

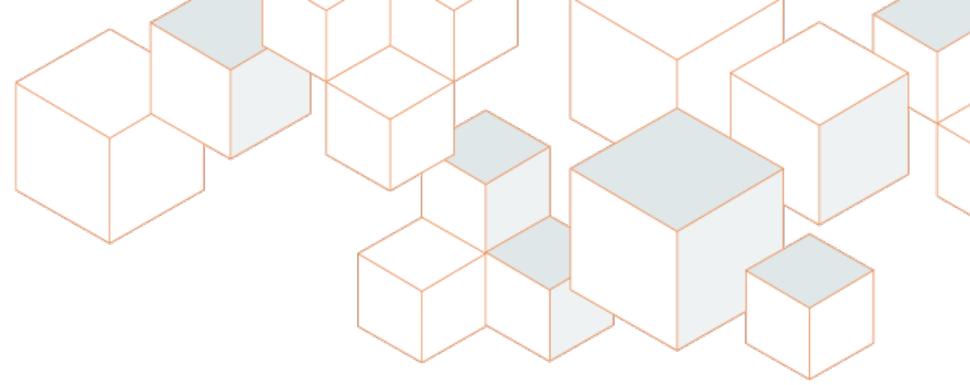
December 13, 2013

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

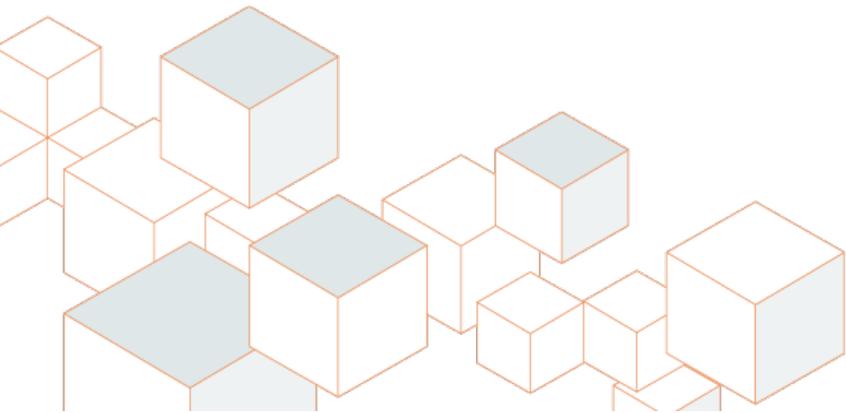
On behalf of ACC and the Center for Advancing Risk Assessment Science and Policy

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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.
 - 1/2 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).
 - 1/2 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.

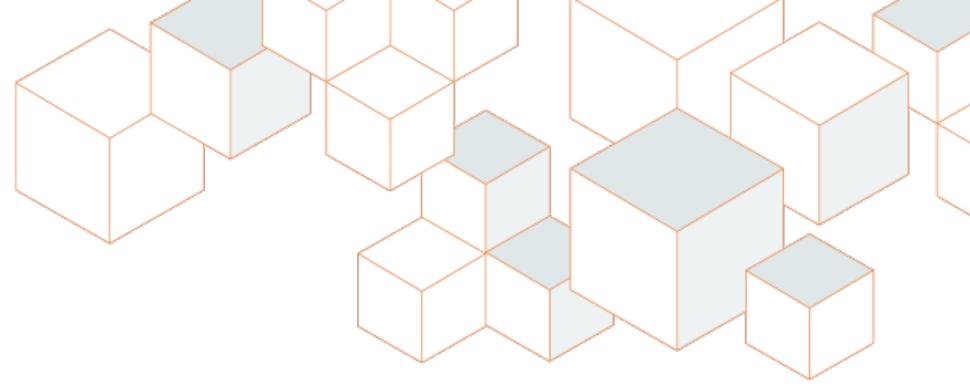
Improving Evidence Tables

- 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!



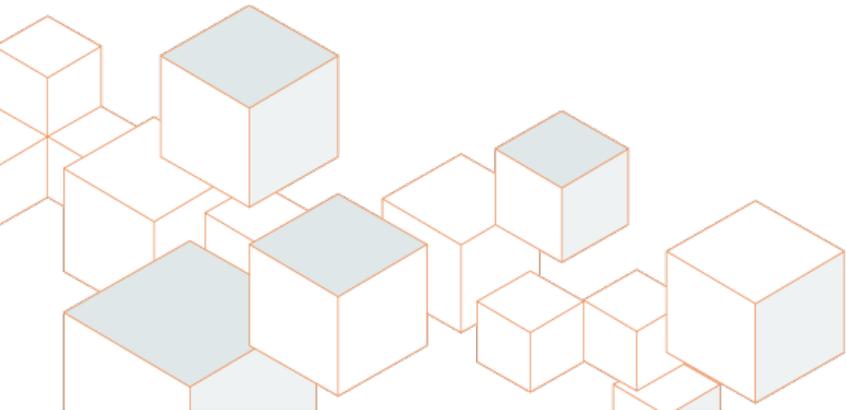
- ❑ EPA has taken a strong first step. However improvements are needed.
- ❑ Consistency with intent of IRIS process enhancements will go a long way towards improving the evidence tables.
- ❑ Most importantly, EPA must conduct a review of the quality and relevance of studies before moving them forward 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.**

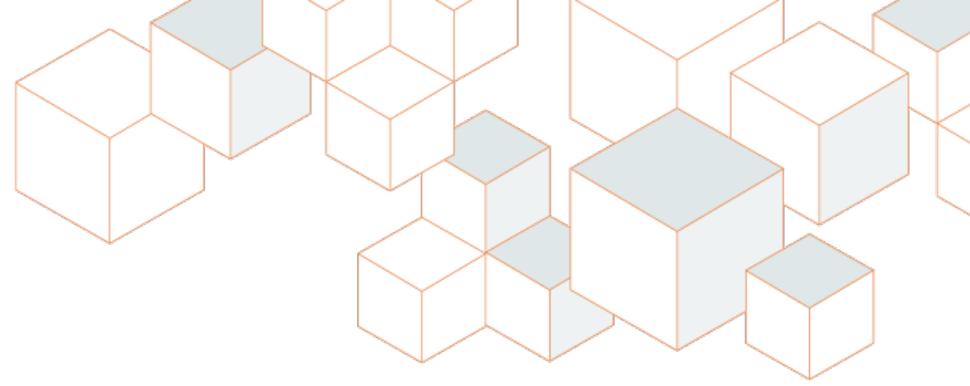


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Willing is not enough; we must do.

-Johann Wolfgang von Goethe





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