

November 30, 2011

NASA thanks EPA for the opportunity to review and comment on the draft final Dioxin IRIS risk assessment. Comments are submitted by NASA Headquarters Environmental Management Division and represent NASA's response in support of interagency review and public comment.

NASA reviewed the draft final Dioxin assessment and submits the following comments:

- NASA strongly supports EPA addressing outstanding technical issues identified during public comment and independent peer review (in this case, the Science Advisory Board or SAB) prior to finalizing IRIS assessments, however, the piecemeal approach proposed for Dioxin is likely to further heighten controversies and confusion, when the IRIS values are applied to specific actions. EPA's decision to split this complex assessment into separate non-cancer and cancer assessments does not reflect SAB recommendations and does not mirror the established EPA IRIS process.
- EPA's decision to split the previously reviewed combined cancer and non-cancer assessments and finalize only the non-cancer assessment caused significant confusion during interagency review. EPA's rationale to split a heavily reviewed document has not been adequately explained and will likely cause widespread confusion and uncertainty when regulators apply only the non-cancer values to new or ongoing remediation efforts.
- Technical review of the now split document which focuses only on the non-cancer assessment is further hampered by EPA's decision to leave not make a clean split between the non-cancer and cancer studies in the draft document under review. Much of EPA's review and assessment of studies forming the basis of the cancer assessment (which is not included in the current final draft) remain throughout the document. NASA questions how to review the current voluminous draft final assessment, especially when there is no ability to evaluate how EPA will use identified cancer studies in its future cancer assessment.
- This unusual effort to split non-cancer and cancer IRIS assessments raises the concern that the Dioxin cancer studies, included in the non-cancer IRIS risk assessment will, in effect be "grandfathered in" as final. EPA has not provided any mechanism or assurance that the proposed future cancer assessment will permit technical review and comment of the fundamental cancer studies and EPA's applications, as these studies would be in a previously finalized Dioxin assessment providing non-cancer values. NASA questions EPA's unusual proposed plan to split the non-cancer and cancer assessments without clear guidance and technical direction as promoting unnecessary confusion among practitioners and the public and limiting independent review.
- EPA, in its response to the SAB peer review, responded specifically to specific identified SAB recommendations only. Detailed SAB comments outlined technical weaknesses and areas for

review and reassessment but EPA did not consistently address these major issues and concentrated only on the recommendations. Generally, independent peer review provides crucial, often detailed input to identify and address technical/scientific weaknesses, confusing or inaccurate approaches, and errors that are necessary to prepare a document for public release. EPA's targeting only recommendations misses much of the SAB's detailed input and technical direction.

- NASA appreciates EPA's effort to clarify and present its assessment in a more concise, substantiated format, a response to National Academy and ongoing interagency comments on IRIS reports faulting their generally excessive size and lack of clarity on decision making. However, in the final draft Dioxin assessment, a bulk of the significant evaluation of scientific and technical issues is now shifted to the Appendices which remain voluminous, difficult to review and lacking ready transparency. EPA's decision to retain a bulk of the studies and evaluation supporting the now postponed cancer assessment in the newly separated non-cancer assessment further undercuts transparency and technical review.
- NASA respects that EPA must access and consider emerging, peer reviewed studies but retain the ability to stop studying to complete and finalize assessments. NASA notes that EPA updated its draft report until October 2009 but EPA also states that it "included evaluations of several studies published in 2010 and 2011". EPA does not provide any substantiation of how these most recent studies were chosen and evaluated. In addition, EPA does not provide clarification of how the Agency chose key studies, an ongoing interagency concern and noted in the recent NAS Report on Formaldehyde. This is in contrast with the SAB direction that EPA to provide clear descriptions of the criteria used to evaluate studies and chose key results.
- NASA notes that four significant and highly relevant studies on over 500 maternal-infant pair offered dose response information not found in EPA's chosen key studies and that these relevant studies were not considered. EPA should consider these studies to establish the NOAEL and minimize the need to apply Uncertainty Factors to address data gaps in EPA's chosen key studies. These studies provide support for the SAB direction that EPA strengthen its analysis by a review across animal and human epidemiological studies which are not readily reflected in the current draft final IRIS assessment. Examples of relevant studies are listed below:
 - Maervoert et al., 2007. *Environ. Health Perspect.* **115**(12): 1780-6
 - Wang et al., 2005. *Environ Health Perspect.* **113**(11): 1645-50
 - Wilhelm et al. 2008. *Mutat. Res.* **659**(1-2):83-92.
 - Koopman-Esseboom et al. 1994. (*Pediatr.Res.* **36**(4): 469-73
- The SAB directs EPA to reconsider and clarify its apparent exclusion of null result epidemiological studies, a long standing technical issue identified through interagency review on

IRIS assessments. NASA sees limited discussion of this crucial issue in the most recent draft final assessment and it remains a significant outstanding weakness in IRIS assessments.

- SAB directed EPA to modify and expand its use of the Emond PBPK model to address outstanding identified issues. EPA's response to SAB direction results in no changes to previous proposed action levels, Uncertainty Factors (UF) or conclusions.
- SAB identified that EPA, in its development and use of a mouse model to estimate TCDD in the body, did not follow established EPA guidance to use only peer reviewed studies and models in its IRIS assessments. Review of the draft final Dioxin assessment does not clearly provide that this model has been peer reviewed or what, if any, impact this required review had on EPA's assessment. Regardless of whether this model is critical to EPA's assessment, use of non-peer reviewed studies and models represents a departure from established EPA policy and should be corrected and any changes be addressed in the assessment.
- EPA's use of a Hill co-efficient of less than 1 was deemed implausible by the SAB who directed EPA to redo its calculations with the more appropriate Hill co-efficient of 1. Additionally, SAB noted that EPA needed to run sensitivity analyses, a normal practice that incorporated this change to the Hill co-efficient. EPA's response to this direction, which the SAB projected to potentially impact on the calculation of an RfD, resulted in exactly the same value previously proposed. NASA notes that EPA's response to the specific technical direction (such as the Hill co-efficient issue) from the SAB yielded no change in proposed action levels, such as the RfD, or UF from previous versions of the draft Dioxin IRIS assessment. In addition, the lack of including required sensitivity analyses remains an outstanding issue in EPA's current draft final Dioxin IRIS assessment and links directly to another significant SAB's concern over the lack of a quantitative uncertainty analysis.

In summary, NASA proposes that EPA address these outstanding issues identified in both public comment and through the independent peer review by the SAB. In the interest of transparency and technical accuracy, EPA should document the re-calculation the RfD to reflect the best available science and approved methodology. EPA's proposed split of the Dioxin assessment into currently a non-cancer assessment with a cancer assessment at a later date does not represent direction from the SAB and will likely create confusion and adversely impact technical review and comment. EPA is encouraged to work to provide one cohesive Dioxin assessment (non-cancer and cancer), reflecting sound science in keeping with the established EPA IRIS process.

Again, NASA thanks EPA for the opportunity to comment on the proposed draft final Dioxin IRIS risk assessment (non-cancer).