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GENERAL COMMENTS AT THE EPA BI-MONTHLY LISTENING SESSION: RDX, ETBE, and tert-Butanol

On behalf of ACC and the Center for Advancing Risk Assessment Science and Policy

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If the same person says the same thing three times, does this create a weight of evidence?

ACC and the Center for Advancing Risk Assessment Science and Policy (ARASP)

ACC:

- Represents the leading companies engaged in the business of chemistry.
- Committed to improved environmental, health and safety performance through Responsible Care®.

ARASP:

- Coalition of 19 organizations focused on development and application of scientifically sound methods for conducting chemical assessments.
- Members include chemical specific panels and other trade associations. See: http://arasp.americanchemistry.com/

IRIS Enhancements

- July 2013 IRIS enhancements are a constructive step forward.
  - Early stakeholder engagement, particularly before a draft is developed will help strengthen assessments and move them to completion in a more timely manner.
  - Planning and scoping will help in understanding parameters that will be assessed.
  - Complex scientific issues will ideally be discussed earlier in the process.
  - Identification of critical studies and their summaries should help stakeholders understand the direction the agency is heading.
  - Appropriate exposure response tables will help provide context.

- The release of evidence tables, while a helpful start, is not sufficiently consistent with the IRIS enhancements.
  - Further improvements are necessary.

IRIS Process Step 1

- The revised IRIS process documentation includes the following in the details about Step 1:
  - Begins with planning and scoping, including public meeting on technical problem formulation and release of planning and scoping summary.
  - ½ Conducts literature search and critical study selection.
  - Develops evidence tables that succinctly summarize the critical studies to be considered in developing the assessment.
  - Publicly releases literature search, literature search strategy, critical study selection criteria, evidence tables for critical studies, and exposure-response figures (which graphically depict responses at different exposure levels for studies in evidence tables).
  - ½ Convenes public meeting to discuss literature search, evidence tables, exposure-response figures, and key issues.

- Step 1 elements are not completed in the RDX, tert-butanol and ETBE releases.

Evidence Table Releases Fall Short (1)

- No planning and scoping summary is provided.
  - There is no understanding of the questions being asked or issues to be addressed.
  - No context is provided in the released evidence tables.

- EPA's definition of a systematic review is related only to the literature search.
  - Document entitled "Systematic review of the ETBE literature" on IRIS takes readers to a HERO webpage for identified studies.
  - Systematic review must be more than a first step literature search strategy.

- All studies identified in the literature search, that provide an endpoint where a change is seen, are deemed 'critical studies'.
  - There are no 'critical study' identification criteria.
  - Study quality must be an essential element of 'critical study' identification.

Evidence Table Releases Fall Short (2)

- Evidence tables present all studies that show a change in an endpoint, not necessarily ‘critical studies’.
  - There is no discussion of which studies should be treated as ‘critical studies’ due to quality, methodology, adversity of effect, or any other criteria.
  - Studies negative for statistical changes are excluded from evidence tables, therefore making them incomplete and misleading.
  - While an approach like this may work where there are limited studies identified in a literature review, as more complex chemicals are reviewed, the EPA approach will be unworkable.
  - Burden is on stakeholders to review and comment on every study identified in the literature review, not just those in the table.

- Evidence tables focus only on endpoints, ignoring all ‘critical studies’ that relate to mode of action (MOA) only.

Evidence Table Releases Fall Short (3)

- Exposure-response arrays are misleading
  - All studies are treated as being of equal quality, when this is not the case.
  - Exposure-response arrays are limited to positive endpoints, ignoring studies with negative endpoint findings and also ignoring all mode of action information.

Improving Evidence Tables

1) Release planning and scoping summary along with evidence tables.
2) Don’t confuse a literature search with a systematic review. Clarify terminology and use it consistently.
3) Determine, *a priori*, criteria for ‘critical study’ identification. This should include not only endpoint specific data, but also mode of action information.
    - It should be more specific than including all relevant studies identified in the literature review.
4) Critical study criteria should include, at a minimum, a review of study quality, methodology, relevance, and adversity of effect (if relevant).
    - This review should be released by EPA along with the evidence tables.
5) Evidence tables and exposure-response arrays should be developed for mode of action information (see Kushman et. al., for example).
6) Exposure-response arrays should include only those studies of sufficient quality (e.g. those meeting critical study criteria) and quality of studies should be clear in the arrays.

Thank You!

- EPA has taken a strong first step. However improvements are needed.
- Consistency with intent of IRIS process enhancements will go a long way towards improving the evidence tables.
- Most importantly, EPA must conduct a review of the quality and relevance of studies before moving them forward as ‘critical studies’ for an IRIS assessment.
- Without changes and improvements, the utility of evidence tables, following the current structure, may not help sufficiently speed the finalization of IRIS assessments.
  - **Small changes, such as those noted in our general recommendations slide will lead to much improvement.**

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Willing is not enough; we must do.

-Johann Wolfgang von Goethe

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