CHARGE QUESTIONS

Health assessments conducted by EPA's National Center for Environmental Assessment critically review publicly available studies to identify adverse health effects from exposure to chemicals (hazard identification) and to characterize exposure-response relationships. Examples of these assessments include the Integrated Science Assessments (ISAs) of criteria air pollutants and Toxicological Reviews developed by the Integrated Risk Information System (IRIS) Program. The type and amount of available data varies considerably among assessments. The information in these assessments can be used in combination with exposure information to characterize the public health risks of a given substance in a given situation, thereby supporting risk management decisions designed to protect public health and the environment. Given this context, please address the questions below relating to incorporating systematic review methods in the development of these assessments.

Panel I: Evaluating Observational Epidemiology Studies

1. What gives you confidence in a study or set of studies? [i.e., what do you look for in a study that makes you comfortable in interpreting the observed risk estimate to be an accurate estimate; what makes you worried that the observed risk estimate is an over estimate or spurious finding; what makes you worried that the observed risk estimate is an underestimate of the actual risk; what criteria would you use to "downgrade" a study (because you're worried it's overestimating, underestimating, or because you don't know how to interpret the results…?]
2. What type of or level of detail (with respect to decisions by the evaluators, and with respect to descriptions of individual studies) would you want to see in an evaluation of study methods/limitations/biases?
3. What thoughts or advice can you offer on addressing the tension between balancing transparency and reproducibility in evaluation of study methods/limitations/biases with the need for flexibility and professional expertise or judgment?
4. Quantitative methods to estimate the extent of specific sources of bias in epidemiology (e.g., misclassification of exposure, selection bias) and the impact on risk estimates have been developed, but are not widely used. What role should quantitative bias assessment play in the systematic review of individual studies and of groups of studies? What minimum data are necessary in order to attempt quantitative bias assessment?

Panel 2: Synthesizing and Integrating Evidence Across Disciplines

1. Some frameworks consider human data and animal data jointly and some frameworks consider human data and animal data independently, and then integrate these results at the end. In what types of circumstance/scenario (e.g., type of data available, or primary study question), if any, would one approach be preferred?
2. The type of evidence available varies for different pollutants. How does the lack or uneven strength of one line of evidence (e.g., human data, mechanistic understanding) impact the weight of evidence and the ability to draw causal conclusions and evaluate hazard and dose-response relationships?
3. The availability of mode of action data can vary across chemicals. Where is the appropriate place in a framework for incorporating mode of action information?
4. How do you allow for flexibility and scientific judgment in developing a framework for integration? What aspects of a framework can be established a priori? What aspects will depend on the data and scenario/questions?