Systematic Integration of Evidence Streams for IRIS

Panel Discussant Comments

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Systematic Integration of Evidence Streams for IRIS

- Very excited and supportive of the approaches that EPA is undertaking with its IRIS revisions
- EPA's open, stakeholder driven embrace of a transparent and scientifically robust assessment process is to be applauded!

Guided expert judgment versus structured processes:

- EPA needs to keep a broad approach to this question. Could be too narrowly defined to miss integrated signals with too prescriptive of a process
- Supportive of a guided expert judgment versus structured approach
- Most structured approaches are just in development by several groups but most have “cherry picked” the examples to date.
- EPA will learn from these processes but very supportive of guided expert judgment

Guided expert judgment versus structured processes (cont.)

- IARC is developing some interesting new approaches for guiding mechanistic evaluations
- Concerns with “lumping” too many concepts within the mechanistic evidence category—still need flexibility but clear guidance, also consider check list for this large category.
- Where is SAR?, QSAR? , and toxicodynamics versus kinetics?

Strength of Evidence across evidence streams:

- NRC provides a good review of approaches for assessment of bias that should be used by EPA, encourage EPA to do so, but realize this will take changes in the scientific community as well as EPA's willingness to do so. EPA should provide guidance based on the approaches reviewed by the NRC to the broader scientific community of practice that they will be using such approaches
- This should not stop process now but provide a path forward for improvement as scientific community practice improves

Best ways to incorporate individual study evaluations in Evidence-Integration process:

- Supportive of guided expert judgment approaches like IARC with structured narrative templates. Supportive of NRCs suggestions on page 105 of the NRC report that calls for organizing the narrative as a statement that clearly supports "argument" or logic for or against compound being a hazard. Suggestions also include consideration of alternative hypotheses.
- Support similar approaches for cancer and non-cancer endpoints, in fact approaches for use of Bradford Hill criteria for causality have been available for non-cancer toxicological studies for many years. See earlier approaches from IEHR evaluative process for non-carcinogens (Moore et al).

Best ways to incorporate individual study evaluations in Evidence-Integration process:

- Essential that when qualitative categorical judgments are used that they are defined with quantitative ranges—see Table 6-5 in NRC report

- Supportive of Bayesian approaches for quantitative considerations but these are still in development and need to be further researched, not all datasets are equally robust and as approaches are developed ensure that these are considered in recommended next steps.
- Meta- analysis of epidemiological evidence for IRIS assessment is useful when epidemiological studies are of similar design and can be considered collectively, not a “cure-all” for bias
- Current approaches in EPA’s most recent risk assessments for quantitative comparisons of cumulative distribution of reference values across endpoints are very useful (like Fig 7-6)