Comments from the Center for Advancing Risk Assessment Science and Policy

June 18 2015
EPA June 2015 Bimonthly Meeting

The Center for Advancing Risk Assessment Science and Policy (ARASP)

ARASP:

- Coalition of 22 organizations focused on development and application of scientifically sound methods for conducting chemical assessments.
- See: http://arasp.americanchemistry.com/ for more information.

Improving Scoping and Problem Formulation

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Scoping and Problem Formulation are cornerstones to the development of a scientifically robust and "fit for purpose" IRIS

Key Questions of Stakeholder Interest

1. What specific guidelines/resource materials is the IRIS Program relying upon to define Scoping and Problem Formulation?
2. Is EPA considering the NRC 2014 Review of IRIS report as the only source for guidance?
3. How is EPA IRIS utilizing the EPA 2014 Framework for Human Health Risk Assessment to Inform Decision Making?
4. How will EPA's approach to scoping and problem formulation be peer reviewed (i.e. as part of the IRIS Handbook that is being developed)?

Improving Scoping and Problem Formulation

According to NRC 2014 and the PCB Preamble "Scoping is intended to seek input from EPA program and regional offices including information and the level of detail needed to inform their decisions."

- While the draft contains general statement that PCBs "are of interest…due to widespread human exposure to PCBs from many sources and through multiple environmental media," no substantive information is presented that would inform the assessment from the individual program and/or regional offices

- Excerpts from a previous ATSDR assessment is not an acceptable surrogate for the detailed information expected from program/regional offices.

Improving Scoping and Problem Formulation

Key Questions of Stakeholder Interest that can impact nature of the assessment:

1. What current exposure scenarios and levels are of interest should be evaluated in the planned assessment?
2. Are there particular levels in fish that are of concern that drive the need for the non-cancer IRIS assessment?
3. Is there concern over a particular inhalation scenario, such as in schools?
4. Are program and/or regional offices considering greater restrictions if PCBs were found to exhibit non-cancers concerns not heretofore identified?
5. What risk assessment products (quantitative and qualitative) are needed by management for informed decision making? What is needed for other analyses (e.g., economic analysis)?
6. Are screening level values sufficient? are best estimates needed? are distributions needed?
7. What schedule will be followed? This will include provision for timely input to the decision making process, as well as timely and adequate internal and independent external peer review, where appropriate.

Improving Scoping and Problem Formulation

Summary Recommendations:

- IRIS should provide guidance on how Scoping is to be approached.
- IRIS should request written information from Program/Regional offices including the level of detail needed to inform their decisions
  - Emphasis should be on exposure scenarios/levels that can inform the "scope" of the assessment
  - Responses from Program/Regional Offices should be placed in the IRIS docket and summarized in draft Scoping Materials for the Stakeholder meeting with an indication of how the proposed scope of the assessment relates to these inputs.
    - Allowing for stakeholder input is an important part of scoping and problem formulation.

Improving Table 1

Note with Asterisks which endpoints will move forward

Note that no adverse effects were identified (-)

Use footnotes to explain why endpoint is not moving forward

	Human Studies		Animal Studies		In Vitro Studies
	Oral	Inhalation	Oral	Inhalation	
Health Outcomes					
Body Weight Effects				✓ (Subchronic)	
Cancer		✓ (Occupational)	✓ (Chronic)	✓ (Chronic)	
Cardiovascular			✓ (Subchronic)	✓ (Subchronic, Chronic)	
Dermal				✓ (Chronic)	
Developmental				✓ (Subchronic)	
Endocrine				✓ (Subchronic, Chronic)	
Gastrointestinal				✓ (Subchronic, Chronic)	
Hematological		✓ (Occupational)	✓ (Subchronic)	✓ (Subchronic, Chronic)	
Hepatic			✓ (Subchronic)	✓ (Subchronic, Chronic)	
Immunological				✓ (Subchronic)	
Metabolic disease					
Musculoskeletal				✓ (Subchronic, Chronic)	
Neurological and Sensory		✓ (Occupational)	✓ (Subchronic)	✓ (Subchronic)	✓
Renal			✓ (Subchronic)	✓ (Subchronic, Chronic)	
Reproductive			✓ (Subchronic)	✓ (Subchronic)	
Respiratory		✓ (Community)	✓ (Subchronic)	✓ (Subchronic, Chronic)	
Other Data and Analyses					
ADME [1]		✓	✓	✓	
Toxicokinetic models [2]					✓
Mode of action hypotheses					✓
Susceptibility data		✓ [3]			
Genotoxicity		✓	✓	✓	✓
Other mechanistic data					✓ [4]

[1] Absorption, distribution, metabolism and excretion (ADME) data also exists for dermal exposure for human and animals

[2] Inhalation PBPKs included

[3] Individuals that may be more susceptible to toxic effects include those with pre-existing hearing loss and diseases of the respiratory system, liver, kidney, or skin; fetuses; young children; pregnant women; and those taking certain medications, such as hepatotoxic medications or drugs (ATSDR 2010).

[4] Adverse outcome models of carcinogenesis and benchmark dose

Improving IRIS Bimonthly Discussions

Improving Transparency

Recommendations:

- We suggest that IRIS, at the close of each panel or session, provide a quick informal summary ("OK, here's what I heard…") of the major points covered by the panelists or speakers
    - specifically in the context of how the information/discussion can be used to inform the IRIS assessment.

- A written summary of the meeting should be posted along with all meeting materials.