July 26, 2013

Response to the September 16, 2009
American Water Works Association
Comments on the
Probabilistic Assessment (PRA) White Paper
Docket No. EPA-HQ-ORD-2009-0645

The American Water Works Association (AWWA) commended EPA for the development of the two draft white papers and its flexible approach in the use of probabilistic risk assessment (PRA) in the regulatory development process. AWWA has previously supported the use of PRA in their comments on several proposed national primary drinking water regulations (NPDWRs) in the past several years.

AWWA offered three specific comments about the draft white papers:

- More detailed guidance is needed on how assumptions or sequences of assumptions should be handled (i.e., whether they are dependent or independent of each other);

- They did not agree with the economic analysis and the underlying statistical model that is discussed in Case Study # 8 "Two-Dimensional Probabilistic Risk Analysis of Cryptosporidium in Public Water Supplies, with Bayesian Approaches to Uncertainty Analysis"; and

- The PRA white papers should clearly acknowledge the need for quality control and quality assurance practices to be in place prior to the collection of any data used to build the PRA distributions. Furthermore, the PRA white papers should also provide a list of clear and simple recommendations that outlines minimum data quality for attaining these objectives.

Response:

The draft white papers are not meant to provide regulatory guidance for decision making, they are intended to provide general reference and descriptive information about Agency PRA use. Additional information about the "Two-Dimensional Probabilistic Risk Analysis of Cryptosporidium in Public Water Supplies, with Bayesian Approaches to Uncertainty Analysis" Case Study can be found in the "Selected References" section at the conclusion of the case study description.

Response to the October 6, 2009
Nuclear Regulatory Commission
Comments on the
Probabilistic Assessment (PRA) White Paper
Docket No. EPA-HQ-ORD-2009-0645

The Nuclear Regulatory Commission (NRC) supports the use of risk-informed and performance-based regulation. The NRC recognizes differences in the manner in which EPA and NRC regulate (e.g., use of a risk range versus use of a specific dose criterion), which may lead to significant differences in the way PRA is used to make certain decisions.

The NRC offered a wide range of general and specific comments.

General comments:

1. It would be helpful to include in introductory chapters a general description of the types of decisions that are being made at EPA that could benefit from a PRA (e.g., to perform cost-benefit analyses for rulemaking; to compare alternatives for remediation; to evaluate compliance against regulatory standards; or to optimize sample collection) and to discuss whether PRA may be more or less suited for these various applications.

Response:
The white paper was revised to include more information about decisions and decision uncertainty.

2. There appears to be a lack of specificity regarding how statistical measures of uncertainty should be considered in making decisions (e.g., evaluating compliance against a regulatory limit). Having recommended metrics in guidance makes it easier for the decision maker and the regulated community to more consistently apply risk information obtained from PRA, providing stability in the regulatory process.

   - *Page 6, Section 1.3, second paragraph.* Statements are made that in the face of uncertainty, decision making is determined not only by science but by Agency policy and where not prohibited by statute, the relative costs and benefits of regulatory alternatives may be considered in making decisions. But it is not clear what policies and statutes may limit the utility of PRA or cost/benefit analysis. Examples could be provided.

     Response:
     The white paper is not meant to provide regulatory guidance for decision making. It is the intent of the white paper to provide general reference and descriptive information about Agency PRA use. The identification of specific policies and statutes is beyond the scope of the document.

   - *Page 7, Section 1.4, sixth bullet.* A statement is made that a decision maker often asks, "What is the percentile of the population to be protected?" It is not clear if there are specific recommendations regarding who is to be protected in EPA guidance or regulations.

- *Page 13, Section 2.2, bullet 4.* Statements are made that PRA might be most useful "When significant equity issues are raised by inter-individual variability." However, it is again not clear what individuals are to be protected.

Response:

The white paper is not meant to provide societal or other values used in a specific decision making context; such details go beyond the scope of the white paper.

- *Page 16, Section 2.8.* States that binary decisions may be perceived to be more readily answered with deterministic analysis as opposed to PRA that present a range of uncertainty. This statement recognizes the difficulty in making decisions when a range of possible outcomes is presented but offers no specific details on how this information should be synthesized or interpreted to make a decision.

- *Page 25, fourth paragraph.* Discusses the evaluation of central tendency and reasonable upper bounds of exposures, effects, and risk estimates, such that the estimates could be for an actual individual in the population of interest rather than a hypothetical Maximally Exposed Individual (MEI). This discussion seems to imply that there is some regulatory flexibility in evaluating risks to potential receptors (does not necessarily have to be the MEI) but introduces ambiguity in the regulatory and decision criteria that might be used in its stead.

- *Page 32, "Resolution" definition.* Discusses an example when an evaluation of upper bound risks may necessitate a geographical-information-system-based modeling framework precise enough to model exposures to individual receptors. One might argue that the necessary level or scale of the analysis would be dictated by regulatory criteria (e.g., maximally exposed individual) and depending on the endpoint, one form of analysis may be more appropriate then another (i.e., deterministic bounding versus probabilistic analysis) and/or would dictate what metrics would be used if a PRA is selected. It is not clear to what extent regulatory criteria (and modeling objectives) are prescribed or if there is some flexibility in evaluating individual risk.

- *Page 58, Case Study 4, second paragraph.* Discusses use of the 95th percentile regulation for lower tiers that do not include percent crop treated to use of the 99.9th percentile for the more refined assessments, which would include percent of crop treated information; but the basis for these percentiles is not provided, and it is not clear if these percentiles are specified in regulation or guidance.

- *Page 60, Case Study 5, first paragraph.* Discusses results of deterministic analysis that exceeds regulatory benchmarks but does not indicate what these benchmarks are or provide information on whether these benchmarks constitute regulatory requirements. The "Results of the Analysis" section presents information on the central tendency individual and reasonable maximum exposure individual, but it is not clear if decisions are based on protection of one or both of these individuals and at what percentage of the PRA distribution of results are these individuals expected to be evaluated.

Response:
As described above, the white paper is not meant to provide regulatory guidance for decision making. It is the intent of the white paper to provide general reference and descriptive information about Agency PRA use. Additional information about each of the Case Studies is available in the "Selected References" section at the conclusion of each case study description.

3. It appears that the focus of most of the PRA case studies presented in the EPA white paper is on a subset of the components of an environmental risk assessment. While uncertainty in these components of the environmental risk assessment is recognized (see bulleted examples below), more emphasis appears to be placed on exposure and consequence modeling in the textual examples and Case Studies.

   - *Page 23, bullet four,* states that "There may be mismatches in the temporal and spatial resolution of each model, which confound the ability to propagate variability, and uncertainty from one model to another," recognizing the challenges of integration and coupling of models.

   - *Page 27, Section A.3.1, "Structural Uncertainty in Scenarios" Section.* Discusses important components of environmental risk assessment models (e.g., source definition, transport, exposure routes, etc.) that constitute forms of structural uncertainty but states that there are no formalized methodologies for dealing with uncertainty and variability (and that qualitative approaches to addressing these uncertainties are common).

   - *Page 27, Section A.3.1, Coupled Models.* Discusses components of an environmental risk assessment model that have varying spatial and temporal scales that are difficult to integrate and can introduce a significant source of structural uncertainty but presents no clear path on how this uncertainty can be addressed.

   - *Page 60, Case Study 5, "Probabilistic Analysis" Section, last sentence.* Discusses the use of mathematical models of environmental fate, transport, and bioaccumulation of polychlorinated biphenyls (PCBs) in the Hudson River to forecast changes in PCB concentrations over time. However, it is not clear that uncertainty in PCB concentrations were propagated over time and how the uncertainty in PCB concentrations compares to uncertainty in angling duration and other exposure factors which appear to be the focus of the Case Study.

   Additional discussion regarding the relative uncertainties expected to be introduced by various components of the environmental risk assessment model for various EPA applications and/or an explanation on why emphasis seems to be placed in particular areas of the risk assessment would be beneficial.

   Response:
   The white paper is not meant to be a handbook. More details on methodology and tools (for both deterministic and probabilistic risk assessments) are available in many of the references

cited. The case studies are illustrative and only briefly summarize each example; additional information on each case study is available in the "Selected References" at the conclusion of each case study description.

4. In many cases, in order to adequately perform PRA to inform decision making, sufficient resources are needed to (i) analyze and synthesize data into forms that are of use to a risk analyst and (ii) create an infrastructure to more efficiently implement PRAs. A summary listing or examples of the types of data that are routinely collected or are planned to be collected and analyzed by the EPA for inclusion in environmental risk assessments; and the types of tools and other resources that are currently being developed to aid in implementation of PRA analyses in the future would be beneficial.

   Response:
   There are revised sections in the white paper dealing with PRA resource needs, tools and techniques.

5. A stated goal of the EPA white paper is to explain how EPA can achieve a broader use of probabilistic methods and address uncertainty and variability by capitalizing on the wide array of tools and methods that comprise PRA. However, while significant information is provided on methods that comprise PRA, less information is provided on the tools of PRA (e.g., off-the-shelf software for performing PRA or EPA sponsored codes specifically designed to execute probabilistic analysis). While this omission may have been intentional, it would be helpful if additional examples of "off-the-shelf" software and additional details on other tools being used to perform these types of analyses is included.

   Response:
   The white paper is not meant to be a handbook. More details on methodology and tools (for both deterministic and probabilistic risk assessments) are available in many of the references cited.

Specific Comments:

6. *Page 9, Section 1 .7, second paragraph.* A statement is made that deterministic risk assessments provide estimations of exposures and resulting risks that address uncertainty and variability in a qualitative manner. Statements in the text regarding the limitations of deterministic analysis and implications that these types of analyses are not science based should be checked and carefully worded (see also page 16, Section 2.8, statement that decisions should be based on the best available science). As discussed in the white paper, in some cases deterministic analyses are adequate and while they may not necessarily reflect the best available science (because best available science is not warranted), they may still be technically defensible and scientific in their approaches.

   Response:
   Information regarding the use of deterministic versus probabilistic risk assessment has been addressed in the white paper. More details on the use of these risk assessment approaches are available in the EPA references cited.

7. *Page 12, Section 2.1.1.* While the 1997 EPA Policy on Probabilistic Analysis in Risk Assessment (EPA, 1997) states that additional study is needed to apply PRA to dose effects (and this policy does not appear to be superseded), several examples are included in this paragraph regarding use of PRA in this manner. Please clarify EPA's current policy and progress in this area.

8. *Page 13, first paragraph on "Model Uncertainty" and page 23, Section 3.4, bullet 2.* These sections of the white paper provide information about model uncertainty and challenges faced in evaluating this type of uncertainty. It should be noted that while model uncertainty and abstraction are important components of uncertainty that should be evaluated, it would be preferable to spend adequate resources up front making sure that the models used to perform the risk assessment are appropriate for their intended application (e.g., that the appropriate level of complexity is captured in the models) and that uncertainty is propagated in the appropriately-selected model. However, in the case of complex systems that must necessarily be simplified and that are difficult to validate using existing data, use of multiple models or scenarios may be warranted and uncertainty in these models should be addressed. While evaluation of model uncertainty is an area in need of continued research, guidance is currently available on the treatment of model uncertainty that can be referenced in this section (e.g., see, for example, Meyer 2004).

   Response:
   The white paper and its relevant references are intended to provide the latest Agency information, not regulatory guidance, on PRA use. Additional information about sources of model uncertainty is available in the white paper Glossary and References.

9. *Page 13, Section 2.2.* Suggest adding a bullet regarding the utility of PRA when model complexity makes it difficult to assess the conservatism of a particular selection of parameter values in a deterministic assessment.

10. *Page 21, Section 3.1.* Statements are made regarding the utility of PRA in evaluating various risk management strategies and alternatives; and that sensitivity analyses can be used to identify influential knowledge gaps. However, no information is provided on how probabilistic analyses are superior in these areas compared to deterministic analyses and/or when it might be appropriate to use deterministic analyses.

    Response:
    Specific guidance regarding the use of deterministic versus probabilistic risk assessment is beyond the scope of the white paper. More details on the use of these risk assessment approaches are available in the EPA references cited.

11. *Page 24, second paragraph, last sentence.* Provide an example of when it would be appropriate to refine an assessment objective depending on the availability of information. It would seem that the assessment objective would be based on some regulatory metric and not necessarily the availability of information. If insufficient information is available one might not be able to make a decision or might manage uncertainty with conservative assumptions.

Response:
Specific guidance and examples of when it would be appropriate to refine an assessment objective depending on the availability of information is beyond the scope of the white paper. Additional information about this issue may be obtained from the EPA references cited in the white paper.

12. *Page 24, "Levels of Analysis" box.* The text should clarify and provide a basis for the ordering of "levels of analysis" (e.g., why is expert elicitation listed last or sensitivity analysis [which can take on many forms] listed first?). The text should note that sensitivity analyses can be either deterministic or probabilistic. It is not clear why Monte Carlo analysis of variability is limited to exposure data and human health and ecological effect data. Define or provide examples of "decision uncertainty analysis" and "geospatial analysis" and provide a basis for where they fall in the ordering of analyses.

Response:
Additional information on the graduated approach to analysis is available in the cited references in the white paper.

13. *Page 25, third paragraph.* "In such a situation, depending on the resource implications of risk management, it might be appropriate to proceed with a more refined, or higher level, analysis. If the cost of intervention is less than the cost of further analysis, then it may be appropriate to simply proceed to the risk management decision as a preventive measure that is also expedient. In some deterministic assessments, for instance, for ecological risks, the assumptions are not well assured of conservatism and the estimated risks might be biased to appear lower than the unseen actual risk." The last sentence above introduces a separate thought and potential problem with respect to deterministic analyses that should be developed on its own (issue with deterministic analyses not clearly being conservative in the face of great uncertainty). Additionally, the thought that additional ecological modeling could be more costly then remediation (making remediation potentially a more attractive option) could be more clearly made in the example. Suggest rewording the sentence for clarity and/or providing a better example.

Response:
Specific guidance regarding the use of deterministic versus probabilistic risk assessment is beyond the scope of the white paper. More details on the use of these risk assessment approaches are available in the EPA references cited.

14. *Page 31, Appendix B: Glossary.* Suggest adding PRA-related terms to the glossary that are used but not well-defined in the text of the white paper: (i) dose response, (ii) target population, (iii) hazard identification, (iv) reference dose, (v) hazard index, (vi) decision uncertainty, (vii) geospatial analysis.

15. *Page 34, "Sensitivity Analysis" definition.* Suggest listing the different types of sensitivity analysis and sensitivity analysis techniques.

Response:
Glossary changes were made to accommodate most of the suggested changes.

16. *Page 53, Case Study 1*. This Case Study explains how sensitivity analysis was used to determine key variables for population exposure variability to arsenic in chromated copper arsenate pressure treated wood. The study found that data needed to be collected on the amount of dislodgeable residue that is transferred from the wood surface to a child's hand upon contact and the amount of dislodgeable residue that exists on the wood surface. It would seem that these parameters would change over time as the integrity of the pressure treated wood diminished. This would be an example of a scenario or structural model uncertainty that might be the most risk significant aspect of the exposure modeling, but if not considered, would not be evaluated as part of the PRA (see general comment 3 above).

17. *Page 62, Figure 1*. It is not clear why this plot which shows the uncertainty in risk estimates to discrete population percentiles (representing inter-individual variability) is not an example of a 2D Monte Carlo analysis (appears to be [albeit a more discrete] version of a 2D Monte Carlo analysis result similar to what is presented in Figure 2 on page 26). On the other hand, the figure on page 73 does not seem to clearly present results of a 2D Monte Carlo analysis related to ozone exposure with only uncertainty in model inputs apparently being presented . Suggest including more illustrative examples of the characteristics of 2D Monte Carlo analysis in the Case Study examples.

Response:
EPA welcomes comments about the case studies. The case studies are meant to be illustrative and only briefly summary the relevant materials in each case study. Specific questions about a case study need to be addressed to the EPA office or region that sponsored the project. Additional information about each case study is available in the "Selected References" section that follows each case study description.

Editorial Comments:

Editorial revisions for consideration include:

- *Page 5, 1st paragraph.* "One can use probability (chance) to quantify the frequency of occurrence or the degree of belief in information." This statement can be clarified to avoid an incorrect interpretation. Probability is not equivalent to frequency. Probability is a value between 0 and 1. Frequency can be greater than 1.

- *Page 6, last paragraph.* A statement is made that "Increased uncertainty can make it more difficult to . . ." perform a cost-benefit analysis. Suggest re-writing for clarity (i.e., what is the increase in uncertainty in relation to?).

- *Page 32, first paragraph, last sentence.* Suggest providing a better example then "logistic models" which has not been defined and may not be obvious to a reader.

- *Page 32, "Resolution" definition.* Check sentence stating "if the grid size selected is too small . . .," should this be "large" not "small" or should reference to the scale be small (as opposed to grid size).

Response:
Relevant editorial revisions were made in the white paper.

Response to the October 15, 2009
Wood Preservative Science Council
Comments on the
Probabilistic Assessment (PRA) White Paper
Docket No. EPA-HQ-ORD-2009-0645

The Wood Preservative Science Council (WPSC) is supportive of the Agency's efforts to develop improved methodologies to assess risks, including the use of probabilistic methods where appropriate. Such methods, when properly developed with appropriate assumptions and underlying scientific justifications, can be helpful in the Agency's decision making process.

The WPSC offered a range of general and specific comments.

General Comments:

The WPSC believes that the white paper mischaracterizes the use of the SHEDS-Wood probabilistic model in relation to risk assessment and decision making for Chromated Copper Arsenate (CCA) wood preservatives and is incomplete in its description of the uses of that model. The WPSC believes that minor modifications to certain statements will better characterize the model's application and use in risk management decisions without diminishing the importance of the development, improvement, and use of probabilistic models.

Under "Results of Risk Analysis" (Case Study 9), the Agency states that the Office of Pesticide Programs used the SHEDs-Wood model for a risk assessment of existing structures and that "This included recommendations for risk reduction (use of sealants and careful attention to children's hand-washing) to homeowners with existing CCA wood structures." However, this does not state accurately what was done in regards to offering advice concerning CCA-treated wood structures. In its April 2008 general advice to consumers, EPA states there is no reason to remove either existing structures or surrounding soil, identifies that there is limited evidence that under some circumstances some coatings may reduce dislodgeable residues but does not recommend their use, and offers the generally applicable good hygiene practice to wash hands after handling any outdoor structures.

Also in this section, the white paper identifies that EPA and the Consumer Product Safety Commission conducted two-year studies to evaluate the impact of commercially-available sealants on residue availability but fails to identify that the FIFRA Scientific Advisory Panel review of those studies at its November 2006 meeting concluded that while those studies provided some evidence that some coatings under some conditions might reduce absolute levels of dislodgeable residues, the studies themselves would not be sufficient to provide advice to the public. The SAP recommended steps to consider if further research in that area is conducted, and the Office of Pesticide Programs concurred with the SAP recommendations that more definitive studies are needed.

Specific Comments:
Specifically under Case Study 9 on pages 70-71 of the white paper, the Agency states the

following under “Management Considerations” - “The modeling product was pivotal in the risk management and re-registration eligibility decisions for CCA, and in advising the public how to minimize health risks from existing treated wood structures.”

In fact, this model and its estimated exposures and risks were not relevant to and were not used by the Agency in any risk management or reregistration eligibility decisions. This was because there have been no registered uses of CCA for treatment of wood used in the scenarios addressed by SHEDS-Wood since 2003. Therefore, these uses were not part of the decision to reregister CCA.

For these reasons, the WPSC recommends that the Agency make revisions to its statements regarding the use of the SHEDS-Wood model in relation to CCA to better reflect the actual use and interpretation of the model estimates in risk assessment and decision making by the Office of Pesticide Programs.

Response:
EPA welcomes comments about the case studies. The case studies are meant to be illustrative and only briefly summary the relevant materials in each case study. Specific questions about a case study need to be addressed to the EPA office or region that sponsored the project. Additional information about Case Study 9 is available in the “Selected References” at the conclusion of the case study description.

Response to the October 15, 2009
CropLife America
Comments on the
Probabilistic Assessment (PRA) White Paper
Docket No. EPA-HQ-ORD-2009-0645

CropLife America fully supports the use of probabilistic methods in human and ecological risk assessments conducted for pesticides in support of registration or re-registration under FIFRA. To date, EPA has seldom used probabilistic methods to refine screening-level assessments of pesticides.

CropLife America offered a range of general and specific comments.

General Comments:

Although the PRA white paper was intended to address the use of probabilistic methods in both human and ecological risk assessment, the paper is clearly written from the human health perspective. There are numerous instances where the text would have benefited from the inclusion of ecological examples or considerations. Only five of the 16 case studies in Appendix D involve the use of probabilistic methods in ecological risk assessments, and only studies 13 and 16 used probabilistic methods to assess risks to aquatic life or wildlife. The others could just have easily been classified as human health or "environmental" case studies (e.g., probability of sea level rise, design of a national environmental monitoring plan, the contribution of atmospheric deposition to watershed contamination).

Response:
A brief summary of the similarities and differences between human health and ecological risk assessments was added to the white paper. Additional details about these risk assessment approaches are available in the cited references.

Given the heavy reliance on the opinion (as expressed through the cited past publications) of the National Academy of Sciences/National Research Council (NAS/NRC) with regard to the use of PRA, it is surprising that this white paper has not been updated to include the more recent opinions/thoughts expressed in the "Silver Book" (Science and Decisions: Advancing Risk Assessment, 2008) as well as the 2008 report entitled Phthalates and Cumulative Risk Assessment: The Tasks Ahead. Since these two volumes represent the latest opinion of the NAS, this white paper should be updated in several areas to incorporate these latest risk assessment reports. Sections that could be improved from consideration of these two reports include, but are not limited to: 1.5; 1.6; 2.4; 2.6.

Response:
The white paper references since 2008 have been updated.

Review of Section 1.8 (page 10) raised many concerns regarding an overall lack of comprehensiveness when considering past EPA efforts in PRA. It is stated that both OPP and OSWER have developed specific guidance in the use of PRA – how have these guidance directly contributed to this white paper? How has the information gained from conducting PRA techniques and methods been synthesized into "lessons learned" to help improve these guidance? For example, from past Agency experience in using these tools, where has PRA been shown NOT to improve upon information generated and decisions made from using deterministic techniques?

The argument put forth mainly in Section 2.9 (but also referenced elsewhere in the document) would benefit from stating the fact that major resources will be required "up front" to develop "Standard Evaluation Procedures" for PRA-based Agency assessments. This is in addition to the upfront resources needed merely to conduct a PRA, relative to a deterministic assessment. Furthermore, this section would be much improved by citing other sovereign government experiences and proof that "ongoing resource cost may be offset by a more informed decision." See *Specific Comment on Page 17, Section 2.10*.

Response:
The white paper is not meant to provide regulatory guidance documents for decision making. It is the intent of the white paper to provide general reference and descriptive information about Agency PRA use.

The recommendations listed toward the end of Section 3.2 are somewhat redundant. All of these suggestions to "improve implementation" fall into one of three general categories: inform, train, and promote. Collapse all suggestions into one of these three major headings to reduce redundancy here.

Response:
The white paper is not an implementation plan for more widespread use of PRA within EPA. While details of PRA implementation are important, this issue goes beyond the scope of the white paper.

The case studies could be restructured to provide more information to the reader. It is recommended that the case study information presented flow as follows:

- What is the problem?
- What is the best PRA tool/technique to solve the problem?
- What was the tool used to solve the problem, assuming the "best" tool was not used for some reason (and explain why it was not used)
- Describe the approach used.
- Describe the management considerations.
- Comment on "lessons learned" and how these can drive improvements in future applications of the approach used.

In many places in the text (particularly in Section 3), the text just asserts the many benefits of probabilistic methods. It would be much more convincing if specific examples (e.g., using text boxes) illustrated the benefits of probabilistic risk methods (e.g., their use led to a more effective decision than did deterministic methods for a particular contaminated site).

Appendix A provides only a superficial overview of probabilistic methods. The text should identify and discuss each of the techniques currently in common use (e.g., first and second-order Monte Carlo analysis, Bayesian methods, etc.) and others that may become useful in the future (e.g., probability bounds analysis, fuzzy arithmetic, etc.).

Response:
The text in the white paper has been revised to incorporate more information about PRA techniques and case study references. The case studies have been structured to improve information flow and provide clarity to readers.

Case study 13 is the only example provided that shows how probabilistic methods have been used to assess pesticide risks to wildlife. The case study describes a probabilistic model (the Terrestrial Investigation Model [TIM], version 2.0) that was developed to estimate the risks of a hypothetical flow of pesticide to birds that forage on treated fields. This case study, however, has several problems, including:

- The material provided is outdated and has been superseded by TIM, version 2.1, which was presented to the FIFRA Scientific Advisory Panel in February 2008. Similarly, the "Chem X" case study, conducted nearly a decade ago, has been updated and expanded upon in an actual pesticide risk assessment (carbofuran), which was presented to the same Panel in February 2008. Although the carbofuran example has a number of flaws, it does represent an improvement over the Chem X case study.
- The last paragraph on page 79 is completely out of place. It has nothing to do with the text describing the terrestrial or aquatic level II models that are described in the surrounding text.
- Little information is provided on the terrestrial and aquatic level II models and their current status of development and use in the Agency.
- The Results section does not mention birds.
- The Management Considerations section is not a balanced presentation of the opinions of the Scientific Advisory Panels that have reviewed the level II models. The Panels have suggested numerous refinements to further improve the level II models, many of which will require significant time and resources to incorporate.

Response:
EPA welcomes comments about the case studies. The case studies are meant to be illustrative and only briefly summary the relevant materials in each case study. Specific questions about a case study need to be addressed to the EPA office or region that sponsored the project. More details are available about Case Study 13 in the "Selected References" section that follows the case study description.

Specific Comments:

Page 4, Paragraph 1. The statement that stakeholders have requested the use of probabilistic methods to ensure a "fuller characterization of risks, including uncertainties, in protecting more sensitive or vulnerable populations and life stages," does not make sense. Better characterization of risks through the use of probabilistic methods will not "protect" sensitive populations and life stages. Only effective risk management actions can accomplish that goal. Probabilistic methods do, however, contribute to a fuller characterization of risks and thus provide useful information that can contribute to effective decision making regarding protection of sensitive populations and life stages.

Page 6, Section 1.3 There is reference to "traditional methods of risk analysis" towards the end of the first paragraph of this section. It should be specified here that traditional methods are synonymous with the deterministic approach to risk analysis. NOTE: This comment should apply to most additional occurrences of the phrase "traditional methods."

Page 15, Section 2.6. The final bullet of this section is somewhat confusing: "By adopting PRA, EPA sends the appropriate signal to the intellectual marketplace …" The white paper clearly lays out the fact that EPA has already adopted PRA techniques in many instances, so the meaning of "by adopting PRA" is unclear. Do the authors refer to some more formal EPA document/proclamation/etc. that needs to occur to "show the intellectual marketplace" that EPA has "officially" embraced PRA? Please clarify. In addition, the terms "appropriate signal" and "intellectual marketplace" are equally nebulous. Finally, "encouraging analysts to gather data" is also confusing … the implication here is that "analysts" (an undefined term – EPA analysts?) will only "gather data" subsequent to some more formal adoption process.

Page 16, Section 2.8. The title of this section is inaccurate. "Why" is explained in this section, not "How." Title should be changed to reflect this.

Page 17, Section 2.10. The final sentence states that PRA "can provide additional interpretations that compensate for additional efforts." Is this demonstrated in the case studies provided along with the white paper? This section/argument would be much improved by citing real-world examples of such compensatory interpretations. See General Comment 3.

Page 17, Section 2.10. The text should note that there are probabilistic methods (e.g., second order Monte Carlo analysis, probability bounds analysis, interval analysis) that can and should be used in data-poor situations.

Page 17, Section 2.11. Provide a reference that supports the statement that PRA "fits directly into a graduated hierarchical approach to risk analysis."

Page 18, Section 2.13. This section gives very little useful guidance on communicating the results of a probabilistic risk analysis to scientists, risk managers, stakeholders and

the public. There is a rich literature on this topic that can help assessors determine what methods will work for different audiences.

Page 21, Section 3.2. Contrary to what is written in the first sentence here, there is little discussion in the paper regarding the methods and tools that are available for conducting a probabilistic risk assessment. Appendix A is insufficient in this regard.

Page 23, Section 3.4. This section briefly describes some of the challenges that must be met for there to be further use of probabilistic methods by EPA. The last three challenges listed in this section, however, are specific to a very narrow topic – addressing model uncertainty. Many broader challenges (e.g., lack of available expertise in the Agency, lack of resources for training, lack of guidance for many programs, etc) are not mentioned but are much more important than the challenges listed in this section.

Response:

Many relevant changes have been made to the white paper text to address the suggested revisions and balance them with suggested revisions by other public and private reviewers.

Response to the October 16, 2009
American Chemistry Council
Comments on the
Probabilistic Assessment (PRA) White Paper
Docket No. EPA-HQ-ORD-2009-0645

The American Chemistry Council (ACC) commends EPA for its efforts to push forward with the development, peer review and eventual adoption of advanced risk assessment methods and improved science-based policies, such as probabilistic approaches in lieu of deterministic methods.

ACC offered a range of general and specific comments.

General Comments:

EPA practices still reflect a reliance on overly conservative default approaches that in many ways are now outdated due to advances in scientific knowledge of toxicology and risk assessment. Despite well intentioned efforts by many within the Agency, considerable improvement is still necessary for EPA to put modern risk assessment methods into practice.

Specific Comments:

On pages 10 and 11of *EPA's Draft Probabilistic RA Guidance Document*, the Agency lists some of the case studies which they have reviewed and which have been conducted by the EPA. It may be useful also to incorporate case studies from outside the EPA that demonstrate additional applications of the PRA approach. In Attachment A, ACC's Chlorine Chemistry Division provides a case in point: *Example Application of PRA to Toxicity Values: A Case Study with Dioxin-Like Compounds.*

In section 2.7 of *EPA's Draft Probabilistic RA Guidance Document*, EPA touches on several limitations in implementing PRA including a lack of resources. ACC acknowledges this as a reality, but it should also be pointed out that if the Agency moves forward with a greater use of this approach there will be incentive to develop methods and tools that may reduce some of the resource demands.

Response:
EPA welcomes references to non-Agency PRA case studies; however, only EPA case studies were included in the white paper because the white paper is designed to provide information on PRA methods and case studies in which the Agency was directly involved.

Response to the
General Electric Company
Comments on the
Probabilistic Assessment (PRA) White Paper
Docket No. EPA-HQ-ORD-2009-0645

Overall, the draft white paper represents a positive advancement in risk assessment, and has the potential to improve risk management by promoting the use of PRA in decision making.

Comments:

Although the draft white paper supports and encourages the use of PRA, it lists a number of challenges, including the application of PRA techniques in toxicity assessment (Section 3.2, p. 23).

One pertinent example is the unwillingness of EPA Region 1, in the context of the Housatonic River Human Health Risk Assessment, to use PRA to characterize the uncertainties associated with toxicity values as recommended by an EPA-convened peer review panel. In reviewing EPA's draft Housatonic River Human Health Risk Assessment, the peer review panel generally agreed that the uncertainties associated with the toxicity values were substantial, and should be included in the evaluation of uncertainties in the risk estimates. EPA Region 1 ignored these recommendations, and did not include a quantitative evaluation of those uncertainties in the final Housatonic River Human Health Risk Assessment, even though GE had commissioned and submitted to the administrative record a PRA that included toxicity distributions.

Case Study 5: One-Dimensional Probabilistic Risk Analysis of Exposure to Polychlorinated Biphenyls (PCBs) via Consumption of Fish from a Contaminated Sediment Site actually is an example of a probabilistic model that lacked transparency, was poorly described, inconsistent with EPA guidance, and inadequate in its characterization of the uncertainties in the exposure estimates. As described in more detail in Section 4.0 of the attached Comments of General Electric Company on Hudson River PCBs Superfund Site Reassessment RI/FS Phase 2 Human Health Risk Assessment (Sept. 7, 1999) (*Hudson Comments*).

In *Case Study 5*, more robust exposure data were available, but EPA chose to use more conservative data in its PRA. *Hudson Comments, Attachment B.* …Results of EPA's 1-dimensional Monte Carlo analysis of exposure to Hudson River sediments via consumption of contaminated fish would have been more realistic if more robust data had been used for fish consumption. Because of these deficiencies, EPA's PRA for the upper Hudson River, as recounted in *Case Study 5*, should not be included in the *Draft white paper* as a positive example.

Sensitivity analysis is an important tool for evaluating the most sensitive inputs. *Case Study 3: Probabilistic Assessment of Angling Duration Used in Assessment of Exposure to Hudson River Sediments via Consumption of Contaminated Fish*, however, is an example of a sensitivity analysis where EPA focused on factors that would only have a minimal impact on the final estimates of risk, and disregarded factors that would have a significant impact.

EPA's PRA for the upper Hudson River, as depicted in *Case Study 3,* is a poor example that should not be included in the final version of this otherwise fine introduction to probabilistic techniques and practices for examining and addressing uncertainty, variability and realism in risk assessment.

Response:

EPA welcomes comments about the white paper case studies. The case studies are meant to be illustrative and only briefly summary the relevant materials in each case study. Specific questions about a case study need to be addressed to the EPA office or region that sponsored the project. Additional information about each case study is available in the "Selected References" section that follows each case study description.

Response to the October 16, 2009
Bayer CropScience US
Comments on the
Probabilistic Assessment (PRA) White Paper
Docket No. EPA-HQ-ORD-2009-0645

Bayer CropScience offered a range of comments.

1. EPA's Experience with the Use of Probabilistic Risk Analysis.
   - The tools used in the application of probabilistic risk analysis (PRA) for some case studies in Appendix D do not meet the criteria stated on page 10 of having "... stood the test of internal and external peer review." Although selected external peer reviewers have been used by the Agency, all interested stakeholders are not offered the opportunity to assess the PRA tools developed by the Agency. Specifically, the example in Appendix D regarding the application of SHEDS in the risk assessment for chromated copper arsenate (CCA) has provided the PRA tools to selected external peer reviewers but has refused to provide access to interested stakeholders including regulated industries impacted by the PRA model.

     Although the Agency did obtain limited external peer of the SHEDS PRA model, interested stakeholders continue to be excluded from the review process. We also cite the statements on pages 17–18 of the document that describes the evaluation process for a probabilistic risk assessment model, that should encompass the entire "life cycle" of the model, that is "… based not only on its predictive value determined from comparison with historical data but also on its comprehensiveness, rigor in development, transparency, and interpretability (NRC, 2007b)."

However, the Agency is to be commended for providing transparency, interpretability and public access to other PRA tools including the Dietary Exposure Evaluation Model (DEEM, Appendix D, Case study 4) developed by Durango Software and Novigen Sciences. Critical to the usefulness of the DEEM PRA model is the quality of input data available for conducting a dietary risk assessment…. Both U.S. EPA's Office of Pesticide Programs and USDA's Agricultural Marketing Service are to be commended as an example of Federal agencies working together to provide an important PRA tool used in the human risk assessment process.

Response:
EPA welcomes comments about the case studies. The case studies are meant to be illustrative and only briefly summary the relevant materials in each case study. Specific questions about a case study need to be addressed to the EPA office or region that sponsored the project. Additional information about each case study is available in the "Selected References" section that follows each case study description.

2. Recommendation for Enhanced Utilization of PRA in EPA.

The recommendations on page 22 of the document describe training resources to educate risk managers at the Agency. These recommendations lack any mention of regulated stakeholders.

We recommend that the Agency not implement such a program without stakeholder participation….The implementation of any probabilistic risk assessment tool developed by the Agency should also include adequate documentation in the form of technical manuals and user guides that describe all aspects of the PRA tool.

Response:
Stakeholder participation is an integral part and required in any Agency regulatory development process. The white paper is not meant to provide regulatory guidance for decision making. The intent of the white paper is to provide general reference and descriptive information about Agency PRA use.

3. PRA Variability and Uncertainty.

EPA's Office of Research and Development, National Exposure Research Laboratory is to be commended for providing concise documentation for the SHEDS PRA model and addressing uncertainty and variability in a complex model used to evaluate pesticide exposures and the risk assessment process. We look forward to additional development of graphical data to describe the uncertainty and variability, and hope that the developers open the peer review process to interested stakeholders.

Response:
No response necessary.