

National Aeronautics and Space Administration (NASA) Comments on the Interagency Science Consultation Draft IRIS Toxicological Review of 1,4-Dioxane (dated May 2011)

Date: June 13, 2011

NASA thanks EPA for the opportunity to review and comment on the updated draft assessment for 1,4-Dioxane. Upon review, we have the following comments and issues and request EPA consider addressing the identified issues, prior to submitting this updated draft for peer review.

Global Issues:

- This updated draft (which now includes proposed RfD and RfC levels) demonstrates the verbosity and lack of ready transparency with a lengthy discussion of the literature but limited clarity on the chosen studies and assumptions. NASA has noted this issue in previous draft assessments and this concern was also identified as a systemic concern in the most recent NAS review on formaldehyde. EPA is encouraged to implement the guidance provided by the NAS to ensure clear presentation of EPA's application of studies in the development of its assessments.
- As this draft was previously subjected to peer review (for the RfD only), NASA encourages a complete peer review to determine if EPA adequately addressed the previous peer review issues and also to consider the new data and study forming the basis of the proposed RfC. Inclusion of new studies (Kano et al, 2009) is a significant change but without peer review, there is no way to know if this significant new addition addresses the peer review issue or raises questions or incompatibilities with the use of Kasai, 2008 and 2008 to estimate the RfC.
- The reader finds it difficult to determine if EPA was responsive to the initial peer review. Redline strikeouts indicate new language for the proposed RfC but little clarification of efforts to address outstanding scientific issues identified during the first peer review.

Specific Issues:

- The draft lacks clarity and discussion on the Kano et al, 2009 study and its relationship (and clarification of) the JBRC 1998a study. It appears that two different data sets were used to make conclusions between the two drafts. NASA questions that use of different data requires significant clarification by EPA and also full peer review.
- As noted in the previous interagency review, use of the Kociba study remains problematic, especially as EPA characterizes its decision to use Kociba as the basis of the RfD as it was "the most sensitive". The updated draft lacks clear discussion of why Kociba was chosen and question what is meant by "sensitivity" and its relevance in this draft. EPA is encouraged to clarify its choice of Kociba and any issues or inconsistencies found when comparing the Kociba and Kasai studies that are the basis for the proposed RfD and RfC respectively.

- The lack of studies (only four are mentioned) for the development of an RfC raises significant concerns that the updated draft's proposed RfC is premature and not supported by scientific literature. The Kasai 2008 and 2009 studies were chosen as the foundation of the RfC development. EPA, by its own admission, states that the lack of any corroborating evidence in other studies for the Kasai result. EPA further notes the weakness in reliance on this one study but setting UFs of 1000 with significant levels of uncertainty in all categories. NASA requests EPA re-consider issuing a draft RfC, based on such limited evidence. We also request an in-depth discussion of how EPA will address peer review responses, should this very limited base (one study) source for the proposed RfC be identified as an outstanding issue.
- The previous interagency review and the peer reviewers of the proposed RfD requested EPA consider non-linear extrapolation. A number of commenters indicated that the Mode of Action (MOA) could not be readily determined but the MOA was likely to be non-linear. EPA's response in the updated draft is to dismiss the peer reviewers input. NASA requests EPA re-visit this issue, in light of the peer reviewers input and the lack of solid, defensible data that indicates a linear relationship. This remains a significant issue and the updated draft needs clarifying language to clearly state EPA's evaluation. Again, the draft text should contain this clarifying language and be subject to peer review again.