

SAB Member Comments received from Dr. Elaine Faustman on March 7, 2013

Quality Review of SAB Advice on Advancing the Application of Computational Toxicology Research for Human Health Risk Assessment- Comments by E. M. Faustman

1) Were the charge questions to the committee adequately addressed?

The reviewers provided significant comments and suggestions on CompTox however this reviewer felt that some sections of the report were very detailed and some sections were not detailed enough to address the charge questions. For example as noted below in my responses to question 4, some details in Section 2 seemed very detailed and not consistent with the level of review and recommendation of the overall report (i.e. recommendation of specific assays).

The report has extensive discussion of the AOP pathways and relationship to disease however the charge questions do not ask that question. The reviewers need to specify why this focus and what charge question(s) it is addressing.

2) Are there any technical errors or omissions or issues that are not adequately dealt with in the draft report?

This reviewer felt that the report was “silent” on general endpoints such as cytotoxicity or oxidative stress that may be components in many types of in vivo endpoints. This reviewer would have liked more clarification on the more simple and less specific endpoints that occur in the assays and how these are interpreted.

The review highlights in several contexts the significance of the early use of the CompTox data for screening dispersants in the Gulf however it is silent of the very large exercise of screening for endocrine disruption that is occurring as a part of the EPA endocrine screening program. Shouldn't the review applaud EPA's approach to emphasize the importance of such evaluations of Comp Tox results for current EPA needs?

3) Is the draft report clear and logical?

See comments above. This reviewer feels more work is needed to organize the reviewer comments and the linkage between the cover letter and the review text. This reviewer supports the five summary points however this reviewer also noted some inconsistencies.

This reviewer noted that the letter to EPA included discussion of a means to evaluate “multiple factors simultaneously” on the first page line 36 yet the review has a much more focused recommendation to establish a “scientifically defensible foundation” on the top of page 9.

The reviewers recommend the development of “data user guides” and this reviewer agrees however this reviewer would eliminate the details on how one of these might be formed as in the reviewers own words these need to be developed for “appropriate use of data in various applications”. The generic list is not that useful but the overall concept is very useful. (Note the text included discusses development of Data Use Guidelines in text pages 10 and 11 and Data Use Guides (DUG) in the cover letter.)

- 4) Are the conclusions drawn or recommendations provided supported by the body of the draft report?

Section 2,

Page 12 lines 4 to 5 Is this statement true? Will the CompTox data not be of “sufficient quality for use in risk assessment” if it does not directly correspond to in vivo endpoints or well-defined AOPs? In this reviewers opinion these assay outcomes could be useful without this stipulation.

Page 12 lines 5 to 7 The logic in this sentence is unclear.

Page 12 lines 9 to 15 This reviewer did not agree with this section of text. Is the text designed to look at “additional endpoints” or same endpoints but now evident during different phases of life course? Are these unique new endpoints or is the causal temporal relationship being emphasized here? Needs clarification. Do we expect that this will be a key strength of these assays? Do we know? Is there a plan to determine if this is true?

Section 4

The review provides well deserved kudos to EPA for establishing User communities as well as request additional usability to data access and interpretation. This reviewer would have liked to have seen more use of the word “dialogue” versus “communication” as it implies a two way exchange that would facilitate the input and use by the program and field offices.

Page 16 lines 15 to 20 This reviewer was unclear on the purpose of this section. Is the review suggesting the prioritization of the CompTox data as follows from this text? “highest to lowest in terms of scrutiny with regard to human relevance as follows: risk assessment, prioritization, screening chemicals and green chemistry”. How did the reviewers decide on this prioritization or are they agreeing with EPA suggestions? Please clarify.

Page 12 lines 11 to 13 This reviewer was surprised that this specific analysis was “highlighted”. What were the criteria to cite this versus so many other very important analyses? Provide rationale.

Typographical Edits:

Page 12, Line 2 Correct the spelling of CompTox