Monday, July 25, 2016

PCB Assessment Team Meeting – MINUTES

In attendance: Geniece, Jenny, Evan, Anu, Laura, Paul, Danelle, Marian, Jeff, Michael Dzierlenga, Prachi Pradeep, ICF (Dave Burch, Joanne Trgovcich, Allison Killius, Anna Engstrom, Cara Henning, Tao Hong), External Experts (Michael Bloom, Todd Jusko, John Meeker, Larry Robertson, Alexander Sergeev)

ICF STATUS UPDATE

- Ongoing: effort to screen and categorize hazard id references continues; we will receive updates to our reference lists biweekly until the effort is complete (due dates in the [HYPERLINK "https://usepa-my.sharepoint.com/personal/lehmann_geniece_epa_gov/_layouts/15/guestaccess.aspx?guestaccesstoken=ydsXosDNLy7jhAwiMgZJIKvK%2b7pN9iFXb1xTy6zxDds%3d&docid=2_128158e3987df4c34a6e61f9f852f3a16"] will be adjusted when categorization effort is complete)
- Ongoing: ADME-specific literature search and screen (due 8/27/2016)
- Expert authors joining our team today:
  - Pamela Lein, UC Davis (neurological effects, tox)
  - Larry Robertson, University of Iowa (hepatic effects, tox)
  - Sharon Sagiv, UC Berkeley (neurological effects, epi)
  - Todd Jusko, University of Rochester (immunological effects, epi)
  - Michael Bloom, SUNY Albany (endocrine effects, epi)
  - John Meeker, University of Michigan (developmental effects, epi)
  - Alexander Sergeev, Ohio University (cardiovascular effects, epi)
- Continuing recruitment of expert authors:
  - Cardiovascular effects (tox) – Michal Toborek (accepted)

NEXT STEPS

- DUE TODAY:
  - EPA Team Members (other than Evan and Laura): Comments on example evidence tables (see meeting minutes from 7/18/16)
  - Authors of animal tox hazard sections: Comments on list of factors important for assessing oral exposure protocols used in animal toxicology studies (see meeting minutes from 7/11/16)
- First-wave evidence table reviews (ongoing; as requested)
- Authors of hazard synthesis sections: develop **literature inventories** and **study quality evaluation protocols** (due dates will be adjusted when categorization effort is complete)

OVERVIEW OF TEAM MEETING PROCEDURES AND RESOURCES

- Outlook calendar invitation is generally updated at least twice: once during the week before the meeting to add the agenda and meeting details; and once during the week after the meeting to add the meeting minutes and to highlight any action items
- When team members miss meetings, they can access meeting materials through the calendar invitation or by accessing the PCB Assessment Team folder (Team Meeting Agendas & Minutes subfolder)

- The PCB assessment tracker is also an important resource to help team members to keep track of ongoing assessment activities and deadlines

UPDATE - Dose-response efforts

- Mixtures Modeling Tool Presentation
  - Tao Hong (ICF) provided an overview of the "Mixtures Similarity Tool (MiST)" for assessing toxicological similarity across PCB mixtures, including a demonstration of the tool using two examples.
    - The tool will implement the methodology described by Marshall et al. (2013) An Empirical Approach to Sufficient Similarity: Combining Exposure Data and Mixtures Toxicology Data. *Risk Analysis* 33(9): 1582-1595.
    - The tool is expected to be useful for estimating and predicting similarities and differences in toxicity across PCB mixtures with different congener compositions.
      - Potentially useful to support reference value derivation and application in future risk assessments
    - Reference mixtures are those for which we have laboratory data on dose response (e.g., different Aroclor mixtures); we may be able to derive reference values for these mixtures
      - Reference mixtures may be compared to each other ("data-rich case") to determine if multiple mixtures are toxicologically similar enough to form the basis for a single reference value or if separate reference values are needed for each mixture
    - Dose-response information may not be available for candidate mixtures (e.g., PCB mixtures found in the environment); these mixtures may be compared to reference mixtures ("data-poor case") to identify the most appropriate reference value to use for exposures to the candidate mixture
- Team Discussion
  - In cases where two mixtures have similar toxicity but different ratios of individual components, the conclusion will be that the mixtures are not similar.
    - According to this approach, similarity depends on both toxicity and mixture composition. This could work well for our purposes. If two reference mixtures are similar in toxicity, but dissimilar in composition, we may want to derive separate reference values for those two mixtures. The reference values would be similar in magnitude and might seem redundant. But, later, when risk assessors are using the tool with environmental PCB mixtures of widely varying composition, we would want to be able to assign a reference value to mixtures similar in composition to either one of the original reference mixtures. So, having reference values available for a variety of mixtures may be useful, even if those mixtures are similar in potency.
  - Because the BMD is an inverse measure of toxicity (high toxicity is indicated by a low BMD) and congener potency values are direct measures of toxicity, it is unclear why the calculation of the mixture potency would be multiplied by the BMD rather than divided by it.
    - Cara Henning offered to follow up on this observation later.
  - The wording used to describe the results of the analysis should reflect the hypothesis testing described in Marshall et al. (2013).
  - Expert judgment is required to establish the "critical value" used to quantify what it means to be "sufficiently similar".

- Because environmental PCB mixtures are much more variable in composition than PCB mixtures used in toxicity testing, we expect that many environmental PCB mixtures will not be found to be sufficiently similar to any of the reference mixtures included in the assessment.
    - For those cases, we may provide guidance to direct the risk assessor to use the most conservative reference value
    - Presently, IRIS offers RfDs for Aroclors 1254 and 1016. Often, when PCBs are measured in the environment, the congener compositions of the environmental mixtures are not similar to either Aroclor. In those cases, risk assessors use a wide variety of justifications for choosing one RfD over the other; there is no standard approach. Use of this tool and associated guidance will standardize this process based on our current understanding of the toxicity of PCB mixtures and the relative potencies of individual congeners.

UPCOMING

- Webinar series
    - (August 25) Effects on social and behavioral responses (Ross Gillette and Michael Reilly)
- Team meetings (suggestions for meeting topics are welcome)
    - (August 8) ADME
        - Based on the results of our literature inventories, we should be able to begin working with the ADME/PK members of the team to figure out what ADME information and models might be most useful to support the assessment
    - (August 15) Preliminary Analysis Plan check-in
        - Including check for consistent dose conversion across tox sections
    - (August 22) Tests of study quality evaluation protocols
    - (August 29) Data Extraction Protocols
        - Gather available information and resources to support data extraction protocol development
        - Review of data extraction requirements for BMD and CatReg analyses
        - At this meeting, we will also discuss health effects in our literature inventories that may be candidates for economic analysis
    - (September 12) MOA check-in
        - Meet to discuss proposed PECO statements and search strings with information specialists from HERO and ICF
        - What is needed from Jenny/TPWG to support MOA analyses?
    - (September 19) Data Extraction Protocol check-in
    - (September 26) Team feedback: Reviews of sample evidence tables from ICF
    - (October 3) Data Extraction Protocol check-in
    - (October 17) Hazard summary introduction
    - (October 24) ADME check-in