.

Another level of uncertainty exists over the use of analytical data from PCB studies covering a time span of approximately 20 years. Because of the limitation of analytical capabilities on PCB detection 10-20 years ago, the "older" results may have considerably large experimental errors.

11.0 Uncertainty Issues

11.1 Exponent

Technical flaws in this risk assessment open to question its usefulness for risk management. Many of the site-specific assumptions are unjustified, and all serve to estimate risk downward. The risk assessment does not include an RME receptor, rendering the risk assessment inconsistent with the NCP, CERCLA and Superfund guidance, such as RAGS.

The exposure point concentration for fish tissue used in the risk assessment is largely based on nine samples of perch fillets (these samples are given 67% of the weight of the EPC). This methodology essentially, and inappropriately, ignores the huge amount of fish tissue data collected at the Site, almost all of which indicate higher PCB concentrations than the nine perch fillets. It certainly neglects the range of exposures that people could receive, such as those who ingest more highly contaminated species or fattier parts of the fish. This selection of data serves to truncate the high end of the exposure curve and to underestimate the mean exposure. Other assumptions in the exposure assessment, including the assumption that PCB_s decrease in fish concentration and PCB_s are lost during cooking, are also deeply flawed and skew the risk estimate downward. The risk assessment does not consider pregnant women and nursing infants as sensitive receptors, and does not compute an appropriate averaging time (acute exposure) to evaluate neurodevelopmental effects, a widely recognized concern. Because the risk assessment is essentially based on nine fish fillets, it is not possible to subdivide the results into different geographic or political districts.

The risk assessment deals inappropriately with the cultural traditions of minority populations in the region, notably the Hmong, by neglecting to include appropriate data and parameters for the parts of fish and fish preparation methods that were revealed in the angler and other survey data. Thus, risk managers do not have an option to develop a special policy directed at that population.

11.2 ThermoRetec

The characterization of the susceptible populations is weak. The identification of subsistence anglers was based on non-site specific data, and targeted known ethnic or racial minority groups rather than those who may be subsistence anglers (if any) on the Lower Fox River. It assumes that all Hmong, racial minorities, and Native American who fish the area are subsistence anglers. The analysis of the subsistence population consisted only of increasing the fish intake rate by 50%, which uniformly gives a 50% higher risk than the recreational anglers. This is incorrect for populations applying different food preparation methods, which appears to be the case based on the survey data presented in the Exponent Report.

ThermoRetec did not include pregnant women (i.e., *in utero* exposures) and nursing infants in its analysis of susceptible populations. This is a critical omission as this is the population that may well drive the risk. Consideration of this population needs to include the appropriate averaging time (i.e., day of exposure) as transplacental and nursing infant exposures are short-term, and the window for some neurodevelopmental effects is also short.

TABLE 1

Assumptions used in Risk Assessments

	ThermoRetec		**Exponent**		
	CTE	**RME**	**mean**	**max**	**distribution**
Fish contaminant data source	skin & fillets	skin & fillets	fillets only		
Exposure duration	30 years	50 years	15 years	80 years	exponential
absorption during fish ingestion	100%	100%	100%	100%	
fish ingestion rate-recreational	15 g/d	59 g/d	7 g/d	26 g/d (upper 95th)	lognormal
fish ingestion rate-subsistence	21 g/d	81 g/d	N/A		
cooking reduction factor	50%	50%	32%		
degradation rate	none	none	0.116/yr*		
CSF/PCB	1 (mg/kg/d)-1	2 (mg/kg/d)-1	1 (mg/kg/d)-1	2 (mg/kg/d)-1	
RfD/Aroclor 1254	2.00E-05	2.00E-05	2.00E-05	2.00E-05	
length of a lifetime	75 yrs	75 yrs	70 yrs	70 yrs	
body weight	71.8 kg	71.8 kg	distribution		

*rate was species dependent

REFERENCES

Arcos, J.C., Woo, Y.T. and Lai, Y.D. 1988. Database on binary combination effects of chemical carcinogens. Environ. Carcinogenesis Rev. C6, 1-150.

ATSDR. 1999. Toxicological profile for polychlorinated biphenyls. U.S. Department of Health & Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry.

Chen, Y-C J., Guo, Y-L., Hsu, C-C. and Rogan, W.J. 1992. Cognitive development of Yu-Cheng (Oil Disease) children prenatally exposed to heat-degraded PCBs. J.A.M.A. 268, 3213-3218.

Cordle, F., Locke, R. and Springer, J. 1982. Risk assessment in a federal regulatory agency: An assessment of risk associated with the human consumption of some species of fish contaminated with polychlorinated biphenyls (PBCs). Env. Health Persp. 45, 171-182.

Elashoff, R.M., Fears, T.R. and Schneiderman, M.A. 1987. Statistical analysis of a carcinogen mixture experiment. I. Liver carcinogens. J. Nat. Cancer Inst. 79, 509-526.

EPA. 1992. National study of chemical residues in fish. Environmental Protection Agency. EPA 823-R-92-008a.

EPA. 1997. Exposure Factors Handbook (Update to Exposure Factors Handbook - May 1989). EPA/600/8-89/043. Office of Research and Development, Washington, D.C.

Fears, T.R., Elashoff, R.M. and Schneiderman, M.A. 1988. The statistical analysis of a carcinogen mixture experiment. II. Carcinogens with different target organs, N-methyl-N-nitro-N-nitrosoguanidine,N-butyl-N-(4-hydroxybutyl)nitrosamine, dipentynitrosamine, and nitrilotriacetic acid. Toxicol. Ind. Health 4, 221-255.

Fears, T.R., Elashoff, R.M. and Schneiderman, M.A. 1989. The statistical analysis of a carcinogen mixture experiment. III. Carcinogens with different target systems, aflatoxin B1, N-butyl-N-(4-hydroxybutyl) nitrosamine, lead acetate, and thiouracil. Toxicol. Ind. Health 5, 1-23.

Fein, G.G., Jacobson, J.L., Jacobson, S.W., Schwartz, P.M. and Dowler, J.K. 1984. Prenatal exposure to polychlorinated biphenyls: effects on birth size and gestational age. J. Pediatr. 105, 315-320.

Finley, B.L., Trowbridge, K.R., Burton, S., Proctor, D.M., Panko, J.M. and Paustenbach, D.J. 1997. Preliminary assessment of PCB risks to human and ecological health in the lower Passaic River. J. Toxicol. Environ. Health 52(2), 95-118.

Fischbein, A., Wolff, M.S., Lilis, R., Thornton, J. and Selikoff, I.J. 1979. Clinical findings among PCB-exposed capacitor manufacturing workers. Ann. NY Acad. Sci. 320, 703-715.

Gan, D.R. and Berthourex, P.M. 1994. Disappearance and crop uptake of PCBs from sludge-amended farmland. Water Environ. Res. 66(1), 54-69.

Gerhard, I., Daniel, V., Link, S., Monga, B. and Runnebaum, B. 1998. Chlorinated hydrocarbons in women with repeated miscarriages. Env. Health Persp. 106, 675-681.

Gaden, B.C., Rogan, W.J., Hardy, P., Thulen, J., Tingelstad, J. and Tully, M. 1988. Development after exposure to polychlorinated biphenyls and dichlorodiphenyl dichloroethene transplacentally and through human milk. J. Pediatr. 113, 991-995.

Harada, M. 1976. Intrauterine poisoning: clinical and epidemiological studies and significance of the problem. Bull. Inst. Constit. Med. (Kumamoto Univ.) 25 (suppl.), 1-69.

Higuchi, K. ed. 1976. PCB poisoning and pollution. New York: Academic Press.

Hutchinson, R. and Kraft, C.E. 1994. Hmong fishing activity and fish consumption. J. Great Lakes Res. 20(2), 471-478.

Hutchinson, R., 1998. Impact of PCB contamination on subsistence fishing in the lower Fox River. Prepared by Ray Hutchinson of ERH Associates for Hagler Bailly Services, Inc., Boulder, Colorado.

Jacobson, J.L., Fein, G.G., Jacobson, S.W., Schwartz, P.M. and Dowley, J. K. 1984. The transfer of polychlorinated biphenyls (PCBs) and polybrominated biphenyls (PBBs) across the human placenta and into maternal milk. Am. J. Public Health. 74, 378-379.

Jacobson, J.L., Jacobson, S.W., Schwartz, P.M. and Dowler, J.K. 1984b. Prenatal exposure to an environmental toxin: A test of the multiple effects model. Dev. Psychobiol. 20, 523-532.

Jacobson, S.W., Fein, G.G., Jacobson, J.L., Schwartz, P.M. and Dowler, J.K. 1985. The effect of PCB exposure on visual recognition memory. Child Dev. 56, 853-806.

Jacobson, J.L., Jacobson, S.W. and Humphrey, H.E.B. 1990a. Effects of *in utero* exposure to polychlorinated-biphenyls and related contaminants on cognitive-functioning in young children. J. Pediatr. 116.38-45.

Jacobson, J.L., Jacobson, S.W. and Humphrey, H.E.B. 1990b. Effects of exposure to PCBs and related compounds on growth and activity in children. Neurotoxicol. Teratol. 12, 319-326.

Jacobson, J.L. and Jacobson, S.W. 1996. Intellectual impairment in children exposed to polychlorinated biphenyls *in utero*. N. Engl. J. Med. 335(11), 783-789.

Kimbrough, R.D. 1995. PCBs and human health: An Update. Crit. Rev. Toxicol. 25(2), 133-163.

Kligerman, A.D., Chapin, R.E., Erexson, G.L., Germolec, D.R., Kwanyuen, P. and Yang, R.S.H. 1993. Analyses of Cytogenetic Damage in Rodents Following Exposure to Simulated Groundwater Contamianted with Pesticides and a Fertilizer. Mutation Res. 300, 125-134.

Kreiss, K., Zack, M.M., Kimbrough, R.D., Needham, L.L., Smrek, A.L. and Jones, B.T. 1981. Association of blood pressure and polychlorinated biphenyl levels. J. Am. Med. Assoc. 245, 2505-2509.

Kuehl, D.W., Haebler, R. and Potter, C. 1994. Coplanar PCB and metal residues in dolphins from the U.S. Atlantic Coast including Atlantic bottlenose obtained during the 1987/88 mass mortality. Chemosphere 28(6), 1245-1253.

Langer, P., Kansitz, J., Tajtakova, M., Kocan, A., Bohov, P. and Hanzen, E. 1997. Decreased blood level of beta2-microglobulin in the employees of a factory which produced polychlorinated biphenyls. Chemosphere, 34(12), 2595-2600.

Lodish, H., Baltimore, D., Berk, A., Zipursky, S.L., Matsudaira, P. and Darnell, J. 1995. Molecular Cell Biology. Third Edition, W.H. Freeman and Company, New York, p. 885.

Loganathan, B.G., Kannan, K., Watanabe, I. 1995. Isomer-specific determination and toxic evaluation of polychlorinated biphenyls, polychlorinated/bromianted dibenzo-p-dioxins and dibenzofurans, polybrominated biphenyl ethers, and extractable organic halogen in carp from the Buffalo River, New York. Envi. Sci. Technol. 29(7), 1832-1838.

McLachlan, M.S. 1993. Digestive tract absorption of polychlorinated dibenzo-p-dioxins, dibenzofurans, and biphenyls in nursing infant. Toxicol. Appl. Pharmacol. 123(1), 68-73.

Nornstein, M.H. and Sigman, M.D. 1986. Continuity in mental development from infancy. Child Dev. 57, 251-274.

Rao, V.R., Woo, Y.T., Lai, D.Y. and Arcos, J.C. 1989. Database on promotors of chemical carcinogenesis. Environ. Carcinogenesis Rev. C7, 145-386.

Schantz, S.L., Sweeney, A.M., Gardiner, J.C., Humphrey, H.E., McCaffrey, R.J., Gasior, D.M., Srikanth, K.R. and Budd, M.L. 1996. Neurophychological assessment of an aging population of Great Lakes fisheaters. Toxicol. Ind. Health 12(3-4), 403-417.

Schmitt, C.J., Zajicek, J.L. and Ribick, M.A. 1985. National pesticide monitoring program. Residues of organochlorine chemicals in freshwater fish, 1980-1981. Arch. Envi. Contam. Toxicol. 14, 225-260.

Takayama, S., Hasegawa, H. and Ohgaki, H. 1989. Combination effects of forty carcinogens administered at low doses to male rats. Jpn. J. Cancer Res. 80, 732-736.

TER. 1999. Memo from J. King, Triangle Economic Research, to V. Carven, Exponent, regarding Fox River response rates. August 24.

Tilden, J., Hanrahan, L.P., Anderson, H., Palit, C., Olson, J., MacKenzie, W. and the Great Lakes Sport Fish Consortium, 1997. Health advisories for consumers of Great Lakes sport fish: Is the message being received? Env. Health Persp. 105(12), 1360-1365.

WDHSS. 1998. Fish consumption exposure assessment study, Sheboygan Harbor and River, May 1998. Final report printed by U.S. Department of Health and Human Services, Agency for Toxic Substances and Disease Registry, Atlanta, GA. Report submitted by Wisconsin Department of Health and Social Services, Madison, WI.

West, P.C., Fly, J.M., Marans, R., Larkin, F. and Rosenblatt, D. 1993. 1991-92 Michigan Sport Anglers Fish Consumption Study. Final report to the Michigan Great Lakes Protection Fund, Michigan Department of Natural Resources. May.

Wilson, N.D., Shear, N.M., Paustenbach, D.J. and Price, P.S. 1998. The effect of cooking practices on the concentration of DDT and PCB compounds in the edible tissue of fish. J. Exp. Anal. Environ. Epi. 8(3), 423-440.

Wong, K.C. and Hwang, M.Y. 1981. Children born to PCB poisoned mothers. Clin. Med. (Taipei). 7, 83-87.

Yang, R.S.H. 1994. Toxicology of Chemical Mixtures: Case Studies, Mechanisms, and Novel Approaches, Academic Press, San Diego, CA, 720 pp.