Final Reviewer Comments

External Peer Review of the

Framework for Human Health Risk Assessment to Inform Decision Making

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I. INTRODUCTION

Federal regulatory agencies often rely on risk assessments as the primary component in their decision-making processes. In order to ensure that human health risk assessments are conducted in a consistent and transparent manner, EPA has developed a *Framework for Human Health Risk Assessment to Inform Decision Making*. This document was produced by a Technical Panel of the EPA Risk Assessment Forum (RAF).

The purpose of the document is to describe a framework for conducting human health risk assessments that are responsive to needs of decision making processes in the U.S. Environmental Protection Agency. The document does not present either a checklist or a compendium or requirements. Rather it includes issues to consider, provides suggested questions to ask during risk assessment planning and execution, and identifies some useful practices.

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II. CHARGE TO REVIEWERS

The EPA RAF is a standing committee of EPA senior scientists established to promote Agency-wide consensus on difficult and controversial risk assessment issues. The RAF has been tasked with formally establishing a framework describing the process for developing human health risk assessments to inform environmental decision making at the EPA. The National Research Council (NRC), in the 2009 report *Science and Decisions: Advancing Risk Assessment*, recommended that to improve the utility of risk assessment that EPA adopt a framework for risk-based decision-making that explicitly recognizes the role of initial problem formulation and scoping, as well as, upfront identification of risk-management options as part of the risk assessment process.

Building from the Agency's experience and NRC's recommendations, the *Framework for Human Health Risk Assessment to Inform Decision Making* is intended to identify the critical aspects of the risk assessment process within a formal albeit flexible structure. The *Framework* is not intended to be an exhaustive reference on all relevant risk assessment guidance. Rather, the *Framework* is intended to clearly describe the overall process, with attention to critical aspects of each component, giving relatively more attention to the description of the less technical and more process-associated components, while identifying relevant references for the more technical components. A draft of the *Framework* is being made available at this time for the purpose of external peer review. At the completion of the external peer review process, the document will be revised in consideration of peer review comments and finalized for publication.

Charge Questions

Please provide a detailed explanation for responses to the charge questions listed below, focusing your recommendations on improving the use, technical robustness, clarity, and efficacy of the document. Please organize your comments in the same order as the charge questions as all comments will be compiled into a comment booklet to be distributed to all panel members and the EPA prior to the public meeting. We encourage you to clearly identify the point of reference in the document, by section number and page, in your comments.

1. Please review and comment on whether the draft *Framework* document adequately captures, describes, and reasonably organizes the key components of the risk assessment process from the perspective of informing environmental decision making to protect human health. Does the draft document appropriately describe the assessment structure, with adequate reference to salient policies, guidance and methods, so as to provide a useful reference for the EPA risk assessors, risk managers, and stakeholders?

2. The *Framework* figure is intended to encompass the broad range of risk assessment contexts and associated approaches within the EPA that includes site-specific assessment for hazardous waste site clean-up decisions under Superfund, as well as national-scale assessments for national air or drinking water standards under those respective statutes. With this in mind, please comment on the adequacy of the *Framework* figure in depicting the key aspects of the *Framework* and the role of these components of the *Framework* in the process of risk assessment. With regard to the aspects listed below,

please comment on the effectiveness of the use of the figure within the document (including the expanded versions located throughout the document), providing any suggestions for enhancement:

a) Accommodation of the Agency's broad scope of work under multiple legal mandates;
b) Recognition of the often iterative nature of risk assessment;
c) Presentation of "Fit for Purpose" as an essential aspect of a risk assessment, and consequently an essential consideration in the process; and
d) Addressing needs of the risk assessor as well as the risk managers, stakeholders and others who need to understand the risk assessment process.

3. Please comment on the extent that the *Framework* addresses the recommendations in *Science and Decisions: Advancing Risk Assessment* (NRC, 2009) related to improving the design and utility of risk assessments.

4. Does the *Framework* document include any scientific or technical inaccuracies in its presentation or description of terminology, assessment structure or methods? Please identify any problem areas and propose revisions or other actions that will result in a scientifically sound document.

5. Please review and comment on the methods and approaches presented in the *Framework*. Do they adequately accommodate consideration of state of the science and provide the flexibility for such accommodation with regard to:

a) Future tools and approaches?
b) Environmental justice and children's health protection concerns?
c) Advances in sustainability and technology innovation?

6. Do you recommend that any additional Agency references or examples be included in the document?

7. Please comment on the overall flow and presentation of the document. Is the document readable, searchable and understandable? Is the level of detail appropriate to the stated purpose of the document?

III. GENERAL IMPRESSIONS

Michael A. Callahan

To start with the positive aspects, the draft Framework is written well, looks nice, and does not have many typos. What is says is technically correct and competent.

Nevertheless, this draft Framework is a disappointment, not for what it contains but for what is missing. EPA has established a precedent for framework documents, which in the past have pushed the science and looked to the future. For example, the *Framework for Ecological Risk Assessment* introduced "problem formulation" into the risk assessment process and spoke to non-chemical stressors in ecological assessment. The *Framework for Cumulative Risk Assessment* introduced the concept of vulnerability to the risk assessment process, as well as discussing non-chemical stressors for human assessments. The Framework being reviewed seems more focused on historical methods, looking back rather than pushing science or looking to the future.

Secondly, for a document titled *Framework for Human Health Risk Assessment to inform Decision Making,* it gives almost all the space to reviewing Human Health Risk Assessment and almost no attention to decision making. This is the lost opportunity for this document to push the science and encourage something new and better for the future. There is (a) no evidence in the document that decision makers were asked what they would like to see and what would be helpful in a risk assessment; and (b) there is no guidance in the document about what risk assessment practitioners need to do to make the assessment useful to decision makers, nor any discussion of what new requirements would be added to make the risk assessment "fit for purpose." Some examples of these requirements might be that the assessment answers specific questions decision makers posed at the planning stage, or the assessment provides clear ways to differentiate among options for action (or the option of no action), or that the assessment specifically addresses the concerns of stakeholders.

Peter L. deFur

Generally, the document is well written and clear. I have a few suggestions to improve:

- Be sure that every use of the word "this" is followed by a noun, to avoid ambiguity and improve clarity.
- Some areas of the text have recommendations for conducting human health risk assessments, yet the language is directive and leaves this reader with the impression that the authors (the Agency) wants the risk assessors to think about or consider some important feature. I would be better able to act on the "recommendation" if the wording clearly stated what the reader should or could do.

This Framework document adds to the existing risk assessment guidance from EPA in a few ways. The Introductory statement and several places in the Framework could point out how the present Framework adds and what the addition serves and why. One major feature that is positive and obvious right away is that this conceptual framework builds on and incorporates characteristics of ecological as well as human health risk assessments.

The Framework would be greatly enhanced by addition of a section that advises risk assessment teams to note and document what the assessment cannot do or will not be addressing. This section is not terribly long, but I think is needed. Not all situations can be assessed with a risk assessment because of one or more logistical factors. This Framework would do well to explicitly address the topic.

Are risk assessments appropriate and necessary in all cases? Sometimes, at least, an exposure assessment is all that is completed, or an effects estimation is the crucial piece of information needed for a decision. In other cases, a risk assessment is an option, but various legal or regulatory considerations can negate the real need for a full risk assessment.

NRC (1996) recommended evaluating risk assessments according to three criteria: substance (science), process and participation. The current Framework document would do well to add these three elements in as design characteristics.

Too much hands-on meddling by or interference from the management level directed to the assessment team can (and often does) alter the conduct and outcome of the RA. By the same token, if the RA is senior, or has greater influence, the influence may go in the other direction. In either case, the RA and RM need to be “fire walled” from each other sufficiently to prevent inappropriate influence.

The RA Framework has to be institutionalized if it is to make a difference. In my experience, all EPA regions currently do not apply existing guidance in the same way, making me nervous that this new Framework has a good chance of not receiving the same level of attention and implementation. Somehow, EPA HQ needs to find a way to have all regions use the Framework document in offices and programs that employ risk assessment.

Page XI:

"Risk characterization: This final, integrative step provides risk managers with a useful, synthesized, set of conclusions about the risk that has been assessed. It is judged by four principles: transparency, clarity, consistency and reasonableness. "

I am sure that I expect more of the RCh than what is described here. I expect to read quantitative (if possible) and qualitative descriptions of risk, explanation of uncertainty and a statement of likelihood, and ideally a numerical probability. NRC also notes the need for science, process and participants to be covered in the RCh.

Penelope A. Fenner-Crisp

This draft Framework document represents a quality product that is head and shoulders above many other Agency efforts. It is spot-on in capturing the history of the development and application of previously-released policy and guidance documents that comprise the background substance for this Framework--including previous iterations of frameworks. It clearly and succinctly counters any criticisms leveled in the past that the Agency may have been "sitting on its hands," so to speak, instead of developing and implementing comprehensive approaches to risk assessment and regulatory decision-making. It provides substantial evidence to show that

not only has a lot of effort gone into developing approaches, as much or more effort has gone into their implementation in many program areas. As noted in the document, whole categories of environmental agents have been addressed, using variations of a comprehensive approach, tailored for the specific situation (e.g., pesticide registration and registration review, HAPs residual risk determinations, drinking water MCLs).

As noted below, the approach taken in writing the document – simple, straight-forward, spare text coupled with text boxes cited relevant references which provide the specific (sometimes, excruciating) details – results in a product easy to read and easy to use to communicate the Agency's approach to the use of, and place for, risk assessment in the decision-making process.

There were no instances in which this reviewer took issue with the conclusions presented.

Patricia M. McGinnis

I appreciate the challenges faced by the EPA committee that authored the Framework, including those to balance the regulatory and statutory requirements of various program offices and historical/ongoing processes for human health risk assessment within the Agency with the recommendations of the NRC (2009). While the intent of the NRC recommendations is to stream line and focus human health risk assessment, there is the potential that the recommendations could enlarge or broaden the scope and depth of EPA risk assessments. Taken too far, the recommendation could lead to paralysis through over-planning and formulation rather than paralysis by analysis. Developing a framework to address the NRC recommendations becomes particularly challenging given the resource-limited environment (whether that be research, data, staff, time, budget) that the Agency currently faces.

The resultant Framework, envisioned to describe an overarching process wherein existing EPA guidance can be implemented, was designed to be broad and flexible. The Framework also takes into account that human health risk assessment must match the scientific depth of the analysis with the depth/complexity/breadth of the risk management decision that needs to be made (so the scope of the risk assessment might narrow in some cases). The intended outcome in implementation of the Framework is for human health risk assessments to be appropriately “fit” or sized to the need of the environmental problem. Additionally, the risk is to be characterized in useable form for risk managers to make relevant and appropriate decisions.

The Framework document is clearly written, well-organized, captures the key components of the risk assessment process, and clearly represents significant consideration and effort on the part of the committee. As a high-level overview, the Framework provides maximum flexibility (so that in some cases it can “retrofit” to existing processes). However, the broadness of the current Framework may lead to inconsistency in application across programs within the Agency. While not being prescriptive, the Framework could be more directive and provide further examples. It is not written to a depth where it could be implemented by some risk management/assessment teams or readily understood by stakeholders or the public. While guidances and policies, and other resources are listed, the Framework does not convey when or how these could/should not be applied. Perhaps this is because the Agency intends to issue further guidance or procedures? Clarification or statements are needed in the Framework as to whether the Agency will develop further guidance or procedures to implement the Framework. If additional guidance is not

forthcoming, then how/when does one discern which existing guidelines, policies, guidance issue papers to apply within the Framework?

Several additions to the Framework could add to its robustness:

- Additional text boxes, diagrams and tables (see Charge Questions #1, 2, 5, 6, 7)
- Two or three hypothetical or generic case studies

Charles A. Menzie

The document provides a comprehensive overview of risk assessment approaches nested within a proposed "framework." The main feature of the Framework is to put forth a common structure for EPA risk assessments while also recognizing that these will differ somewhat based on "fit" for a decision or regulatory need. The most significant contribution of this Framework is that it recognizes a single risk assessment approach that can accommodate all risk assessment approaches across the Agency. In some cases, this approach would be "behind the scenes" as when a program office is developing criteria; in other situations the approach could inform policies; and finally, the approach would serve to support risks assessments of individual stressors (chemical and others) as well as multiple stressor or cumulative risk assessments. In short, a single framework would accommodate these and would permit a common language to be used.

I think the information is accurate.

I do not believe the document offers "conclusions" but rather proposes a path forward.

The document accomplishes two things:

1. Provides a common approach for risk assessments that relies upon terms and steps that make sense. Essentially, these reflect the evolving understanding of steps needed to produce a useful risk assessment that can inform a decision. The document does a good job at pointing out how assessments may differ.

2. Provides a nice set of links to various guidance documents.

While the document is useful as a resource, I think it is too long for providing a succinct framework and is light on the nature of EPA decisions and the manner in which risk assessment is intended to inform them. I also think that the assessment does not deal enough with understanding the full scope of risks related to decisions. The document handles other risk management factors at the end and indicates these are outside the bounds. I don't agree. A risk assessment that is outside the management process (or just a line of information to consider) is not well integrated and may not be as useful as one that is. I also don't think the assessment provides enough information on phased approaches. The Framework would benefit from more up-front discussion of the nature of decisions and how risk assessment can inform them. I agree with other commenters that the document would benefit from input from individuals in the Agency that commonly make decisions or formulate policies.

An additional key feature of the Famework is the emphasis given to problem formulation. Much of the discussion the panel had on "fit for purpose" and my comments on understanding the decisions can be addressed by folding these into problem formulation. Problem formulation is also the place to consider how best to approach the assessment (e.g., using a tiered approach or the value of a probabilistic approach). Therefore, I think in addition to the provision of a common structure for risk assessments, the document would greatly benefit from a more thorough development of the problem formulation. This should be the part of the assessment within which there is discussion regarding 1) purpose, 2) how best to inform the decision, 3) general approach, and 4) the need to consider other management factors to make the risk assessment information most useful for decision-making. In short, I would place all of these activities within problem formulation and eliminate the confusion caused by a separate fit for purpose step.

Gregory M. Paoli

Overall, the EPA document is well-organized, well written and makes good use of exhibits such as text boxes and figures. One negative component of the document is that it is constantly making reference to other documents such that in places (not everywhere), it seems to read more like a webpage whose sole purpose is to provide links to other documents. The balance between the description of the Framework and the linkages to other documents seems to lean more toward the latter at times.

With respect to the soundness of the conclusions, this is addressed below. As an overall comment on the document, it would be very useful if the document could point out where, if at all, it deviates from past guidance, or past practice. There is no succinct answer to the question, which might colloquially be phrased, "What's new here?"

The Framework contains some expanded thinking on the design of risk assessment, but is largely silent on any other component of risk assessment. The change to the overall understanding of risk assessment is sufficiently small as to make questionable the consideration of it as a "new framework" particularly if no significant changes are made to the expectations for, or the practice of, the core risk assessment steps, as a consequence of adopting this framework. The authors may believe that the changes are substantial and will have a significant impact, but it is not clearly stated what the expected impacts will be. The document must admit to some shortcomings that are addressed by the Framework, if it is to be seen as having any real impact on practice.

IV. RESPONSE TO CHARGE QUESTIONS

Question 1. Please review and comment on whether the draft Framework document adequately captures, describes, and reasonably organizes the key components of the risk assessment process from the perspective of informing environmental decision making to protect human health. Does the draft document appropriately describe the assessment structure, with adequate reference to salient policies, guidance and methods, so as to provide a useful reference for the EPA risk assessors, risk managers, and stakeholders?

Michael A. Callahan

As a list of guidance documents, the Framework succeeds. As a primer on risk assessment structure, the Framework succeeds. As a guide to crafting risk assessment to inform decision makers, it fails fairly spectacularly. There are no criteria for what a risk assessment that's made for informing risk assessors looks like, just vague questions. Someone needs to do some work in this area to find out before a framework that claims to be about the subject gets published.

Peter L. deFur

Yes to the question. I do have a few suggestions for further improvements that enhance or add to the current document.

Having read the Framework twice, I find that the document is complete, concise and accurate, appropriately covering the material. I will use this document for new employees, interns, in class and in dealing with Agency efforts. The authors are to be commended.

I recommend lists or checklists for ease and to avoid confusion. Lists also give the newer assessors a benchmark.

Some references and boxes are a distraction – I suggest moving to appendices if possible. Check the way text reads with and without the text boxes.

Penelope A. Fenner-Crisp

In this reviewer's mind, the draft document is one of the best that has been crafted by the Agency in a very long time. It reflects an intelligent and substantial understanding of the risk assessment process, as it should be practiced to achieve the goal of protection of human health, based upon consideration of relevant credible science and other information. It nicely avoids the usual outcome of endless detail weighing down the message by presenting the information efficiently, then deferring to the relevant references cited in easily-identified accompanying text boxes as the source of those details if desired by the reader.

This is not a "How-to" document. But, then, it's not meant to be one. Those can be found elsewhere. And, as is evident, the relevant material is cited, but not laboriously summarized, in the document. This Framework document is intended to serve as a summary vision of, and roadmap for, a process composed of a number of parts and an articulation of how those parts relate to one another. An understanding of the Framework will be a necessary prerequisite for

participation in its implementation of a specific case, no matter what role one will be playing-internal or external to the Agency.

The Framework is presented and described in an orderly, logical way, pegged at an optimal level of detail.

During the course of the peer review meeting, one or two of the reviewers noted that the text boxes containing lists of the EPA documents relevant to the topic under discussion were a distraction/interruption to the flow for them. The suggestion that these boxes be removed from the body of the text and reformatted into appendices is a good one. There could be a separate appendix for each subject (e.g., Text Boxes 1-2, 2-1, 2-2, 2-5, 2-6, 2-8, etc.). The integrated reference section beginning on page 61 of the draft document should be retained.

Patricia M. McGinnis

The Framework document is clearly written, well-organized and captures the key components of the risk assessment process. The assessment structure is adequate and is similar in structure to the *Guidelines for Ecological Risk Assessment* (and Framework) (US EPA, 1998) and the *Framework for Cumulative Risk A*ssessment (US EPA, 2003). It is a thorough and useful compendium of guidelines, issue papers and policy memorandums throughout the Agency's history for risk managers, risk assessors and stakeholders. The Framework presents a process for human health risk assessment at a very high level. While useful as an overview, it is not presented at a sufficient level for those who would have the charge to implement or operationally manage the risk assessment process described therein. The salient references are provided, the overall broad structure is set, but the next level down – the level between the overview and the detailed implementation of the various guidelines – is missing. When are the guidelines applied? Text boxes note, for example, other framework documents (Text Box 1-2) references and examples for planning and scoping (Text Box 2-1 and 2-2), but how does the team involved in planning and scoping choose amongst the options? Is there one that represents "best practices" or is "best of breed?" Without providing too many details, the next step or level that leads the team to the relevant guideline seems key to implementing the framework. Can common or important elements be teased-out and delineated in the Framework, perhaps as additional figures showing expansion of the various elements? Without additional direction in the Framework, it may not be possible to have a consistent application of the process across the Agency.

Charles A. Menzie

The document provides a very useful and I think more complete overview of how human health risk assessment should be considered. And this structure accommodates other assessments – ecological, multiple stressor, integrated, and cumulative. However, the document does not spend enough space to discuss linkage between the risk assessment and decision making. I think that linkage could be stronger and could be integrated with other risk management factors. This can all be accommodated by writing a more comprehensive problem formulation piece (for the document) that explicitly discusses the decision context for the assessment. The "fit for use" component **does not fit** and should be eliminated. That idea – fitting the assessment to the

problem and to the needs of the decision – is typically an aspect of problem formulation and should be incorporated into that part of the Framework.

Gregory M. Paoli

Overall, the document meets the above objective. The core aspects of risk assessment are minimally covered (not surprising for a framework document) and are consistent with the stated purpose of the document. The main question is whether the document adds sufficient new content to justify the notion that it is a new "Framework."

The document is somewhat heavy on 'process' as opposed to developing any important conceptual content, though this is not unexpected given the Framework's stated intent of focusing on the design of risk assessment and the goal of maximizing utility for decision-makers, similar to *Science and Decisions* (NRC, 2009). Given that any changes to risk assessment practice are expected to come in the form of new or updated guidance documents under the umbrella of this Framework, this should be stated early in the document, so that the reader is not expecting to see them here.

Question 2. The Framework figure is intended to encompass the broad range of risk assessment contexts and associated approaches within the EPA that includes site-specific assessment for hazardous waste site clean-up decisions under Superfund, as well as national-scale assessments for national air or drinking water standards under those respective statutes. With this in mind, please comment on the adequacy of the Framework figure in depicting the key aspects of the Framework and the role of these components of the Framework in the process of risk assessment. With regard to the aspects listed below, please comment on the effectiveness of the use of the figure within the document (including the expanded versions located throughout the document), providing any suggestions for enhancement:

- ***a) Accommodation of the Agency's broad scope of work under multiple legal mandates;***
- ***b) Recognition of the often iterative nature of risk assessment;***
- ***c) Presentation of "Fit for Purpose" as an essential aspect of a risk assessment, and consequently an essential consideration in the process; and***
- ***d) Addressing needs of the risk assessor as well as the risk managers, stakeholders and others who need to understand the risk assessment process.***

Michael A. Callahan

a) This diagram is like many that have appeared in EPA guidelines and frameworks over the years. Like them, it is so broad, it can accommodate any program.

b) The diagram is so brief it doesn't really highlight the iterative nature outside of having arrows pointing everywhere. Very few will intuit the iterative nature of risk assessment from the bare bones of the diagram. Not that they should; no one will be doing risk assessment solely from that diagram.

c) "Fit for Purpose" is a bad term. It is a coined term nobody has heard before and has little intuitive "eureka" meaning. (And please, if the document must claim repeatedly that the phrase comes from NRC (2009), provide a specific page reference. Word search does not find it at all in that document.) In addition, "fit for purpose" is presented like a step in the process, which it is not. It is a mind set to be applied to what is happening in the process (see more detailed comments below). I realize that without "Fit for Purpose" in there, the diagram becomes just one of the many generic risk assessment diagrams. What *should* be happening in the diagram is that the planning step for "an assessment that informs decision makers" generates a lot of *extra specific requirements* for the assessment to fulfill if it is to be useful for decision making. How well it meets these requirements will be a measure of its usefulness for decision makers. The decision makers will be the ultimate judges of how well it meets those requirements, so there should be a link between planning and the decision makers with an evaluation step.

d) The diagram is what it is, just like all the others like it. It won't help a lot for neophytes trying to understand risk assessment except in the most general way.

Peter L. deFur

The Figure is acceptable as it is, but there are two parts that are not yet perfect: the initiation or "signal" is not depicted at all. Without a starting point or a clearly labeled beginning, some ambiguity remains, especially for a naive reader.
Secondly, I do not find the term "Fit for Purpose" to be particularly useful. This feature is important, by all means and I heartily agree that risk assessments will be improved greatly by determining the fitness of the assessment. But my description would be that the design has to match the decision needs of the situation, leading me to explain that the design must match the decision.

Neither the figure nor the text includes a reference to a risk hypothesis, which is of course part of the conceptual model. Is this omission intentional or an oversight? I think the risk hypothesis helps frame the assessment and focus the work on what the team believes to be the causal relationship(s).

“Fit for purpose” (I do not like the term, and suggest using “appropriate.”) is not a single step and certainly not confined to any part of the process. How can the figure portray application across all phases? Perhaps some symbol inside every box/step.

Multipurpose assessments may or do have different characteristics than single use or single purpose assessments. The Framework would be improved with a simple note to that effect.

The figure does not show iteration – can it?

Undue influence between RA and RM will be mitigated by larger groups with more members, open processes and a team approach.

Penelope A. Fenner-Crisp

The basic framework figure, displayed as Figure 1-1 (page 6), does not, as a stand-alone visual, convey the message that its application **"is intended to encompass the broad range of risk assessment contexts and associated approaches within the EPA that includes site-specific assessment for hazardous waste site clean-up decisions under Superfund, as well as, national-scale assessments for national air or drinking water standards under those respective statutes."** A knowledgeable reader may garner the hint of scope, if s/he is already aware of the NRC 2009 report's discussion of the concepts of "fit for purpose" and "utility" and is otherwise quite familiar with the structure, legislative authorities and responsibilities of the Agency. The basic figure reflects a view from high altitude-serving as the lid on an interesting and challenging potpourri of possibilities. Generally, it does provide a proper, but spare, introduction to the key elements of the risk assessment process and how they are envisioned to interact with one another. One aspect that could benefit from some additional "art," would be double-pointed arrows or something similar which would capture the iterative nature of the process. The current visual appears too linear, except for the relationship with stakeholder involvement.

On the other hand, inclusion of the subsequent figures which include the "exploded" text boxes introducing the key considerations of each of the components of the framework are very useful for summarizing what will be covered in each of these areas (i.e., Figures 2-1, 2-2, 3-1, 4-1 and 5-1). They mesh well with the accompanying text on these topics. A simple, but impactful device.

As was discussed during the peer review meeting, creating a figure which adequately conveys a complex process is very difficult, if not impossible. As noted earlier, the present one is too linear, although it is acknowledged that if one were to truly capture the iterative nature of this process, it would look like the scribbling of a two-year old. Dr. Paulson, the Agency's Science Advisor, commented that he had asked the design team in RTP to help the RAF writing team to devise a more compelling visual.

One specific area that drew a lot of attention and dissatisfaction was the "fit for purpose" box. Several reviewers didn't like the term and challenged the Agency to find another phrase that captures this principle. Whatever that choice of phrase may turn out to be, it would be better displayed in a wrap-around visual to emphasize the point that this element must be considered repeatedly at every step along the way.

Patricia M. McGinnis

The expanded versions showing Key Considerations for each key element (e.g. Figure 2-1, 2-2) are effective. A table that shows the goal and output/outcome for each element would add to the effectiveness.

The section on Conceptual Models (Problem Formulation) is at the appropriate level for the Framework. (Whereas, the specificity and details as described in Region 8 Superfund Technical Guidance [1995] for Site Conceptual Models is too detailed and at too low of a level for this Framework.) The Conceptual Model Section has more specificity than some of the other sections and describes not only the considerations, but provides a bulleted list of what one should include, and examples (Figures 2-3 and 2-4, and Text Box 2-9), and a list of resources. In contrast, the other component of Problem Formulation, Analysis Plan, does not show any examples or resource list that would be helpful to the risk assessment team or stakeholders.

A generic goal of each element in the Framework needs to be articulated. This may be most efficiently accomplished in a table that states the goal for that element and the outcomes/outputs (products), and then how that output feeds into the next step in the process. For example, the Cumulative Risk Assessment Framework (on page 24) shows a text box that lists the SAB's desired outputs for Problem Formulation for an environmental decision-making exercise. A similar table conveying the hypothetical output of a problem formulation for a human health risk assessment would enable the risk assessment team and stakeholders to better visualize this element. Text Box 3-9, page 38 of the Ecological Framework, shows management goals and may be another example that could be adapted to this Framework.

Involvement of the public, stakeholders and community at various stages of the risk assessment process is thoroughly considered in Section 4 of the Framework. Peer review/consultation of Planning and Scoping and Problem Formulation elements would seem particularly useful to the

Agency prior to undertaking the Risk Assessment. I'm not sure to what extent that is currently practiced.

How do programs like HPV and SIDS (or other tiered approaches) fit into Framework?

It seems that development of schedules and milestones would be important elements of Planning and Scoping, but no mention is made of those in the Framework (see *NAAQS Integrated Review Plan for Particulate Matter*, 2008).

Charles A. Menzie

With the removal of "fit for use," I think the figure is appropriate. It might be useful to distinguish between situations where the figure is used to underpin programs and situations where it is used for specific assessments. For the former, the process may occur "in the background" and serve to support a policy.

A better job can be done at reflecting iterative approaches. This might be accomplished by incorporating this idea within the Framework, by including this as an aspect of problem formulation or scoping, or by simply footnoting this thought.

Fit for purpose is important, but this also drives the need for particular types of assessments that may not have all the elements reflected in the figure. I suggest eliminating this component and instead weaving this concept into problem formulation. That is actually how this is dealt with for most risk assessments.

I think the figure provides a useful starting place for discussion and communication.

Gregory M. Paoli

a) The document maintains a very broad perspective to avoid limiting its scope to certain programs or assessment types. Inevitably, perhaps, this is both a strength and a weakness. It certainly achieves breadth, but at the expense of depth.

b) The figure, itself, does not imply a great deal of iteration. With no arrows indicating a feedback loop, iteration may be assumed but it is definitely not explicit based solely on the figure. The fact that the "fit for purpose" part of the figure is located alongside the risk assessment phase may imply iteration, but that would be speculation on the part of the reader.

   While the document makes specific reference to iterative aspects of risk assessment, this is not stressed by the figure. A key question of "fit-for-purpose" assessment is establishing a sufficiently robust basis for stopping a risk assessment, since there will always be an inclination to tinker with various aspects of the risk assessment to achieve some technical improvement, or to accommodate some newly available data or theory or stakeholder input. As important as iteration may be, the need to provide timely information should be equally stressed, in the figure and in the text. A loop concept, with an explicit decision point for

establishing "sufficient" (far from perfect) information to support decision-making. This might also help to explain some aspects of the "fit-for-purpose" concept.

c) The figure is somewhat confusing in a number of regards:

- A section of the diagram entitled "planning and scoping and problem formulation" (PS&PF) suggests that this is one step, but in the text these are distinct steps.
- By placing the PS&PF title above the text "Risk Assessment," it is not clear whether the PS&PF comes entirely before Risk Assessment, or if it is considered the first step in Risk Assessment.
- The grey box with the dotted border has an ambiguous relationship with the other boxes. One might assume that the box refers to "Fit for Purpose" assessment (linking the risk assessment to the decision), but this is far from clear given that the box contains many other words with equally bold text. It may be possible to link the "fit for purpose" with the concept of "iteration" to indicate that the process is continually monitored for "fitness" until this is satisfied and then it proceeds to the "informing decisions" phase.
- In short, the role of the concept of "Fit for Purpose" is not made clear by the figure.
- As discussed below, the Informing Decisions may be illustrated as an outcome rather than a "Step" since it appears, as written, to be largely redundant to Risk Characterization.

d) The figure makes clear that the risk manager is the primary audience of the risk assessment, which is appropriate and consistent with the Framework. By simply providing two-ended arrows between the risk assessment process and stakeholders, the figure says essentially nothing about how various stakeholders might expect to participate in the process, though this is so variable as to be impossible to communicate in a figure. It seems likely that most stakeholders could understand the risk assessment process, especially with the various sub-figures that expand on the various elements of risk assessment with regards to what question each element of risk assessment is intended to answer.

EPA may want to find a way to indicate in the figure that public, stakeholder and community involvement is not a significant part of every risk assessment at every stage, as the figure suggests. Determining the costs and benefits of various roles for stakeholders and the public should be part of the risk assessment design process and can be included under the umbrella of "fit for purpose" considerations.

Question 3. Please comment on the extent that the Framework addresses the recommendations in Science and Decisions: Advancing Risk Assessment (NRC, 2009) related to improving the design and utility of risk assessments.

Michael A. Callahan

Ostensibly, this is *the purpose of this document*. The document was requested of EPA in Chapter 8 of NRC (2009) by nearly this exact title. In the Executive Summary of the Framework, it gives two purposes:

1. [The Framework] is intended to facilitate implementation of existing [U.S. EPA] guidance for conducting human health risk assessments, and

2. To improve the utility of risk assessments in the risk assessment process.

Unfortunately, when reading the draft Framework, the fact that this is being written to emphasize the use of risk assessment in decision making is mostly lost in an avalanche of EPA guidance and risk assessment steps. Nor do all the things requested by NRC in Chapter 8 (and 9, which seems related but defined out of this Framework) seem to be included in the draft Framework. The Framework, as now written, reads like a primer in risk assessment, including links to guidelines and guidance on various topics (the links are done quite well, by the way), but little else.

Most of the specific recommendations in NRC (2009) have been ignored or at best partly addressed. For example, on page 58, 3rd bullet of NRC (2009), it recommends that EPA establish training programs on risk assessment and decision making. This Framework is silent on that recommendation, even though it is highly relevant to this subject matter. Even assuming that the only references in NRC (2009) to be addressed are those from Chapter 8 (page 256), these were only partly or not at all addressed.

Peter L. deFur

Pretty much addresses the NRC recommendations.

A lot of emphasis is placed on Chapter 8 from NRC 2009, *Science and Decisions* – too much so? The Preface or Introduction to the Framework is a good place to provide a few brief sentences explaining the context relating the NRC book and the Framework document.

Penelope A. Fenner-Crisp

In Chapter 8 of the 2009 NRC report, there is a figure (Figure 8-1) depicting a "framework for risk-based decision-making that maximizes the utility of risk assessment." To this reader of the NRC report, the accompanying text in the NRC report suggests that this framework is a new and novel approach. The draft EPA Framework indirectly and quietly dispels this notion, by including reference to many relevant and key Agency policy and guidance documents that were developed and issued *prior* to the publication of the 2009 NRC report (e. g., Text boxes 2-1, 2-2, 2-5, 2-7, 2-8, 2-11, 2-12, 2-13), along with a few others issued since. These documents, in the

collective, address the concepts presented in the NRC's Phase I: Problem Formulation and Scoping and Phase II: Planning and Conduct of Risk Assessment, as well as provisions for stakeholder involvement. The topics related to NRC's Phase III: Risk Management generally have been imbedded in the other areas by EPA. The NRC framework, however, did incorporate a level of detail not seen in most of EPA's previous framework documents, including specific questions in each of the three phases. That difference has now been mitigated by inclusion of the expanded figures and accompanying text in the present draft Framework.

The present document adequately presents and describes those few new NRC recommendations, that is, those related to fit for purpose and utility, with which the Agency agrees and now proposes to incorporate into its Framework principles going forward. These are captured visually in text boxes (e.g., 2-15) and summarized in the accompanying text.

During the peer review meeting, a significant amount of time was spent discussing the concepts of Problem Formulation and Planning and Scoping, the order in which each should occur or whether one was actually imbedded in the other. Taking the reviewers' and public commenters' feedback into consideration, the Agency will have to reach a decision on how these aspects will be displayed and discussed. However that turns out, it is imperative that the Agency clearly define these two concepts and articulate why they have decided to present them as they do. They should not feel compelled to accept the NRC's version of this component of a framework if it does not/will not reflect the Agency's current or future practices.

Patricia M. McGinnis

The NRC charge was to propose ways to improve risk assessment at EPA. Recommendations were focused primarily in two areas: technical (Chapters 4-7 of Silver Book: Variability and Uncertainty, Unified Approach to Dose-Response Assessments, Selection and Use of Defaults, Implementing Cumulative Risk Assessment) and in the design and utility or risk assessment (Chapters 3 and 8 of Silver Book: Design of Risk Assessments, and Improving the Utility of Risk Assessment). EPA has made significant strides in addressing the recommendations related to design and utility of risk assessments.

The Framework places considerable emphasis on both the design and utility of human health risk assessment with the inclusion of the elements of Planning and Scoping and Problem Formulation. It is consistently emphasized in the Framework that the design level and complexity of the risk assessment should be consistent with goals of decision-making in order to increase the relevance (utility) of products of risk assessment. More specifically, development of the Framework demonstrates EPA's commitment to the committee's recommendation for Design (page 90, Silver Book) to "strengthen its commitment to risk-assessment planning" "by formalizing and implementing planning and scoping and problem formulation in human health risk assessment". NRC recommendations for adoption of formal VOI methods were not addressed in the Framework; these however, seem more appropriate as the subject matter for subsequent EPA guidance.

In Chapter 8 of the Silver Book (page 255), NRC offers the following recommendations:

- "The technical framework for risk assessment presented in the Red Book should remain intact but should be embedded in a broader framework in which risk assessment is used principally to help to discriminate among risk-management options.
- The framework for risk-based decision-making (Figure 8-1) should have as its core elements a problem-formulation and scoping phase in which the available risk-management options are identified, a planning and assessment phase in which risk-assessment tools are used to determine risks under existing conditions and with proposed options, and a management phase in which risk and nonrisk information is integrated to inform choices among options.
- EPA should develop multiple guidance documents relevant to the framework, including a more expansive development of the framework itself (with explicit steps to determine the appropriate scope of the risk assessment), formal provisions for stakeholder involvement at all stages, and methods for options development that ensure that a wide array of options will be formally evaluated.
- EPA should phase in the use of the framework with a series of demonstration projects that apply the framework and that determine the degree to which the approach meets the needs of the Agency risk managers, and how risk-management conclusions differ as a result of the revised orientation."

EPA has addressed the first two recommendations for utility of risk assessment. The EPA Framework bears many similarities to that proposed by NRC (Figure 8-1). It is not clear whether EPA will develop multiple guidance documents relevant to the Framework, or conduct demonstration projects.

The Framework very briefly touches on Variability and Uncertainty (Section 2.2.2.5) and provides some Agency resources, but does not address the NRC's technical recommendations. Perhaps these recommendations are the subject of forthcoming guidance from EPA?

Charles A. Menzie

I believe the Framework is consistent with those recommendations and emphasis on planning. I would expand the problem formulation part of the Framework to provide a richer discussion of the decision context and how to insure that the assessment is providing the right content and form of information.

Gregory M. Paoli

In a general sense, the Framework addresses the recommendations relatively thoroughly as they pertain to the design and utility of risk assessments. Notably absent are the notions of "stopping criteria" for risk assessments, and the concept of value of information. These are not critical, though would be useful in operationalizing the concept of "fit for purpose."

This question is addressed in more details, together with Question 4, below.

Question 4. Does the Framework document include any scientific or technical inaccuracies in its presentation or description of terminology, assessment structure or methods? Please identify any problem areas and propose revisions or other actions that will result in a scientifically sound document.

Michael A. Callahan

The document is sound for what it covers, which is mostly restatements of old material. The problem is that it covers so little new ground and gives so little guidance in the very topic it was designed to cover (see #3).

Peter L. deFur

None found thus far.

Penelope A. Fenner-Crisp

The answer to the question is "No." While one might take issue with the nature and accuracy of the content of one or more of the technical guidance and policy documents cited as resources for implementation of the Framework, it is outside of the scope of this document and its review to offer a fix to those problems.

Patricia M. McGinnis

I did not see any scientific or technical inaccuracies. Please clarify: it seems that at least some part of Hazard Identification occurs in Scoping and Problem Formulation prior to the Effects Assessment.

Charles A. Menzie

I did not detect inaccuracies. My main concern with the document is utility. It may be too long. I feel that much of the document is a restatement of old materials and that detracts from the impact of the document. A shorter crisper document that addresses the key ideas is more desirable than a catalogue. The key ideas are: 1) common structure, 2) a problem formulation step that connects the assessment to the decision and/or management context, and 3) aligning elements of the assessment with the needs of the decision/management as articulated in problem formulation. Therefore, the assessment could have shortened sections on exposure, effects, etc. and direct the reader to supporting appendices for links to historical documents that may be of value. Problem formulation discussion should be expanded and perhaps the figure could include key bullets such as “define decision context”.

I think the Framework does miss the concept of holistic risk assessment including the possible need to consider countervailing risks. Those ideas can again be aspects of problem formulation.

Gregory M. Paoli

Overall, the Framework could be much clearer as to what precisely is expected in the early phases of risk assessment (or pre-risk assessment, a semantic question largely but worth clarifying). While this process is somewhat hard to specify, it might be more clearly communicated in the form of particular "deliverables" from each step. For example, "Products from planning and scoping (e.g., the conceptual model and analysis plan), …" Based on other text, the P&S process results in a much more ambiguous deliverable described as "scope," "boundaries" and so on, whereas the Problem Formulation phase results in the conceptual model and analysis plan.

The framework has P&S coming before PF, which is consistent with past EPA guidance (in ecological risk assessment for example). As discussed below, it may be worth considering whether the distinction between P&S & PF can be meaningfully maintained.

The Framework makes reference at various points to "overarching considerations" such as Children's Environmental Health, Sustainability, and Environmental Justice, to suggest that these are very important things that all risk assessments should attempt to include. At the same time, the Framework provides no real content to address these topics which suggests that the status quo of risk assessment activities that support these considerations would be considered appropriate. Given that the working linkage between Risk Assessment and Sustainability is quite vague and of limited penetration into standard risk assessment practice, the Framework would suggest no change to that situation. Without something in the Framework to provide a path forward, there is little real movement in this direction.

<u>Section 2.1.1: Context, Purpose and Scope</u>

This section provides an opportunity to include a broader scope of questions that might trigger a risk assessment. The context described in the section as examples, "environmental events, newly identified circumstances of potential public health concern," are largely reactionary as opposed to preventative triggers. If risk assessment is to be a true contribution to Sustainability or Environmental Justice, the risk assessment process needs to be opened up to questions which are entirely different and not merely reacting to newly identified problems. Risk assessment can be constructed to support proactive decision-making: instead of asking "How much impact can we tolerate from product/chemical X?" the question would be "How can society achieve benefit Y, with the least adverse impact on people and the environment?" Here, benefit Y would be the presumed reason for tolerating any exposure to product/chemical X, but in this context/purpose/scope, chemical X is but one of several ways of achieving benefit Y. A similar argument can be made for questions of environmental justice. The incremental approach (one chemical, one media, one time point, one exposure route) is the means by which environmental injustice can creep in over time, and is how we get to the point of requiring special consideration of environmental injustices. No specific tool, approach or expectation is suggested for accommodating a consideration of environmental justice other than its reiteration as an overarching consideration.

The key here is that the Framework is largely silent on contexts/purposes/scopes of this type. One might reasonably ask if the reader should take seriously the Framework's intent to be particularly accommodating to the "overarching concerns" that are described.

Section 2.1.4: Decision Points and Scientific Peer Review

The concept of "Decision Points" is not elaborated beyond the idea that peer review may be considered at multiple points. Given that the entire section is about peer review, the additional concept of a "decision point" is not needed since the reader might expect something more than just a decision about whether to, or when to, peer review a risk assessment.

Section 2.1.6: Past Experiences and Assessments

Given the desire for consistency, efficiency, timeliness and other attributes of utility, this reviewer was struck by the lack of attention (or lack of emphasis) on this tremendous resource. The Risk Assessment Forum should consider how often the Agency is conducting a risk assessment that is truly novel in any regard. Moreover, the Forum should consider how often they are conducting a risk assessment for which a significant portion of the conceptual, scientific, biological, behavioral and mathematical constructs have not been used many times before. This question could become one of the first questions that arise during the design phase of a risk assessment: "Which component of the risk assessment is expected to be, in any important way, truly novel for which no prototypes exist?" One might surmise that the number of truly novel risk assessment elements is rather a small proportion of the risk assessment activity. The analysts in a particular situation could reasonably be asked to justify why they would not simply re-use conceptual model elements, computation algorithms, software and full risk assessment templates from recent risk assessments of similar scope. Similarly, it might be worthwhile to suggest that a key efficiency in risk assessment is to use tools that are, technically speaking, very transparent and user-friendly to be updated given new information.

Planning and Scoping (Figure 2-1) refers, in the "Key Considerations" box, to the question, "What are the Risk Management Goals?" This question may be considered to transcend the line between risk assessment and risk management, whereas the question, "What options are under consideration by the risk manager?" might be considered a "safer question to be pondered by the risk assessor. It also reinforces the statement in the document (and as the document cites *Science and Decisions*) that a key purpose is to help the decision-maker "discriminate among risk management options." This is a key question of the border between RM and RA, and is a key component of the definition of "fit for purpose."

Overall Question for the Section on Planning and Scoping

The section on Planning and Scoping makes reference to a great deal of interaction between the risk assessor and the risk manager to foster an assessment approach that is "fit for purpose." In addition, the assessor and risk manager are expected to be mindful of the important distinctions between their roles. Given that the concept of "fit for purpose" relies heavily on the concept of knowing what would be helpful to the decision-maker, yet the decision-maker is not to be prescriptive of scientific judgment and activity, there is a great deal of success and failure

relying on the notion of an exchange of information between the risk assessor and the risk manager.

The key operational question is: What precisely does a risk assessor need to know about the decision from the risk manager in order to meet the oft-cited, but poorly defined, goal of producing a risk assessment that is "fit for purpose" in "informing the decision?" Is it sufficient to simply have a meeting, get a vague notion of what the risk manager is trying to achieve, understand various legal constraints, get a vague notion of what timeframe is involved and then go back and do the same risk assessment you would have otherwise done? If not, the Framework should suggest what sorts of decisions or determinations that are executed by a risk assessor would be appropriately influenced by the risk manager. How exactly is the risk manager expected to influence the risk assessment?

One must also address: In what ways should a risk manager NOT influence a risk assessment? Can the risk manager narrow the scope of a risk assessment even if it excludes an important source, pathway, or route of exposure just because they deem that it is not "in scope"? Can a risk manager exclude the contemplation of countervailing risk (e.g., product substitution, disinfection byproducts versus microbes, transfers of pollutants from one media to another) even if the risk assessor has reason to believe that the countervailing risk is important and worse than the risk being controlled?

Equivalently, it is important to consider what elements of risk management should not be usurped by the risk assessor. Who should decide what level of biological change should be considered sufficiently adverse to provide the basis for a protective limit? Who should decide what level of certainty should be considered "reasonable certainty"? What percentile of the population should be protected? When, if ever, is the number 95% an appropriate default number for establishing percentiles of variability among humans or confidence limits in quantitative criteria when dealing with matters of public health protection? Should the IRIS process provide one number, or a set of numbers that have different levels of protection associated with them, in order to avoid making hidden policy determinations that are ultimately matters of societal value judgment?

By placing a premium on the value of frequent and non-trivial interaction between risk assessor and risk manager, and at the same time mandating that their differing roles be "respected," the Framework puts the science-policy interface directly at center-stage. Currently, the Framework is largely devoid of guidance in this area, even by example. These are difficult issues to be sure, but it is the essential ingredient to successful implementation of the Framework's vision.

Section 2.2: Problem Formulation

The main deliverables of the problem formulation activity in the Framework are the conceptual model and the analysis plan. The conceptual model, as described, is largely focused on the source-pathway-route-endpoint combinations that will be considered in the model. This set of combinations might be considered the technical "scope" of the risk assessment. As such, it is not clear what elements of scope are decided in the "Planning and Scoping" phase.

One impression of the various activities described in the PS&PF sections is that the distinction amongst all of these activities is very blurry and may be practically non-existent or highly variable across activities. The relative order and role of these two activities is different between past EPA guidance and the framework espoused in *Science & Decisions*. Rather than trying to choose between conformance with past guidance and accommodation of S&D, by allocating specific determinations to each named activity, and to strictly order them in what should probably be (and probably is) a highly iterative set of activities and decisions, it may be worth simply dropping the distinction and focusing on the output of the process. Exactly ***How*** one arrives at an appropriate set of risk metrics, decisions as to how to treat population variability, what percentile of the population to protect, and critical questions of scope are far more important than the order in which they are done, or the label one chooses to assign to the activity. For example, on page 35, the Framework suggests that, "The upper end of the distribution used for risk characterization may vary depending on the needs of the assessment (e.g., the 90^{th}, 95^{th} or 99^{th} percentiles). This, as just one example, is a critical determination which is not, by usual understanding of the distinction between assessor and manager, a decision to be made by risk assessors. However, there is little guidance as to how this number should be chosen, with the consequence that the 95^{th} percentile is chosen (though it seems "scientific" by sheer repetition) except when otherwise specified (and it very rarely is). Such a determination could be made by the risk assessor, the risk manager, or could be determined in advance during the PS&PF stage. If the Framework is to have real impact on "informing decisions" while "respecting roles," this type of issue needs considerable attention.

In sum, the Risk Assessment Forum may wish to merge these two activities into one overall activity without attempting to clearly delineate which specific determinations are made during Planning and Scoping and which during Problem Formulation. By specifying the goals and deliverables of the activity, the purpose of the activities can be described without making distinctions that perhaps don't exist in reality, and to provide flexibility going forward for implementation of the Framework.

Section 2.2.2.5: Uncertainty and Variability

This section is so brief as to be essentially absent from the Framework. The distinct impression left by the document is that uncertainty and variability are minor features or trivial details of risk assessment. In many cases, the greatest challenge in risk management decision-making is making complex tradeoff decisions (cost, benefit, risk-risk) while coping with the extent of uncertainty, particularly as it pertains to the extent of variability. The primary ethical obligations of the risk assessor are to ensure that they have adequately accounted for (often through computation) and described the extent of variability in risk, and specifically to describe the uncertainty in the levels of protection (to individuals and the population) that are afforded by different risk management options (including choices of exposure thresholds like RfDs and RfCs).

As with other essentially technical sections, the authors should consider stating high level expectations for the treatment of variability and uncertainty in risk assessment, even if the details are left to other guidance material.

Section 2.3: Fit for Purpose

The bulleted list at the bottom of the page includes two bullets which seem identical. "Does the assessment [meet/have] the … [objectives/attributes] identified in [problem formulation/planning]?" This is suggestive of the lack of any meaningful concrete distinction between these two phases (P&S versus PF). What attributes in 'planning' would not be found as objectives or attributes in the problem formulation step?

The last bullet, "Does the assessment inform choices among risk management options…?" is the essential characteristic of "fit for purpose" as long as "informing decisions" is the primary goal. Many of the other bullets are off-topic ("How will it be communicated?", "Was it appropriately peer reviewed and responded to?"), or otherwise redundant to this determination.

The Framework dedicates a half-page to the notion of a distinction between risk assessor and risk managers, with strong references to "in no way … influenced" and "does not allow for the manipulation." While these distinctions are important, EPA should also indicate how it manages inappropriate influences in the opposite direction, where risk assessors inappropriately "influence" or "manipulate" determinations that should be the purview of risk managers. There are considerable opportunities for risk assessors to make choices that prescribe risk management determinations with little consultation with the risk management function.

A significant fraction of what might be described as risk management determinations (e.g., choosing the level of protection in the form of percentiles of the population and the level of confidence in establishing a threshold value) are essentially made by scientific staff with no explicit guidance on the level of protection that is desired. In this rather influential part of EPA's activities, there is considerable influence of risk assessors into value judgments that would by most definitions lay clearly on the risk management side of the "conceptual distinction." While this is not an easy challenge to overcome, it is certainly a key consideration if the "conceptual distinction" is to be held up as a significant pillar in EPA's design of risk assessment processes.

Section 3: Risk Assessment

The first paragraph revisits the question of whether the problem formulation activities (specifically the development and, as indicated, frequent revision of the conceptual model and analysis plan) are actually distinct from the risk assessment process, or if they should be more properly considered the first step in risk assessment that is frequently revisited. It is difficult to argue that a decision to update the conceptual model and revisit the analysis plan is somehow distinct from the task of risk assessment itself.

Section 3.1: Exposure Assessment

The level of detail for exposure assessment (1/2 page, and one small text box) is quite low, in an absolute sense and relative to the discussion of effects assessment. While it is understood that other guidance material will provide the details, the Framework should provide some expectations for this activity, otherwise it is not really "framing" anything beyond mimicking the table of contents of a risk assessment.

One key element of exposure assessment is the appropriate consideration of variability in exposures, in order to adequately address the relative frequency of what may be disproportionately high exposure in a small fraction of the population of interest. These exposures are important in their own right (e.g., in meeting the obligation to appropriately describe extreme exposures in the population) and in the fact that they may contribute in large measure to the overall population risk. Failure to adequately describe such extremes can lead to an inevitable failure to adequately characterize risk.

As such, one would expect the Framework to establish some sort of minimal standard for what is to be achieved in an exposure assessment. For example, Box 3-1 provides the example of Monte Carlo simulation as an optional exercise to be considered if the analyst so chooses. The Framework could set the expectation that the exposure assessment derive estimates of the probabilities of extremes in exposure through appropriate means such as Monte Carlo analysis, or demonstrate how exposure variability can be *appropriately* estimated through other equivalent means. At present, the Framework suggests "anything goes."

Section 3.2.2: Dose-Response Assessment

A section on dose-response assessment that is less than a full page, while providing no indication or framing discussion of how EPA might estimate dose-response differently, is unexpected. With no change in the process (let alone expectations, or even aspirations) of dose-response assessment, it is difficult to imagine how the Framework will lead to any significant change in the information provided to decision-makers.

The only indication that the Framework provides of any contemplation of changes to risk assessment are in Text Box 2-4: Risk Assessment for Economic Benefits Analysis. This box suggests that during the conduct of economic benefits analysis one might include:

- "Identifying a set of human health endpoints that are economically meaningful …"
- "Estimating changes in the probabilities of human health outcomes rather than measures such as reference doses and reference concentrations that do not estimate potential risk…"
- "Producing expected or central estimates of risk … rather than conservative estimates"

The key question for EPA to clarify, in the description of the framework, is whether they would assign any merit to these two activities outside of the context of an economic benefits analysis? The apparent indication from the inclusion of these key issues in this Text Box (and nowhere else) is that if they were to do such analysis it would be because "the economists made us do it." It would be desirable if EPA could address this issue head-on and not hidden within a Text Box dedicated to "economic benefits analysis." Everyone at EPA and every stakeholder would benefit each and every time EPA could explain what an RfD or RfC actually means in terms of public health protection. One does not require a formal economic analysis to have an interest in a quantifiable meaning for these critical intermediate products of risk assessment.

Section 3.3: Risk Characterization

The section on Risk Characterization suggests a largely narrative process of "integration" and "synthesis." It should be stressed that there can (or should) be a significant computational

component to the exercise, particularly if variability and uncertainty are to be appropriately accounted for.

The section refers frequently to "qualitative or quantitative" expressions of risk. Essentially, up to this point in the document, there is very little or no mention of the outcome of risk assessment being a qualitative expression of risk, and every reason to believe that the result should be quantitative. If qualitative risk assessment is to be understood as an important and frequent outcome, some guidance is surely needed, and some mention of the pros and cons of each earlier in the document, particularly during the "fit for purpose" discussion.

Section 5: Informing Decisions

The distinction between Section 5 and "Risk Characterization" is unclear. If the risk characterization is following the conceptual model and the analysis plan, then the characterization of risks for risk management options should be entirely embedded in the process of risk characterization (making Section 5.1 redundant). If the intent is to have a section on communication issues, this might be a better title and focus, but this is dealt with in Section 4. As it is, the entire steps would seem to be largely redundant to the conduct of a full risk characterization that includes quantitative and narrative components. The bulleted list on page 57 simply reiterates the content of the narrative component of a risk characterization.

Given that Section 5.2 simply refers to the fact that there are other issues involved in decision-making (a point made earlier), the whole of Section 5 might be considered redundant.

Question 5. Please review and comment on the methods and approaches presented in the Framework. Do they adequately accommodate consideration of state of the science and provide the flexibility for such accommodation with regard to:

a) Future tools and approaches?
b) Environmental justice and children's health protection concerns?
c) Advances in sustainability and technology innovation?

Michael A. Callahan

Future tools and approaches are largely ignored in favor of past ways of doing business. Nothing is said about possible game-changers such as the -omics research. Other than a definition, nothing much is said about non-chemical cumulative risk or why that might be done, what an environmental justice assessment might be about, what sustainability means in terms of risk assessment or decision making, etc. Right now, there is a definition or two and some references, but there is no answer to "why should I bother to concern myself with new technologies or approaches?" "What might they have to offer to risk assessment?" Even more important, "How might these new tools or approaches change the way decisions are made at EPA?" With the current document, one is left with the impression that they won't change anything.

Peter L. deFur

All three of the above areas are in the document in some form or fashion, and future developments or additions could easily be added to the present document without any major structural modifications.

The last section (5.2) on other factors needs to more specifically address the above 3 elements, especially justice, equity and sustainability.

Children's risk, environmental justice, sustainability and cumulative risk are briefly covered in the Framework, but the sections are not satisfying for a risk assessor who needs direction on how to account for each of these factors. I suggest providing some language, just a sentence or two for each that indicates the current options for addressing these four areas.

Add some language explaining how and where to account for children, environmental justice, full scope sustainability and cumulative risk, e.g. during the planning and by recognizing the appropriate factors in the analysis.

Penelope A. Fenner-Crisp

The draft text actually says relatively little about these three areas with regard to specific methods and approaches, other than providing definitions where needed and including citation of relevant documents, along with inferring a commitment to incorporate consideration of these areas in the risk assessment process, as appropriate. This level of detail is consistent with the treatment of topics elsewhere in the document. If the reader needs/wants more detail, then s/he can consult the relevant references cited.

Upon further reflection on comments from some of the other peer reviewers, I agree with the criticism that these areas seem to be included as "blow-off" afterthoughts that might or might not be addressed in a risk assessment. This impression might be dispelled if some brief examples were included on children's health, noting, for instance, that women of childbearing age are factored into every pesticide occupational risk assessment (>700), and specific "findings" for children are made for every pesticide tolerance assessment (~10, 000) or drinking water health advisory and standard (>200). In addition, environmental justice issues surface frequently in Superfund or hazardous waste site clean-up cases. Is there, in fact, an example in which sustainability has been integrated into the assessment and decision process?

Patricia M. McGinnis

The Framework, because it is so broad and flexible, appears to adequately accommodate future tools, environmental justice, children's health, sustainability and technology innovation. Relevant guidance documents are cited in accompanying text boxes (2-5, 2-6) for those sections. Citations in the text of the Environmental Justice Section could also be put into a text box.

Charles A. Menzie

The document is a framework and as such should be able to accommodate all of these. I think the introduction and problem formulation sections should indicate that these are aspects that might be included.

The document provides a useful portal to various approaches. I would suggest a much shorter document to help with clarity and relegate much of the meat of the document to a set of supporting appendices where the reader could find useful links for specific applications.

Gregory M. Paoli

The actual Framework does not contain sufficient detail to extrapolate how these issues might be accommodated. While there is some reference to current and future in vitro toxicity testing paradigms, there is no indication of its role in the Framework apart from the expectation of relying on defaults until the science is well understood (which might be seen as a clear indication of the Agency's level of interest in change).

Environmental justice is mentioned but no discernible change in the expectations for risk assessment practice is implied by the Framework. Children's Health Protection is addressed only by reference to past guidance and legislative requirements, but is not distinctly addressed as a matter of altered expectations for risk assessment in this Framework.

Sustainability is similarly addressed in the sense that there is no discernible change in the expectations for risk assessment practice. The fact that sustainability considerations and life cycle considerations are not in themselves one of the problem contexts that EPA includes in the planning and scoping section is further indication that no change in expectations are implied by the Framework.

Question 6. Do you recommend that any additional Agency references or examples be included in the document?

Michael A. Callahan

The bibliography is astonishingly one-sided with EPA references; one is loath to recommend yet others. Some outside references are needed for balance; research on risk assessment and especially the application of risk assessment to policy decisions has not taken place only within EPA for the past 30 years. If the idea is for the EPA document to contain the non-EPA references, a statement at the beginning of the reference section should be added to that effect.

Peter L. deFur

Yes. Two documents that are not Agency documents and would be helpful references, and that I use, are these:

Jasanoff, Sheila. 1986. *Risk Management and Political Culture: A Comparative Study of Science in the Policy Context.* Social Research Perspectives: Occasional Reports on Current Topics. Russel Sage Foundation. New York. 94p.

National Research Council (NRC). 1996. *Understanding Risk: Informing Decisions in a Democratic Society*. National Academy Press. Washington, DC. 249p.

Document flow is in places interrupted by citations and text boxes. I suggest minimizing the text boxes by placing some in appendices and incorporating others into the text, with the emphasis on how the text reads. Text boxes are not intended to be necessary, as are figures and tables. If the text box is removed, and the resulting document is greatly altered, then the box is necessary for the meaning and the authors should consider using a table, bullets or other device to present the information.

Hold a copy of each reference, for the record, so that if a source goes away or fails to maintain archives and records, EPA has a copy.

Penelope A. Fenner-Crisp

Examples relevant to most of the Agency's major legislative mandates are included in the paper-except for RCRA. Are there any RCRA examples that could be added?

Additionally, the existing examples are very Headquarters-focused. Only two regional examples are noted (Region VIII's PCBs Conceptual Model; Region III's MIRA Approach). Another one or two regional examples would be helpful in providing a broader and better balance of acknowledging past and ongoing activities representative of the Agency as a whole.

Patricia M. McGinnis

The authors were thorough in citing references and the reference section serves as a good compendium of Agency guidelines, policy issue papers, and current websites. However, some of

the references are websites containing numerous documents. This makes it confusing and frustrating for the reader to find the specific (or even most relevant) document that is referenced in the text. For example, U.S. EPA 2011n and 2011o list six and 29 documents, respectively. There may be others like this; only the specific reference for the text should be cited. Ancillary references can be listed in an appendix.

The Framework would benefit from two to three hypothetical or generic case studies and further examples (text boxes or diagrams) for each of the key elements: Planning and Scoping and Problem Formulation (Conceptual Model and Analysis Plan), and Risk Assessment (Exposure and Effects Assessment, Risk Characterization). These additions would help those tasked with implementation of the Framework (within the Agency) as well as help stakeholders outside the Agency to better understand the process and expected outcomes. More examples like the Case Example for Review of the NAAQS in the text box on page 9 of the Framework are needed. Figures 2-3 and 2-4 are particularly helpful and illustrative of Conceptual Model outputs.

Charles A. Menzie

The document is light on putting forward the decision context and the nature of decision making and decision science. I suggest that these areas be expanded in the introduction and in the problem formulation sections. To that end, those sections would benefit from literature citations. I believe EPA has a number of documents that bear on these subjects.

I think that the extensive set of links to documents be placed in appendices that can be referenced briefly in the main body of the Framework. I find that these in-document references dilute the main messages and also imply that the cited documents are the ones to go to for guidance. These may be out of date or may go out of date. Thus, getting the key ideas down is important for the Framework, but the lists of links etc. can be relegated to examples of existing guidance that is potentially helpful. Placing these in a well-organized appendix would serve that purpose.

Gregory M. Paoli

On the contrary, the Framework should avoid becoming over-shadowed by more external references, unless its primary purpose is backward-looking as opposed to establishing a forward-looking framework. There is ample reference to EPA guidance documents.

Question 7. Please comment on the overall flow and presentation of the document. Is the document readable, searchable and understandable? Is the level of detail appropriate to the stated purpose of the document?

Michael A. Callahan

One cannot get into excruciating technical detail in a Framework document, so the level of detail is about right. The flow could be improved in some places. Certainly the short sections on public participation and communications do not belong at the end, as they are part of the planning process (see RAF white paper on Planning and Scoping done for the RAF's cumulative risk committee).

Peter L. deFur

The Framework is presented in the same format as risk assessment guidance documents and risk assessments themselves. As such, the structure of the document is straightforward, sensible, easy to follow and logical. I probably would have used a similar format and structure if I were to start this Framework document on my own. I did not search the document as if I were looking for advice on some aspect of the HHRA process, but I had no trouble moving through the document at all.

Please add a list of figures with page numbers to accompany the list of text boxes.

Take out text boxes in places to improve the flow of the reading process. Communication and public participation are part of the entire process and come in across the RA process.

Add a note/statement about the intentional alignment between ecological and human health risk assessments.

Penelope A. Fenner-Crisp

Yes. And, yes. As noted in this reviewer's comments to Question #1, the draft Framework hits the target for optimal level of detail, organization and length.

Patricia M. McGinnis

The Text boxes generally amplified points made in text or provided valuable resources.

An expanded figure for each element (such as Figures similar to Figure 2-1, page 15, Cumulative Risk Framework or Figure 1-2, page 5, Ecological Risk Framework) would be valuable to the risk management/assessment team, stakeholders and public.

Charles A. Menzie

The document is readable searchable and understandable. However, I suggest a reorganization to tighten up the main aspects, the addition of appendices, and the inclusion of materials on how risk assessment is used in decision-making in an integrated fashion.

Problem formulation should be a key focus as this step sets the stage for all types of assessments. Therefore, I recommend an expansion of this section and the inclusion of key themes and options here.

Gregory M. Paoli

The document is well produced (readable, understandable, and useful application of figures and text boxes, even if the central figure requires some improvement). Overall, the document would benefit greatly from clarifying altered expectations for the practice of risk assessment, even if the details of how those expectations will be met will be found in other, or future, guidance documents.

V. SPECIFIC OBSERVATIONS

Michael A. Callahan

Page	Paragraph or Line #	Comment or Question
x	1	The title of this Framework is at odds with the purposes listed in the first paragraph of the Executive Summary. I find it odd that the first purpose is to "facilitate the implementation of existing USEPA guidance." This is pursued relentlessly in this Framework, as guidance after guidance is cited, as if that alone will facilitate things. At the end of the first paragraph it says, "by citing and discussing existing guidance in the context of the full framework, this document is intended to foster increased implementation of Agency guidance." The actual purpose of this Framework, the one that was requested by the NRC in Chapters 8 & 9 of their report *Science and Decisions*, is "to improve the utility of risk assessment in the decision-making process." The first purpose above would not support writing a Framework document by itself. But it seems relatively little focus is on this second, and more important, purpose.
x	2	Planning and scoping. This notes that "a broad range of technical experts working as a team may be involved," yet participation is not presented as part of the planning stages in this report. Instead, it is shuffled off to the end as if it is an afterthought.
xi	2	Again, why is public participation not part of planning?
xi	4/4	I was unable to find the term "fit for purpose" in NRC (2009).
1-3	Sec. 1.1	This is mostly a listing of previous EPA and some NAS documents. This adds to the feeling that nothing is new here. Where is the discussion about how risk assessments interact with decision making? Is there no history of that?
3	Sec. 1.2.1, Sentence 1	The first sentence gives a different purpose from the first one in the Executive Summary. This is more like what was asked for by NRC (2009). Most of the following paragraph talks about previous guidance.
5	Para. 1	This summary dwells almost exclusively on existing guidance, and "improving" the *way it is used*. The final sentence brings in linking the planning to the decision to be made, but it is not the "major objective" here, seemingly.
6	Fig. 1-1	The only thing new here is the coined term "fit for purpose," which now seems to be a step in the process rather than a mind-set (i.e., a mindset similar to "data quality"). "Fit for Purpose" here is very confusing, and it is the *only* thing in this diagram that is new and part of what should be the main focus of this diagram, which is helping people construct risk assessments that inform decision making. That is not very evident in the diagram. See general comment 2c above.

Page	Paragraph or Line #	Comment or Question
6	Last para.	It would seem that at least a text box could be helpful here. What are the things that are helpful in constructing a risk assessment that informs decision making? It seems many of them are listed in this paragraph. These items listed here are discussed in much detail in the RAF white paper on Planning and Scoping (Lawrence Martin has this; it was accepted by EPA in early 2012). The text box could be constructed as "What does a risk assessment that informs decision making look like?" It has the following things... (1) a clear discussion of the specific environmental issue; (2) a clear discussion of the legal framework, etc. etc. This would be much more informative than just saying "fit for purpose", which hardly means anything to most people.
7	Para. 1	The following sentence is circular: A key aspect of the Framework, "fit for purpose," is consideration of the usefulness of the assessment for its intended purpose, to ensure that the assessment produced is suitable and useful for informing the needed decisions. In other words, consideration of the usefulness of the assessment ensures the assessment is useful. Actually, the *process employed for planning the assessment* should ensure that the assessment has *specific requirements* that need to be achieved if it is to be useful for decision making. It should consider the things necessary to make it useful (see recommended text box above). "Fit for purpose" doesn't help lift the fog here.
7	Para. 2	I realize the statement starting "Where there is a need for such review..." was adapted from the NRC (2009) diagram (e.g., Fig. 8-1), but this is not good wording for an EPA document here trying to say "we're doing things a new and better way." Many people outside the Agency would read this as an arrogant and condescending statement that says, in effect, outside participation (from, for example, communities) is likely to be of such poor quality that it compromises the assessment. While I realize this statement is literally true as it stands, it needs to be said differently.
7	Last para.	The communication strategy is tacked on to the very end of the process. This is not how it should work; it should start in the Planning phase - see RAF Planning and Scoping White Paper.
10	Sec. 2.1	RAF P&S white paper gives a more comprehensive history of P&S. It also gives an indication of what needs to be accomplished at each step. That is missing in this Framework. Instead of just citing guidance, it would be useful to indicate what needs to be accomplished at each step. By giving general guidance about what specifically needs to happen in each step, it gives the team flexibility in tailoring the assessment to make it happen in a way that's appropriate for that situation/purpose/technical abilities, etc.

Page	Paragraph or Line #	Comment or Question
15	First part para.	"That is, the utility of [the] risk assessment is a function of how well it informs the decision for which it was designed" again seems tautological: it's useful because it's useful. This whole section (2.2.1) seems to go around like that without really saying anything. How about a list of criteria for an assessment being useful? What makes it useful? The answer is *not* that someone has done a "fit to purpose" analysis. The answer will be things like: (1) it answers specific risk questions proposed by risk managers at the start of the process; (2) It provides clear ways to differentiate between a series of control and no-control decisions; (3) it specifically considers concerns of the stakeholders; (4)...
16	Sec. 2.1.2	Overarching considerations. While there's nothing specifically wrong with what is said about environmental justice, children's health, cumulative risk, and sustainability, there is a certain "tacked on" feel to these discussions as if these aren't really part of the risk assessment methodology, just some odd things that you might come across while doing a "real" assessment. If this Framework was really looking forward (like other frameworks), it would integrate these points into the whole, because they are all actually here today and becoming more important as time passes. The writers of this document need to choose whether they want a Framework that will stand up for many years, or one that will be quickly obsolete. In addition to citing guidance documents, there needs to be a discussion about what kind of decisions will need these kinds of analyses, and what types of questions need to be answered during planning to address these needs.
21	Sec. 2.1.3	When talking about the assessment team, I'm astonished that after all the effort EPA has made in the last 20 years about participation, outside-EPA coordination is still relegated to last, and then only if EPA is forced to do it: "Coordination with...other stakeholders also may appropriate, depending on the type of assessment." This viewpoint has a long history in EPA, and it is deeply imbedded in EPA culture. [It would be quite interesting to see a discussion here of what types of assessments need *no participation by anyone outside EPA*, and send it out for public comment to see who agrees.] Again, this gives the impression that nothing's changed at EPA. Indeed, NRC (2009) p.13, under "stakeholder involvement," makes a specific recommendation *for this document* that has been totally ignored.
24	Sec. 2.1.5	See above comment.
37	Sec. 2.2.2.5	Most of the sections, starting with 2.2.2.1, do little except cite EPA guidance documents. For a document that purports to have considered and incorporated the recommendations from NRC (2009), what happened to all the recommendations on uncertainty and variability (p. 121-122 of that book)?

Page	Paragraph or Line #	Comment or Question
38	Sec. 2.3	Again, I fail to find "fit for purpose" in NRC (2009) by doing word searches on that phrase or related phrases. For a term that is so widely used in this report and continually referenced to NRC (2009), please provide a specific reference somewhere. And again, this section (whatever it's called, and I hope it doesn't end up as "Fit for Purpose") would be much more useful to the reader if rather than a series of questions, there were a set of performance criteria established for such an assessment. These are the *criteria* for an assessment that informs decision making (see comment for page 15 above). Just because someone asks questions doesn't mean anything happens. Performance criteria are a different story; it either meets them or it doesn't. An example for the risk communication bullet for the planning stage might be: Development of a written communication plan, including who is authorized to speak for the project and who is responsible for coordination among team members and seeking collaboration from outside groups or individuals.
40-49	Sec. 3	There is little new here. Most of this was written 10-20 years ago. Where is the value added by discussing how this is related to decision making?
50-55	Sec. 4	Little new here; points to EPA guidance, mostly.
56-58	Sec. 5	This section would be a lot stronger if more than just talking about risk characterization (from a risk assessor's viewpoint) were discussed. For example, *from a decision maker's standpoint,* what constitutes an assessment that is useful for decision making? Has anyone asked them? What kind of *criteria* would they list? How can a document claim to be about making risk assessments more useful to decision makers when there's *nothing in it from the decision maker's point of view?* On this one point alone, this Framework fails.
60	Last para.	Flexible is one thing; saying so little that anyone can do what they want is another matter.
61-72	Refs.	The bibliography is almost devoid of any references that are not EPA, NAS, prepared for EPA, written by EPA scientists, or other government documents (I counted two outside documents in an 11-page reference section). The reason this Framework diverges so radically from other Frameworks in terms of the bibliography needs to be explained.

Peter L. deFur

Page	Paragraph or Line #	Comment or Question
7	Para. 1	The guidance calls on confirming the usefulness of the RA for management purposes, rather than waiting until the end and ask managers "Is this what you meant or wanted?" I understand the need for confirmation through the process and that confirmation must not mean that management can continually alter the RA process, substance or output. This step is ideally conducted by the RA team and only back to RM for clarification. EPA still has the problem of managers telling assessors what results can or will work for the decisions they want to make.
9	Box	I suggest removing the acronyms.
11		Planning and scoping to set the conditions of the assessment is not always such an agreeable process. In fact, when the input from stakeholders and interested parties is included, reaching agreement may be a long and arduous process. Note this fact.
17	Text box 2-4	The general message in this box is vague. Does the document mean to indicate that these analyses should be conducted, or conducted in this way? If so, then the text would be more clear by using more specific language.
17	Text box 2-4	Bullet 3 is not clear. The box presents considerations for economic benefits analysis and this bullet says: "Producing expected or central estimates of risk for a given population rather than conservative estimates. The *Science Advisory Board (SAB) Advisory on EPA's Superfund Benefits Analysis* highlights the issue of using conservative risk assessments in benefits analysis (U.S. EPA 2006b)." Does the bullet mean that the SAB issue is wrong? Or is the point simply that the difference between conservative and central tendency is significant and conservative assumptions will produce skewed benefits estimates?
38	Bullets	These bullet items are great evaluation questions and considerations. I suggest modifying the wording in such a way that the risk assessment team easily applies the questions before, during and after the risk assessment is conducted, as noted earlier in the document.
49	Text box 3-5	The section on cumulative risk needs additional language on what areas have not been developed, either within EPA or by professionals in the field. Many areas of cumulative risk assessment lack methods to truly combine different sorts of risk. Examples of situations that cannot be assessed include chemical and biological threats/risks; psycho-social and chemical risks; and predicting novel responses that only occur in complex cumulative risk situations. The field of risk assessment cannot directly assess these issues at present.

Page	Paragraph or Line #	Comment or Question
52-53	Sections 4.1.1 and 4.1.2	It is not clear to this reviewer how the Framework might address a systemic problem within EPA, but the topic should be raised in review. Community involvement is one of the most uneven and unpredictable features of EPA programs, across regional offices, among projects, and from program to program. Should this Framework be more directive and explicit, stating that there is no situation in which the public is to be actively excluded, treated with scorn or ignored?
58	Bullets	Justice and equity need to be included on the list of factors considered.

Penelope A. Fenner-Crisp

Page	Paragraph or Line #	Comment or Question
x	Line #2	Add "and future" after "existing," to reinforce the flexibility aspect of the Framework.
x	Line #6	After "(NRC, 2009)," add "and those put forth in earlier NRC reports (e.g., NRC, 1994)."
3	Line #3 in Sec.1.2.1	Add "and future" after "existing," to reinforce the flexibility aspect of the Framework.
6	Paragraph #1	This discussion infers that "signals" and possible subsequent activity come only after the agent is already "out there" in the environment. What's the signal for OPPT and OPP for new, not-yet released agents?
16	Last two sentences of Section 2.1.1	Not enough said about these two important elements. Enhanced discussion of cross-program (and, perhaps, also cross-government-both domestic and international) participation in a particular planning and scoping exercise should be made. The possibility of multi-media presence of an agent is high, and choices must be made as to who should be responsible for what tasks/decisions. For instance, characterization of relative source contribution would inform where the greatest source of exposure lies and biggest bang for remediation buck could be had; that reality should be dealt with collaboratively. OPPT has to make decisions related to Section 9 of TSCA- the mechanism by which regulatory responsibility is referred to another federal Agency. Furthermore, some Agency programs engage in work-share activities with outside governments (e.g. OPP with Health Canada's PMRA and the EU's EFSA). Also, in this section, there should be some discussion of the criteria/process by which a "hard stop" to activity can be imposed at certain points *before* every stage of Planning, Scoping, Problem Formulation and Risk Assessment is completed. Right now, the document reads as if one must complete all of these tasks before selecting a "do-little or nothing" option.

Page	Paragraph or Line #	Comment or Question
15	Line 4	Change the "and" to "a."
22	Second last line of last Para. in Section 2.1.3	Change "should" to "shall" or "must." Isn't the Agency now obligated to do this every time the issue of human data comes up?
24+	Section 2.1.5 and Text Box 2-7	The definitions seem a bit parochial and narrow. Too U.S.-centric. Need to acknowledge and include non-US bodies as potential partners such as Canada and Mexico via NAFTA; OECD; the EU via EFSA and ECHA; FAO, WHO and CODEX.
26	Line 8 of last Para.	Insert "may" between "among others," and "include." Not every chemical is a Q*'d carcinogen.
34	Line #1 of Para. 3 Last line of Para. 3	Replace "all" with "many." There are no risk assessment guidelines for a number of important, but generally ignored, toxicity endpoints such as those affecting the immune or cardiovascular systems, as well as outdated existing ones such as for mutagenicity. Put more oomph in this statement by replacing "may" with "should" or "shall."
36	Last line above Text Box and title of Text Box	Unless the resources listed in the text box include a discussion of risk communication and risk management in addition to risk assessment, these should be labeled risk *assessment* resources. "Risk analysis" currently is defined globally as a tripartite concept: risk assessment, risk management and risk communication.
41	End of last Para.	The sentence "Available toxicokinetic information also may be characterized and internal doses calculated." is present in the text twice.
53	Para. on IRIS	Isn't a step missing? Is there not a step between nomination and review and comment on draft assessments which provides the opportunity for entities to submit new or existing data for consideration in the assessment of potential hazard, with concomitant responsibility of the Agency to examine them and determine their appropriate role in the assessment?

Patricia M. McGinnis

Page	Paragraph or Line #	Comment or Question
xi 38	Line 4 of last paragraph First paragraph	While conceptually the NRC discusses “fit for purpose,” this term is actually not used the report (at least I didn’t see it in my recent reread. Need to rephrase as “conceptually refers to” rather than “uses the term.”
7	Line 1 of 2nd full paragraph	Suggest to replace “assessed via” with “evaluated via.”

Page	Paragraph or Line #	Comment or Question
12	Text Box 2-2	Please note that U.S. EPA 2011o is not a guidance document, but a web site listing approximately 30 documents, of which one of those relates to human health planning and scoping.
12	Text Box 2-2	Text in box needs further editing.
15	Line 4	Last sentence- delete "and."
20	Line 6, 2nd paragraph	Add "risk" after cumulative at end of sentence.
38	Line 9, 2nd paragraph	Clarify/Rephrase "…informational needs for the assessment are being met by the information being generated by the assessment."
42	Figure 3-1	Effects Assessment, first bullet. Replace "agents" with "stressors."

Charles A. Menzie

None provided.

Gregory M. Paoli

None provided.