Notes Updated July 1, 2019

Summary of Meeting and Action Items

Event Title: Stakeholder Meeting: Chloroprene Request for Reconsideration (Follow-up)
Date: June 12, 2019
Time: 2:00 PM – 4:00 PM
Location: NCEA/ORD/EPA, Research Triangle Park, NC
Keywords: IRIS, chloroprene

Attendees:

Paul Schlosser - NCEA/ORD/EPA
John Vandenberg - NCEA/ORD/EPA
Kris Thayer - NCEA/ORD/EPA
Sonja Sax – Ramboll
Jerry Campbell – Ramboll
Cynthia Van Landingham – Ramboll
Patrick Walsh – Denka Performance Elastomer, LLC (DPE)
Harvey Clewell – Ramboll
Ken Mundt – Cardno ChemRisk
Mel Andersen – Andersen ToxConsulting
David Gray – R6/EPA
Allen Davis – NCEA/ORD/EPA
Belinda Hawkins – NCEA/ORD/EPA
Tina Bahadori – NCEA/ORD/EPA
Alan Sasso – NCEA/ORD/EPA
Kevin Kirby – OMS/EPA
Victor Morozov – NCEA/ORD/EPA
Madison McGovern – NCEA/ORD/EPA
Lou D'Amico – ORD/EPA
June Sutherlin – Louisiana Department of Environmental Quality
Ted Broyles – Louisiana Department of Environmental Quality
Lourdes Iturralde – Louisiana Department of Environmental Quality
Elliot Vega – Louisiana Department of Environmental Quality
Robinan Gentry – Ramboll
Dustin Kapraun – NCEA/ORD/EPA
Amanda Bernstein – NCEA/ORD/EPA
Kate Saili – OAR/OAQPS/EPA
Darcie Smith – OAR/OAQPS/EPA
Vicki Soto – NCEA/ORD/EPA
Paul White – NCEA/ORD/EPA

Meeting Agenda:

1) Introductions (all)
2) Overview of updates to the PBPK model (DPE consultants)
3) Focused Q/A discussion of the model updates (led by the EPA/ORD PK team)
4) Other questions/comments (all)

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Summary of Meeting Activities:

- Ramboll/DPE presentation (attached)
    - Additional discussion was prompted by DPE to update the current inhalation unit risk (IUR) from the 2010 IRIS assessment of chloroprene.
        - EPA responded that this meeting was set to discuss next steps in finalizing the physiologically based pharmacokinetic (PBPK) model for chloroprene in order to move forward with the request for reconsideration (RFR). Discussions related to the risk evaluation or assessment will occur in future meetings.
    - On slide 15, EPA inquired about the number of samples from human lung studies for microsomal metabolism of chloroprene used in the Ramboll report.
        - Ramboll clarified there was one study of chloroprene metabolism in human lung tissue, published by Himmelstein et al. (2004a). In this study, a single sample consisting of pooled lung microsomes from 5 individuals was used.
        - Ramboll discussed similarities with methylene chloride and other chemicals where this type of in vitro scale-up approach has been applied, noting that both the EPA Office of Pesticides and FDA use these approaches. EPA clarified that there are distinctions among different EPA offices (e.g., NCEA, Office of Pesticide Programs) and agencies (e.g., Food and Drug Administration) regarding access to data sets and study validation.
- EPA presentation (attached)
    - Slide 3 indicates EPA's concern over mixing methods for the In vitro mass transfer experiment conducted by DPE at EPA's request. Ramboll indicated the mixing is circular to decrease chances of protein degradation, claiming no loss of Vmax due to consistency and coherence of data.
        - EPA asked if the procedures and data would appear solid to biochemists experienced in microsomal methods; agreed that it would be addressed during peer review.
        - EPA and Ramboll agreed that additional attention should be given to the approach to and uncertainties associated with estimating the levels of metabolism in the human lung.
    - Based on slide 4, DPE/Ramboll discussed moving forward with their submitted publication for the PBPK model.
        - EPA responded that Ramboll may publish, but that would be independent of the EPA review process. EPA will continue forward with the QA process and the letter-peer review of the draft model before proceeding with decisions regarding the RFR and the chloroprene IRIS assessment.
    - Ramboll raised discussions from the previous meeting with EPA (July 19, 2018) and their understanding that EPA would use the PBPK model as-is, provided that it was in a form acceptable to EPA and it was to be published in a peer-reviewed journal (slide 5).
        - EPA clarified the peer review following QA is not the same as that for a journal publication and the PBPK model would still undergo EPA's process of peer review.
        - EPA indicated that they would employ a contractor to perform the peer review.
- DPE requested the status of the RFR.
    - EPA explained the RFR is currently being held open until EPA has had an opportunity to examine, assess and peer review the supplemental information now provided with the PBPK model.

        - EPA suggested the RFR could potentially be closed or withdrawn and potentially revisited as a new RFC or RFR once the model is ready.
        - DPE expressed the desire to continue with the current RFR process and continue an open dialogue as the QA process continues.
        - EPA agreed to communicate this to IQG managers.
- DPE asked if EPA is making their requests a priority.
    - EPA informed DPE the Agency is prioritizing the QA process of the PBPK and the response to RFR with respect to the chloroprene PBPK model.
- EPA and Ramboll discussed potential conflicts of interest in the peer review process due to small pool of qualified experts available.
    - Ramboll indicated they would consider withdrawing their submission for publication and wait for EPA to complete QA process and begin peer review of the PBPK model.
    - Ramboll will send final draft of the model report to EPA's pharmacokinetic (PK) workgroup for comments and feedback before resubmission.
- DPE asked if EPA would remove the 2010 IRIS assessment or its IUR value only based on the outcome of discussions.
    - EPA stated the IRIS assessment will not be changed or removed unless science presented since the Request for Correction necessitated reassessment.
    - The process was reviewed (slide 7/EPA): peer review model and address feedback; apply model to assessment (if appropriate); update IRIS assessment (if appropriate), building on earlier response to RFC; peer review IRIS Update (if appropriate).
- DPE asked if the meeting notes were to be posted on the web as had been done before.
    - EPA responded that meeting materials would be publicly available.
- DPE requested if press could be directed to the posted meeting materials for viewing or potential articles.
    - EPA did not have an issue with pointing to public documents.
- DPE asked whether EPAs consideration of the RFR included the interpretation of the occupational epidemiology studies of workers exposed to chloroprene.
    - EPA reiterated that those issues were addressed in the response to the Request for Correction; unless there were any new studies or results, the epidemiology would not be revisited.

<u>Action Items:</u>

- EPA will complete QA of PBPK model and communicate status with Ramboll/DPE.
- EPA will develop peer review charge questions and provide DPE/Ramboll an opportunity to review and before beginning the peer review process.
- Additional details on slide 7 of EPA presentation.