



July 24, 2014

Public Statement from Angela Lynch, MSPH, PhD, on behalf of the American Chemistry Council to the Chartered Scientific Advisory Board and Board of Scientific Counselors Regarding the Discussion of Office Research and Development Strategic Research Directions

I appreciate the opportunity to provide comments on behalf of the American Chemistry Council, which represents the leading companies engaged in the business of chemistry. I have four points I would like to present regarding the Office of Research and Development's (ORD) Human Health Risk Assessment Strategic Research Action Plan (HHRA Strategic Action Plan).

- 1) The HHRA Strategic Action Plan appropriately recognizes that ORD hazard and risk assessment outputs are used frequently in a statutory and policy context by the Agency. In order to improve the quality and timeliness of the Agency's chemical risk assessments, ORD must consider the recently finalized EPA Human Health Risk Assessment (HHRA) Framework¹ in the development of these important assessments. The HHRA Framework emphasizes the importance of scoping and problem formulation to inform risk management decisions and recommends providing a broad range of risk estimates, including central estimates, and information to account for human variability and uncertainty. Transparency and communication are important throughout the entire chemical assessment process. Risk managers and stakeholders should understand what the results actually mean to inform how they can be appropriately applied in different situations. This can only be accomplished through clear communication. The HHRA Framework specifically states, "All steps, key assumptions, limitations and decisions, as well as associated rationales, should be presented clearly." All of these points have been recommended by ACC and the National Academy of Sciences (NAS) over the past several years and were recently reiterated by the NAS in its May 2014 report on the IRIS program. We hope that your review will help steer ORD towards incorporating this critical information into the hazard assessments produced by the Agency.
- 2) ACC supports continued investment of research resources to improve development and application of 21st Century technologies to enable more efficient and scientifically relevant hazard, exposure and risk estimations, and to more accurately determine the probability of adverse health outcomes at environmentally relevant exposure levels. Our key recommendations that relate to EPA's strategic planning as follows:
 - a. Build from the NexGen work and the OECD Adverse Outcome Pathway (AOP) activities to develop draft guidance which addresses the development, evaluation and use of AOPs for defined purposes such as prioritization, formation of categories for read across, integrated testing, and screening level hazard/risk assessment.

¹ <http://www.epa.gov/raf/frameworkhhra.htm>



- b. Focus efforts on incorporating exposure into the next generation of risk assessment approaches, by building from the consumer model in the European Center for Ecotoxicology and Toxicology of Chemicals (ECETOC) Targeted Risk Assessment exposure tool and the tiered exposure assessment approaches developed by the ILSI-Health and Environmental Sciences Institute RISK 21 project
- c. Develop the framework the Agency will use to establish and document the scientific confidence that is needed for these methods and prediction models to be used for regulatory purposes.
- d. Employ a more open stakeholder engagement process by maximizing open meetings, broadening consultations and collaborations and conducting peer review in accordance with Agency procedures for influential risk assessments guidance and policies.
- e. Care should be taken that these new technologies are not deployed prematurely to classify hazards and risks without adequate confidence not only in their sensitivity to predict an adverse outcome but also in their specificity to avoid an unacceptable level of false positive responses, lest the public and scientific community lose confidence in these new approaches.
- f. Use mode of action (MOA) as an organizing principle. We encourage the work of EPA and others in developing and building scientific confidence in MOAs and AOPs. ACC has consistently urged EPA to employ MOA analytical constructs, such as the Key Event Dose Response framework or the Hypothesis-Based Weight of Evidence framework, in risk assessments to ensure that key events, dose-dependent transitions and 21st Century knowledge of the biology of molecular, cellular and organ responses form the foundation of human health risk assessments. AOPs are also promising tools that can be used to describe the sequential steps and linkages between initial events, intermediate events, key events, and adverse outcomes, and to document methods to measure key events.

3) Regarding the IRIS program, as noted by the NAS in May, there is much more work to be done for EPA to maintain their trajectory for improvement. The most critical area for IRIS reform is evaluating and integrating scientific evidence in a transparent and robust manner. For example, IRIS has identified study quality considerations for certain types of scientific evidence, but the assessments have program has not systematically and transparently evaluated studies against these considerations. NAS recommended this in 2011 and again in 2014. IRIS assessments also need to consistently address mode of action. To date, EPA's approach to integrating evidence has left stakeholders guessing as to how mode of action and mechanistic information will be used. If IRIS assessments are designed well from the start, the Agency can organize the available information to evaluate the plausible alternative hypotheses that may be supported by the data. Better study design can also help ensure more timely assessments.



- 3) Finally, I would like to comment on peer review as we all recognize its importance in the scientific process. In 2012, this committee made comments to ORD regarding improving peer review of the HHRA program.² To our knowledge, EPA has not addressed these recommendations. We encourage you, consistent with previous recommendations, to recommend that EPA put in place strategies to ensure that recommendations from the public and peer reviewers are appropriately addressed. The joint SAB and BOSC report notes the NAS example of an independent review monitor to provide critical guidance on addressing comments. Similar to the role of a journal editor, the NAS review monitor helps to ensure that comments from reviewers have been appropriately and sufficiently addressed. The IRIS process, for example, currently lacks an independent review monitor and further improvements in this area are necessary to help strengthen the IRIS program and ensure that all public and peer review comments are appropriately addressed.

Thank you again for the opportunity to provide comments.

² See SAB/BOSC 2012 report available at:
[http://yosemite.epa.gov/sab/sabproduct.nsf/3822EB089FCCB18D85257A8700800679/\\$File/EPA-SAB-12-012-unsigned.pdf](http://yosemite.epa.gov/sab/sabproduct.nsf/3822EB089FCCB18D85257A8700800679/$File/EPA-SAB-12-012-unsigned.pdf).