



Beyond Science and Decisions: From Problem Formulation to Dose-Response Report from Workshop VII

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Webinar

Report Prepared By:

Toxicology Excellence for Risk Assessment (TERA)

Lead Rapporteur and Report Author : Oliver Kroner (kroner@tera.org)

Supporting Rapporteur: Lynne Haber

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Overview

The workshop series, *Beyond Science and Decisions: From Problem Formulation to Dose-Response* continues and expands upon the discussion initiated by the National Academy of Science report: *Science and Decisions: Advancement of Risk Assessment* (NRC, 2009). The workshops utilize a multi-stakeholder format to support the development of a practical and solution-oriented compendium of risk assessment methods. Conducted under the aegis of the Alliance for Risk Assessment (ARA), the workshop series explores both currently available and evolving methodologies, through the development and application of case studies. The workshop series is based on the fundamental premise that the appropriate methodologies for dose-response assessment need to be based on objectives specific to the intended application; this will include varying levels of analysis.

The workshop series continues to advance the framework of ARA (2012) on problem formulation and dose-response analysis (beta version available at <http://chemicalriskassessment.org/methods/>).

The purpose of this workshop report is to document and communicate the workshop results to the workshop participants and interested others. The report contains summaries of the Science Panel discussions with the authors of invited presentations. The draft Workshop report was reviewed by the panel and presenters, and their comments have been incorporated into the final report.

Science Panel

The standing Science Panel chosen by the ARA Steering Committee prior to Workshop IV continued its service for Workshop VII. Panel biographies are provided in Appendix 1, as well as at <http://www.allianceforrisk.org/Workshop/Panel.htm>. The Science Panel for Workshop VII consisted of the following:

- ▶ Michael L. Dourson, *Toxicology Excellence for Risk Assessment* (Co-chair)
- ▶ Annie M. Jarabek, *U.S. EPA, Office of Research and Development* (Co-chair)
- ▶ Richard Beauchamp, *Texas Department of State Health Services*
- ▶ James S. Bus, *The Dow Chemical Company*
- ▶ Rory Conolly, *U.S. EPA National Health and Environmental Effects Research Laboratory*
- ▶ R. Jeffrey Lewis, *ExxonMobil Biomedical Sciences, Inc.*
- ▶ Bette Meek, *McLaughlin Centre for Population Health Risk Assessment, University of Ottawa*
- ▶ Gregory Paoli, *Risk Sciences International*¹

¹ Member of the NAS *Science & Decisions* panel

ARA Dose-Response Framework Presentation

Oliver Kroner introduced the revamped ARA Dose-Response Framework 2.0, available as *beta* at www.chemicalriskassessment.org/methods. As a centralized source of risk methods from different organizations, the database is intended to catalogue, organize, and highlight key elements of risk methods, providing an overview of the method's utility and limitations, and a case study to demonstrate real world application.

The revised framework addresses several of the shortcomings of the original tool, offering:

- A search-oriented interface, with the ability to search and sort the database by method or keyword
- Keyword tags, to allow case studies to be grouped and cataloged
- A rubric for quantifying and comparing different aspects of the methods
 - The rubrics included in the *beta* were presented as placeholders for a panel-vetted system for scoring methods.
- A sitemap of all methods included in the Framework
- A list of key publications relating to Framework keywords
- Automatic translation of the site's content into French, German, Mandarin, Spanish

Questions Posed to the Panel

Following Mr. Kroner's presentation, the Science Panel was asked to offer feedback on a number of questions in several areas (content, features, rubric) and other considerations. The Panel offered their thoughts on the following topics.

A. Content

1. Is the organization of the site sensible? Is the layout intuitive? How can it be improved?
2. What information is missing or could be enhanced (for the material that is presented)?¹
3. The initial summary paragraph for each case study is currently copied from the case study prepared. Is this appropriate? Should we use the more targeted summaries (which contain less context) from the summaries of the discussion at the workshops? Or some other approach?

B. Features

4. What features (e.g., advanced search methods) are missing or could be enhanced?
5. Are additional changes needed to make it easier to search for methods to address specific issues/problems? If so, what?
6. The site was designed without emphasis on the chemicals featured in the various case studies. Would it be useful to allow users to sort and filter methods by chemical for identifying chemical specific information?

C. Rubrics

7. The Framework currently includes measurements of applicability, data requirements, accuracy, and precision for each case study, on a four point scale. (See, for example - <http://chemicalriskassessment.org/methods/human-kinetic-variability-trichloroethylene/>)
 - a. Are these useful metrics? What other metrics would be useful?
 - b. What is the best method for establishing a “score” for these metrics?
 - c. What other critical elements can be brought forward?

D. Other Considerations

8. Is Dose Response Framework an appropriate name?
9. Should methods related to exposure assessment or other aspects of risk assessment (e.g., value of information, risk communication, etc.) be included?
10. How can we proceed to make this a sustainable project?

Panel Feedback

A. Content

The Panel expressed general approval of the revised framework, calling it “a step in the right direction” and more intuitive than the initial version. A few panelists indicated that the purpose of the site was not immediately obvious, and asked for stronger visual and written cues, particularly on the landing page, to help the visitor understand the site’s intent and function. Panel recommendations included:

- The framework should emphasize the role of problem formulation and “fit for purpose” methods. Bette Meek offered to share a revised problem formulation figure for consideration.
- Inclusion of a schematic to help visitors understand the structure of the site and how it fits within the risk assessment paradigm.
- Inclusion of the words “environmental risk” or “human health risk” on home page.
- The case study summary paragraphs, as extracted from the authors’ summary, were deemed appropriate for use as a synopsis of the method. The Panel asked Lynne Haber to review the summaries for accuracy and consistency.
- Panelists asked about the possibility of creating an instructional video demonstrating the purpose of the site and how to use it; Oliver Kroner noted that this is quite feasible.
- One panelist indicated that a weakness of the Framework is that it only includes methods that have been reviewed by the Science Panel, omitting many valuable risk methods. The panel discussed methods for incorporating other methods into the Framework, including the possibility of panel members offering short synopses of new methods that they come across in the literature, with the panel vetting the short synopsis. Jim Bus volunteered to create a draft method review for panel consideration, and other panel members were also encouraged to synopsise one or two papers of interest. These synopses could be used to elicit sponsors (either the paper authors or others) who might be interested in developing

a case study based on the methods.

- The Panel also suggested an organized effort to identify gaps in the available methods, and creating placeholders on the site to indicate need for risk methods in this area. Lynne Haber offered to share a list of gaps identified during previous Panel discussions.

B. Features

The Panel offered several recommendations for adding or enhancing the functional features of the site. Those suggestions included:

- Strengthening the emphasis on problem formulation/fit-for-purpose risk assessment, which could potentially be done using a “schematic,” or increasing the focus on problem formulation on the case study pages.
- Offering users the opportunity to provide feedback via survey or comment form.
- Making the translation feature more prominent. The translation feature is useful, but is not conspicuous. The Panel suggested possibly relocating the translation tool to the top of the screen.
- Offering an inventory of tools available to risk assessors (e.g, Benchmark Dose Software), with links and tutorials as feasible.
- Offering abstracts of key references cited, or links to where the reference can be found, as done by U.S. EPA’s HERO Database.

On the question of whether or not to highlight the specific chemicals featured in the case studies, the Panel members were of mixed minds. Some thought that the chemical-specific information was highly useful to users, and should therefore be featured. Others expressed concern that the chemicals featured in the case studies were only used as vehicles to demonstrate the method, and that the focus of panel conversation had been around the method, not the chemical data. A compromise was proposed in which a list of the featured chemicals would be provided, preceded by a prominent disclaimer that the panel did not review any chemical-specific outcome. The disclaimer shall read as “Panel members provide input on the utility of the case study methods to address specific problem formulations, and identify areas for additional development of the case study and/or method. Inclusion of a method or case study in the framework as an illustration of a useful technique does not imply panel acceptance of the chemical-specific outcome, and chemical specific numbers do not represent the opinion of the Panel or of the Workshop sponsors.”

C. Rubrics

The rubric system was appreciated in concept, but there was agreement among the Panel that further thought was needed to determine which method metrics were appropriate to highlight, and to develop a process for quantifying those metrics. It was suggested that the placeholder rubrics be taken down during the beta testing, to allow the panel time for consideration. Jim Bus and Annie Jarabek offered to develop an initial approach for rubrics and metrics. Lynne Haber will point them to some relevant information from case studies. Lynn Pottenger (an audience

member and a member of the Dose-Response Advisory Committee) suggested that it may make sense to have a broader list of rubrics, but apply only the ones relevant for each case study. She offered to work with the Panel leads on this topic as needed. Some points of consideration identified include:

- Rubrics should have some focus on problem formulation.
- Possible rubrics may include:
 - Method's level of acceptance (e.g., new experimental method, well-established)
 - Human-relevance
 - Extrapolation assumptions
- Given the methods were developed for different problem formulations, they may require different metrics depending on the methods intended use.

D. Other Considerations

- Reflecting on the name of the database, the Panel considered the inclusion of terms such as “problem formulation,” “science,” and “fit-for-purpose,” but there was no clear consensus on an alternate name.
- One panelist questioned whether the movement toward a “catalog” of risk methods warranted reconsideration of the Panel constitution and format.
- The Panel agreed that exposure assessment methods could fit neatly within the existing Framework structure, needing only exposure-related key terms to help highlight where exposure methods are already included in the Framework. TERA will identify which of the case studies in the current framework include exposure methods. It was also suggested that Richard Beauchamp bring in his method as a case study. ExpoBox from the EPA is also a useful resource.

Next Steps

The Panel called for a “mid-term review” to evaluate what has been accomplished, and what areas still need attention. The workshop Co-chairs volunteered to plan a Panel review for early 2014.

The Panel recommended sharing the *beta* Framework with workshop sponsors for testing and review. After preliminary feedback is addressed (home page changes to emphasize human health risk assessment, hiding rubrics), the Panel suggested a promotional push including an announcement at the Society for Risk Analysis annual meeting in December 2013, and possible promotion on the Society for Toxicology blog.

The Dose Response Advisory Committee is currently planning Workshop VIII for May of 2014.