

Summary of Recommendations from June 2019 Consultation with Members of the EPA Chartered Science Advisory Board and the Chemical Assessment Advisory Committee (arranged by topic)

Process and format:

- *Update all guidance and provide it in a central location*
- *As EPA develops new guidelines, create a “readers guide” to the available guidance*
- *Organize new guidance along the lines of the 2014 “Framework for Human health Risk Assessment to Inform Decision-Making”*
- *Consult the 2004 Staff paper to identify areas to revisit*
- *Leverage recommendations from NAS, etc. on how to best inform risk assessment guidance*
- *Obtain stakeholder practitioners input*
- *Ensure adequate review and input from public*
- *Use outside experts to develop health assessments to avoid back and forth peer review*

Problem formulation and scoping:

- *Reconsider the overall process of evaluating risk – bifurcation of risk and safety assessment*
- *Reconsider the practice of “ensuring that risk is not likely to be underestimated” as it inappropriately impacts multiple facets of risk assessment*
- *Develop better scoping and problem formulation processes to identify fit for purpose approaches and allow for reality checks*
- *Consider incorporating a “reality check” into risk assessments to control for overly conservative toxicity factors*

Harmonization:

- *Develop “harmonized” guidelines for cancer and noncancer effects, including dose-response*
- *Utilize transparent criteria and consider scientific utility if cancer and noncancer classification schemes are revised or developed*
- *Consider whether a phased scoring approach for characterizing WOE for cancer and noncancer would be better than use of descriptors*

Cumulative and mixtures risk assessment:

- *Expand the 2014 “Framework for Human health Risk Assessment to Inform Decision-Making” to include cumulative approach advances*
- *Further develop cumulative risk assessment practices*
- *Address issues of mixtures and confounding factors*

General cancer issues:

- *Update Cancer Guidelines, particularly statistical methods section*
- *Finalize the 2007 Draft Guidelines for a Mutagenic MOA for Carcinogenicity*
- *Develop an agency-wide uniformity in applying Cancer Guidelines, particularly with respect to MOA and application of a threshold approach*
- *Reconsider the linear-no-threshold (LNT) approach as a default for low-dose extrapolation*
- *Reconsider animal models for low-dose determination of cancer potential*

- *Convene panels to inform and develop specific guidance for examining the human relevance of animal tumors*
- *Address New Alternative Methods (NAMs) and cancer risk assessment*

Specific cancer issues:

- *Redesign the WOE narrative – currently an impossible task as described in Cancer Guidelines*
- *Expand/do not expand the application of ADAFs for early-life susceptibility*
- *Revisit the “bar for a mutagenic MOA” as it is different in Cancer Guidelines than that proposed in the 2007 draft framework for a mutagenic MOA*
- *Update cell proliferation MOA information in guidelines to support determination of threshold response for multiple carcinogens*
- *Consider MOA and threshold approaches even for DNA reactive carcinogens*
- *Reconsider LNT as a default approach for non-DNA reactive carcinogens*
- *Use linear dose response when there is uncertainty about the shape of the dose-response*
- *Re-evaluate practices for determining statistical significance for common tumors*
- *Develop guidance for the evaluation of historical controls for cancer*
- *Develop guidance for the use of initiation-promotion studies for cancer*
- *Place greater emphasis on context (route, exposure conditions) for classifying potential carcinogens*
- *Add recent advances in AOPs to cancer guidelines*

Summary of Specific Comments on Radiation Risk Assessment

- *Look at issues with current risk assessment practices for estimating risks from low doses of radiation:*
 - *practices for estimating risks from doses near or below background that are contrary to expert advice*
 - *inaccurate claims of a scientific consensus supporting current Agency policies*
 - *logically fallacious reasoning*
 - *reliance on outdated information*
 - *inconsistencies between the Agency’s practices for estimating low-dose radiation risk and those for other carcinogens*
 - *ignoring evidence for dose-response models other than the LNT model.*
- *Issues are significant enough to warrant a comprehensive review by EPA’s SAB and/or the RAC.*