SAB Consultation
Updating EPA's Cancer and non-Cancer Risk Assessment Guidance

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EPA Administrator's Request (April 2019)

- "SAB advice regarding upcoming actions related to an update to 2005 EPA *Guidelines for Carcinogenic Risk Assessment* and creation of a guidelines for non-cancer risk assessment" (Letter to SAB, 4/19/2019).
- EPA's Science Technology Policy Council (STPC) nominated Agency experts to augment an existing Risk Assessment Forum (RAF) oversight committee to address the Administrator's request.
- The committee is considering what new guidance or aspects of existing guidance should be updated.

Risk Assessment Forum

Administrator

Science and Technology Policy Council

Risk Assessment Forum

Health Effects **Exposure** **Ecological Effects**

Technical Panels

Special Subcommittees

Risk Assessment Forum's Mission

- To address risk assessment issues
- To develop Agencywide risk assessment guidelines, guidance, and methods in support of Agency decision making in its mission to protect human health and the environment

Guidelines for Carcinogen Risk Assessment (2005)

- RAF Guidelines cover steps from problem scoping, thru analysis of studies, to conclusions and quantification.
- Topics include:
  - Assessment of human data
  - Assessment of animal data
  - Analysis of other data, including mechanistic
  - Evaluation of evidence for modes of action
  - Consideration of susceptible populations and lifestages
  - Reaching and describing weight of evidence conclusion
  - Modeling of dose-response in the observable range
  - Extrapolation to below the observable range when appropriate.
- There is a supplement on cancer risk from early-life exposure.
- The Guidelines recognize that other EPA Guidelines and method reports are also relevant.

* External review draft published in 1999; final revision released in 2005.

Noncancer Guidelines

There are some RAF Guidelines for other specific (noncancer) health effects.

- Guidelines for Developmental Toxicity Risk Assessment (1991)
- Guidelines for Reproductive Toxicity Risk Assessment (1996)
- Guidelines for Neurotoxicity Risk Assessment (1998)

Overarching Questions

1. Are there particular aspects of existing Agency risk assessment guidance related to cancer and other endpoints that should be revised or augmented to incorporate updated scientific information (based on experience in usage, new information, or scientific advances)?

2. Are there important topic areas that the existing Agency risk assessment guidances related to cancer and other endpoints do not address and that current information would support addressing?

Additional Questions

Additional questions identified by Agency leadership:

3. Are any key elements of hazard and dose-response analysis —including analytical limitations, heterogeneity, natural variability, and non-ambient exposures (i.e., endogenous or indoor exposures)—not adequately characterized in guidance?

4. Current guidance discusses how to describe confidence in hazard conclusions (see, for example, the Cancer Guidelines, section 2.5 “Weight of Evidence Narrative” or Guidelines for Developmental Toxicity, Table 3) and discusses presentation of uncertainty in dose response (see for example the Cancer Guidelines, section 3.7 “Dose Response Characterization”). Examples of current practice can also be seen in various recent EPA assessments of specific chemicals or pollutants.

   i. Do SAB members have recommendations for better ways to characterize conclusions and uncertainties in a transparent way?
   ii. Do SAB members have recommendations for better ways to analyze uncertainty, qualitatively or with quantitative analysis?
   iii. What role should statistical analysis play in this characterization?
   iv. Are there methods SAB members recommend for better analyzing and communicating compounded uncertainty, including the use of uncertainty factors, in the hazard identification and dose response process?

Additional Questions (cont)

5. The current Agency-wide guidance includes a guideline on cancer assessment, several guidelines for specific noncancer endpoints (e.g., reproductive toxicity, developmental toxicity, and mutagenicity), and guidances or reports on aspects of assessment common to many assessment endpoints (e.g., inhalation dosimetry, body-weight scaling of oral doses, benchmark dose technical guidance, risk characterization).

    i. Are there specific areas within these documents on which there have been advances in risk assessment that should be reflected in updated guidelines?

    ii. Are there areas of overlap or disagreement between these guidelines?

    iii. What issues or guideline documents would SAB members prioritize for update?

6. Given current understanding of how risk assessments are used in decision making, are there considerations or changes to existing guidance with respect to problem formulation, assessment, data integration, and risk characterization that SAB members recommend EPA consider? Do SAB members have specific recommendations as to questions of importance to decision makers that are not being addressed by current risk assessments?

Additional Questions (cont)

7. The purpose of some risk assessments (to quantify dose-response or reference values protective of the most sensitive receptors) and the purpose of the assessment of risk to inform benefits in an economic analysis (to create a predictive analysis for judging the effectiveness and feasibility of a regulatory action) can be quite different. As a result, the evaluation methods and key decision points can be quite different. For example, risk assessors may choose an benchmark dose at the high end (>95 percentile) of a distribution in order to define a level likely to avoid adverse effects, while economists may prefer risk assessors characterize the entire distribution or, at a minimum, use benchmark doses in the middle of the distribution, to inform benefit analyses.

    i. Do SAB members think risk assessments are providing the information needed by risk managers and those estimating the benefits of potential decisions? If not, what do SAB members recommend might make hazard and dose response analyses more useful to decision makers?

    ii. Should EPA's guidance direct staff to consider as part of the development of the assessment the questions decision makers need answered in the end use of the assessment?

Summary

- With these questions guiding, but not limiting, your review, please provide input on:
  - Scope and topics
  - Prioritization of our effort
  - Process (NOTE - The Agency recognizes this effort could be very large, lengthy and resource intensive, thus it is considering a phased approach to this work)
- Timing
  - We would like the SAB members to provide any written feedback within 30-days