Early Scientific Peer Consultation and Stakeholder Engagement in EPA's IRIS Assessment Process

Joseph V. Rodricks[1] and James Solyst[1]

[1]ENVIRON International Corporation, Arlington, VA 22203, USA

This article reviews some recent NAS reports, as well as internal EPA guidance and documents, and presents recommendations for improving both the IRIS product and process. Our principal recommendation is for greater stakeholder involvement, particularly early in the IRIS process. We believe this will result in more credible and widely accepted assessments, and help EPA address the issues cited in the NRC reports. Many stakeholders are at the forefront of methodological developments in risk assessment, and are able to offer useful input regarding emerging methods, such as weight-of–evidence evaluations of epidemiology, toxicology and mode-of-action data, and the application of mode-of-action data to improve the scientific basis for the various forms of extrapolation required to complete risk assessments. In addition, early stakeholder involvement increases the likelihood that the design of the assessment reflects the level and complexity necessary to inform the decision-making process. Greater attention on design in the formative stages of risk assessment, specifically during planning, scoping, and problem formulation, will result in a more useful and credible scientific product. As stated in one influential NRC report: "Good design involves bringing risk managers, risk assessors, and various stakeholders together early in the process to determine the major factors to be considered, the decision-making context, and the timeline and depth needed to ensure that the right questions are being asked in the context of the assessment." (1)

1. Overview and Current Situation Broadly

In recent years EPA's Integrated Risk Information System (IRIS) has received considerable attention from an impressive array of authorities and stakeholders, including Congressional committees, federal agencies, and the National Academy of Sciences (NAS). The reason for this attention is that the IRIS program produces toxicological assessments that are used to assess chemical risks, and those assessments are usually the principal scientific input to the decision-making process. As stated on the EPA web site: "Through the IRIS Program, EPA provides the highest quality science-based human health assessments to support the agency's regulatory activities." (2)

The decisions made by the EPA to regulate industrial chemicals and environmental contaminants often have huge economic and public health consequences, so the scientific bases for those decisions must be highly credible. Some NAS committees, operating from The National Research Council (NRC), have offered recommendations for improving the manner in which IRIS assessments are designed, and on the process the EPA employs in receiving and considering information and analysis from key stakeholders, including industry, NGOs, and the broad scientific community.

The EPA has conducted internal analyses of how it conducts risk assessments (3) and has funded several NAS committees to examine the risk assessment process in general, as well as specific IRIS assessments. The first of several risk-related reports was 1983's *Risk Assessment in the Federal Government: Managing the Process*, often referred to as the "Red Book." (4) Although this report was not funded by the agency, it established a pattern of EPA funding NAS committees and charging them with addressing aspects of the risk assessment process. These committees produced notable reports, including 1994's *Science and Judgment in Risk Assessment.* (5)

The trend of EPA relying upon NAS committees for advice on risk expanded in the past five years, and a handful of highly influential reports have been issued, including the 2009 "Silver Book", *Science and Decisions: Advancing Risk Assessment.* During this timeframe two other key reports were issued by committees established to examine cumulative risk (*Phthalates and Cumulative Risk Assessment:*

The Task Ahead) (6) and future data needs (*Toxicity Testing in the 21st Century: A Vision and a Strategy*) (7)*

The importance of the IRIS program was recognized early by the Obama administration, and EPA Administrator Lisa Jackson cited "Assuring the Safety of Chemicals" as one of seven priorities for EPA's future. The Administrator specifically references the IRIS program as a means of making "strong progress toward rigorous, peer-reviewed health assessments on dioxins, arsenic, formaldehyde, TCE and other substances of concern." (8)

Arguably the most influential NAS effort was conducted by the Committee to Review EPA's Draft IRIS Assessment of Formaldehyde; the report offered relatively serious criticisms of the EPA's description of and analytical support for its ultimate conclusions. The Committee also found it necessary to comment on the quality of IRIS assessments in general and the need for improvements. In its 2011 report *Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde* (9), the Committee devotes an entire chapter—Chapter 7, *A Roadmap for Revision*—to "general recommendations for changes" and "suggestions for improvements". The Committee also stated that: "The persistence of limitations of the IRIS assessment methods and reports is of concern, particularly in light of the continued evolution of risk assessment methods and the growing societal and legislative pressure to evaluate many more chemicals in an expedient manner."

Chapter 7 has received considerable attention and most importantly has been the subject of Congressional hearings and actions. The EPA testimony from the hearings commits the agency to fully addressing the suggestions in Chapter 7. In the aftermath of the attention received by the Formaldehyde report, EPA has announced it has funded the establishment of an NAS committee to conduct a review of the IRIS assessment development process, and of the changes that are currently being planned by EPA in response to recommendations set out in the formaldehyde report. The EPA also asked NAS to review current methods for weight-of-evidence analysis, and to recommend specific approaches for weighing scientific evidence for identifying chemical hazards and modes-of-action.

The agency has also asked its own Science Advisory Board (SAB) to form a new standing committee—SAB Chemical Assessment Advisory Committee (CAAC)—to provide advice regarding the development of IRIS assessments. The involvement of independent scientific bodies in seeking improvement to the IRIS program is essential, given the challenging environment that currently exists. Seemingly all IRIS stakeholders except NAS are perceived as having inherent conflicts that result in their actions and motives being questioned. The EPA itself is in the difficult position of defending the IRIS program against attack, while yet acknowledging the need for change.

The agency has offered testimony to Congress that it will implement the recommendations in Chapter 7 of the Formaldehyde report, but has so far not agreed with critics that it has an overly precautionary, default driven approach to conducting IRIS assessments. Industry is often viewed as obstructionist, interested only in slowing down the decision-making process. NGOs are often perceived as having extreme views that are driven primarily by precaution, not science.

Although some of the criticism and perceptions of EPA and key stakeholders is understandable, it is essential they be encouraged to work together to address the pressing issues identified by NAS and SAB committees. Scientists engaged in risk assessment-related studies, and who work in academia or for government or regulated parties, have and will continue to contribute to the development of risk assessment methodologies. Many are active in their respective scientific associations, and have served on NAS and other independent scientific committees, including those that produced the Red Book, Silver Book and the Formaldehyde report. Moreover, they have demonstrated a

* The "Silver Book" has a large Appendix listing all of the many NAS efforts, over 25 years, related to EPA's risk assessment programs.

willingness to work together in organizations such as the Alliance for Risk Assessment (ARA) that is a collaborative effort seeking to foster the development of technically sound risk assessments. The EPA should be encouraged to seek out and take maximum advantage of all such activities.

2. The Case for an IRIS Stakeholder Engagement Model

EPA, and particularly the IRIS program—which is organizationally part of the Office of Research and Development (ORD) National Center for Environmental Assessment (NCEA)—has responded to the recommendations offered in the NRC reports, particularly those from Chapter 7 of the Formaldehyde report. The changes EPA is committed to making will undoubtedly lead to more credible and useful IRIS assessments. However, the recommendations offered to date are just a fraction of what the agency can expect in the coming years.

The IRIS-related scientific review bodies being established at NAS and SAB will generate a great deal of interest within the scientific, governmental and political communities, including key Congressional committees, the General Accountability Office (GAO), and the White House Office of Management and Budget (OMB). This level of interest is a healthy and productive element of the governmental decision-making process.

During this time of change, it would be wise for the EPA to implement a formal process for stakeholder involvement that is truly based on dialogue and exchange of ideas. The key parties listed above have all addressed, and will likely continue to address, the critical role of stakeholders in the IRIS process. EPA has publically stated a willingness to engage stakeholders, but to date has not developed a process that allows the agency fully to benefit from stakeholder involvement.

There are two fundamental reasons why greater and more formal stakeholder engagement is beneficial: it demonstrates EPA's openness and a confidence that the IRIS program is headed in the right direction; and it provides a mechanism for the agency to receive information and analysis from professionals steeped in risk assessment and involved in related emerging scientific and methodological developments. All stakeholder involvement is not equal, and there will be some questionable science and judgment presented; but a truly open exchange of ideas between EPA and stakeholders should allow the agency to be able to separate the wheat from the chaff.

EPA, and its IRIS program, has historically had a process for receiving stakeholder input. EPA has relied upon stakeholders to serve on a variety of peer review activities. Stakeholders from academia, state government, and to a lesser extent industry and NGOs, serve on SAB committees and the Board of Scientific Counselors. Stakeholders, provided they don't have a conflict of interest, also serve on chemical specific peer review bodies, including those that review IRIS assessments.

The IRIS program staff also routinely meets with stakeholders that will be affected by a particular chemical assessment. Often these meetings provide an opportunity for a stakeholder to stress the importance of an assessment and how it could affect business or human health and the environment. These meetings are essential, and fundamental to an open and transparent process, but they do not necessarily result in the clarification of the scientific evidence essential for conducting an IRIS assessment. Too often these meetings involve only passive "listening" by EPA staff, not active engagement and attempts to work collaboratively to reach understanding of agreements and disagreements.

EPA also meets with scientific peers who have a considerable amount of information, research, and analysis that can greatly benefit the IRIS assessment process. Such peer consultations have a tremendous potential, and have been recognized by the agency as an integral part of future stakeholder engagement. As stated in the August 2011 *IRIS Progress Report*, EPA is committed to "add an early peer consultation

step to the IRIS draft development process. This will facilitate the early involvement of scientists in the draft development process, informing the development of early drafts of IRIS assessments." (10) The peer consultation concept is elaborated upon in the June 2012 report *EPA's IRIS Program: Progress Report and Report to Congress* (11) which describes how workshops will "focus on state-of-the-art science for a particular chemical or provide a forum for discussion with experts about certain cross-cutting scientific issues that may impact the development of a scientifically complex assessment."

The concept of early peer consultant is not a new idea: it has been recommended often, and is a major feature of the 2009 Silver Book (2). The importance of early peer consultation is cited throughout the report, but most notably in Chapter 3, *The Design of Risk* Assessment, which stresses the importance of EPA strengthening its commitment to risk-assessment planning. The committee concludes that increased attention to the design of risk assessment in its formative stages is needed, and states that "good design" involves "bringing risk managers, risk assessors, and various stakeholders together early in the process to determine the major factors to be considered, the decision-making context, and the timeline and depth needed to ensure that the right questions are being asked in the context of the assessment." Early peer consultation in the design phase, is viewed by the committee as an opportunity to improve the assessment process and product, not simply to demonstrate EPA's willingness to meet with stakeholders.

Of course it is one thing for a NAS committee to recommend early peer consultation and quite a different thing to actually design and implement a peer consultation process that withstands challenges from critics and also benefits the assessment process. And although EPA has publicly promised to establish an early peer consultation process, the agency has not scheduled a consultation nor described the goals and operations of the consultations. Stakeholders who would likely be invited to peer consultations have expressed great enthusiasm for the prospect, but are growing frustrated by the slow pace of implementation. Thus, the timing is right for EPA to accelerate the process and for stakeholders to offer their own model for a peer stakeholder process.

As the agency goes forward in accelerating the stakeholder involvement process it should acknowledge there are subtle but distinct differences between peer review, peer consultation, and peer engagement. Peer review, as conducted by EPA, is a formal, well-established process that is mandatory and typically results in an improved product, but could use some improvement (which is addressed later in this article). Peer consultation—as addressed in this article—is the concept of involving stakeholders early in the process to increase the quality and credibility of the assessment. Peer engagement presents a higher bar: it requires the stakeholder to be highly knowledgeable, to be a peer of the involved EPA scientists, thereby allowing for true and beneficial peer exchange

3. The Early Peer Consultation Model

As previously stated, the fundamental recommendation presented in this article is that early peer consultation with stakeholders will contribute to the preparation of a high quality assessment. It is reassuring that the IRIS program is committed to early peer consultation, but the process for achieving the commitment is still evolving. We suggest that in developing the process EPA follow the suggestions and framework presented in Chapter 3 of the NRC Silver Book. (2)

In Chapter 3, the Silver Book committee suggests that a key to ensuring EPA risk assessments provide the desired utility and are of high technical quality is to ensure the necessary "inputs" into the process are done early and follow well documented procedures. Of particular importance is the provision and application of the "best scientific evidence and methods", which EPA should "acquire and interpret" by "using established, trusted, and formal methods." EPA seemingly agrees with this suggestion to document information

collection and interpretation procedures, as demonstrated in its June 2012 Progress Report and Report to Congress, where a revised approach to literature search and weight of evidence is presented. The report describes a revised IRIS document structure that includes a detailed description of the literature search strategy and study evaluation process that EPA uses to develop IRIS assessments. The agency commits to describing how the scientific literature was gathered and emphasizing how studies were selected to be included in the document, and, if applicable, explain the rationale for excluding potentially relevant studies from the assessment.

Also in the June 2012 Progress Report and Report to Congress the agency states it is "taking a more systematic approach to analyze the available human and animal toxicity data in IRIS assessments" and is specifically developing a formal framework to establish conclusions about weight of evidence for health effects other than cancer. This is consistent with the core message of Chapter 3, which states that a formal framework informs the design phase of an EPA risk assessment. However, it is uncertain whether the EPA process for soliciting input from stakeholders will achieve the benefits addressed in Chapter 3 of the Silver Book.

EPA's approach for receiving stakeholder input regarding weight-of-evidence, as stated in the June 2012 Progress Report and Report to Congress, is to convene a workshop and "identify the various approaches that are currently in use and compare their strengths and weaknesses." Although this approach is necessary and possibly useful, it falls short of true peer consultation. Stakeholders will be allowed to provide written and oral comments but the workshop is by no means a collaborative effort; rather it is an EPA-designed and implemented event, to which stakeholders are invited.

The EPA designed workshop approach is also the basis for the proposed early peer consultations. As stated in the June 2012 Progress Report and Report to Congress, workshops will "enhance the input of the scientific community as assessments are designed." Although this is a commendable objective, the approach is designed to focus on scientific issues rather than the specific assessment of concern to a stakeholder. We believe both approaches—workshop addressing key scientific issues, and a design discussion with stakeholders—are necessary to achieve true peer consultation as envisioned in the NRC Silver Book and the NRC Formaldehyde report.

The protocol we recommend is that a peer consultation occurs during the development of the draft plan, when the agency is conducting data acquisition, determining the objective of the assessment, and preparing a data evaluation and analysis plan. We envision a meeting in which the agency describes how it is implementing the formal procedures it has developed relating to data analysis. EPA staff would describe how the procedures will be applied for each type of study (e.g., in vivo animal toxicological studies, in vitro mechanistic studies, epidemiological studies) to establish relevancy and reliability, with citations to applicable agency guidance. During this session EPA would describe the *a priori* inclusion/exclusion criteria that will be used to select the studies which meet the relevancy and reliability criteria. We assume that EPA would be able to describe the methods that will be used and be able to identify the most likely issues to be resolved. Particular attention would be paid to hazard identification and dose-response, including mode of action and extrapolation modeling. In addition, exposure assessment, uncertainty analysis, including defaults and data-derived methods would be addressed.

During this early peer consultation EPA would be presenting its "blue print" for the IRIS assessment, and providing assurance the assessment will be conducted in a timely fashion without jeopardizing technical quality. EPA should expect that stakeholders would be willing to accept the rules and contribute to ensuring the quality of the assessment. The resources stakeholders can devote to contributing to the process will vary, but the expectation should be that a subset of stakeholders—such as companies that manufacture and use the

substance being assessed—will provide useful research and analysis. EPA should anticipate, for example, that these stakeholders will provide studies that may not have been identified in the initial literature. It should also be expected that stakeholders will offer technical comments on the data acquisition strategy and methods of data analysis employed by the agency.

Stakeholders may also present ongoing or planned research that is relevant to key areas of the assessment and perhaps fill potential data gaps. The timing of such research can be problematic. The IRIS program is committed to preparing high quality assessments in a timely fashion. Stakeholder research may contribute to the quality of the assessment but could delay completion of the assessment, thereby helping one but impairing the other objective. Ideally, stakeholder research was initiated with the assessment timeframe in mind, and it would be hoped that EPA is willing to accommodate slight changes in the timeframe in order to improve the quality of the assessment.

If a stakeholder has been particularly vigilant and vocal about a methodological aspect of the assessment process the stakeholder should be prepared to provide research and analysis to make a compelling case. For example, many regulated parties have long denounced EPA's pattern of relying on default assumptions when chemical-specific scientific information is available. The chemical industry in particular has stated that adequate knowledge of a chemical's mode-of-action, coupled with an understanding of relevant background processes, would allow for the development of dose-response models with an acceptable degree of accuracy and precision. Industry has funded research that provides valuable insights into toxic modes-of-action and inter-and intra-species variability associated with specific chemicals. Such research often has as its objective the replacement of one or more generic defaults by chemical specific information. This is an issue highlighted in the Silver Book and in subsequent NRC reports.

The Silver Book, in Chapter 6, describes well the long-standing problem of apparently irreplaceable defaults. The 1983 Red Book made it clear that default assumptions are needed to make inferences in many areas of the risk assessment process where chemical-specific scientific information is lacking. The agency has specified a need for default assumptions used for difficult matters of extrapolations across species, from high-dose responses to low-dose responses, and to account for population variability in response. EPA has correctly stated that in the absence of chemical-specific data, risk assessments cannot be completed without invoking defaults.

But the Red Book itself, and more specifically the Silver Book, recognized that, with scientific advances, it is possible for research on specific chemicals to provide data that might be used to replace one or more defaults in the chemical risk assessment. This issue is very important for improving IRIS risk assessments, and much stakeholder research is focused on data (often mode-of-action data) that could be used to develop a more fully science-based, and less default-driven, assessment.

The Silver Book points out that although default replacement has had limited success at the EPA, the failure of the agency to specify the criteria that should be used to judge whether chemical-specific information can be used instead of the default assumption has resulted in major impediments to the creation of risk assessments that can be widely regarded as the best science can offer. Stakeholders with large investments in research sometimes find their work rejected by the EPA for unclear reasons.

This state-of-affairs is undesirable. The Silver Book recommended that the EPA establish clear criteria for judging the acceptability of scientific information intended to replace one or more defaults, and gave guidance to the agency on how this should be done. It seems essential for the EPA, working with stakeholders, to move ahead on this issue, to break a long-standing deadlock.

4. Peer Consultation beyond the Design Phase

Consultation with stakeholders should continue after the early data acquisition, evaluation and analysis meeting. Once a draft IRIS assessment is completed the agency should solicit review and comments, and anticipate meetings with stakeholders to discuss the draft. Those stakeholders who met with the agency during early peer consultation should be expected to comment on whether the consultation is reflected in the draft assessment. For example, is there an indication the agency fully considered the stakeholder's input relating to data analysis protocols and procedures, inclusion and exclusion criteria, mode-of-action, dose response analysis, and low-dose extrapolation methods.

Stakeholders should also be expected to comment on the EPA peer review process; particularly the charge questions given to the review panel. Of most importance, however, is how the agency responds to the review prepared by the peer review panel, as well as comments offered by stakeholders during the process. The agency should be empowered to make decisions regarding which peer review comments they find useful and applicable. However, the agency should at least respond to each credible comment and explain why the comment was not acted upon.

5. Conclusions

Stakeholder involvement—particularly during the assessment design phase—will improve the technical quality of an IRIS assessment. It will improve the scientific process, resulting in enhanced quality, consistency, and clarity of the assessment. The EPA promoted concept of early peer consultation is sound and has an opportunity to greatly enhance the assessment process. We believe the early peer consultation workshop approach will prove useful; however, EPA must also offer the opportunity for a single stakeholder to meet early in the process to comment on—and ideally contribute to—the data acquisition, evaluation and analysis plan.

The case we present clearly benefits the stakeholder; particularly the stakeholder that has evidence and analysis to share. But we feel the early peer consultation approach also greatly benefits the agency. In addition to gaining useful evidence, the stakeholder process may also result in greater acceptance of the assessment, certainly by the regulated community; but also perhaps by other key audiences, including Congress and the broad scientific community.

6. Acknowledgements

Support for preparation of this white paper was provided by the Center for Advancing Risk Assessment Science and Policy of the American Chemistry Council. For more information on the Center see: http://arasp.americanchemistry.com

References

1. National Research Council, Sciences and Decisions: Advancing Risk Assessment (2009) (Washington, DC: National Academies Press).

2. U.S. Environmental Protection Agency 2012. Integrated Risk Information System. Accessed June 2012, http://www.epa.gov/IRIS/

3. U.S. Environmental Protection Agency Risk Assessment Task Force, Examination of EPA Risk Assessment Principles and Practices (2004).

4. National Research Council, Risk Assessment in the Federal Government: Managing the Process (1983) (Washington, DC: National Academies Press).

5. National Research Council, Science and Judgment in Risk Assessment (1994) (Washington, DC: National Academies Press).

6. National Research Council, Phthalates and Cumulative Risk Assessment: The Tasks Ahead (2008) (Washington, DC: National Academies Press).

7. National Research Council, Toxicity Testing in the 21st Century: A Vision and a Strategy (2007) (Washington, DC: National Academies Press).

8. U.S. Environmental Protection Agency, Administrator's web site

9. National Research Council, Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde (2011) (Washington, DC: National Academies Press).

10. U.S. Environmental Protection Agency, August 2011 IRIS Progress Report (2011).

11. U.S. Environmental Protection Agency, EPA's IRIS Program: Progress Report and Report to Congress (2012).