

Office of Management and Budget (OMB) and Office of Science and Technology Policy (OSTP)
Comments on the Interagency Science Consultation Draft IRIS Assessment of *tert*-Butanol (dated September 2014)

Date: November 21, 2014

November 20, 2014

Interagency Review (Step 3) of EPA IRIS Toxicological Review of *tert*-Butanol

Dear EPA IRIS:

Thank you for the opportunity to provide comments on the draft Toxicological Review of *tert*-Butanol. We have comments on both the Preamble and the dose-response assessment.

Preamble Comments

As noted in the comments on the Preamble for ETBE and RDX, there are statements in the Preamble that amount to policy positions or decisions rather than scientific ones. Those comments are not reproduced here, but should be considered as part of this record.

- For consistency with RDX and ETBE, the page numbers should be lower case Roman numerals (the Preamble begins in lower case Roman numerals, but then switches to Arabic numerals).

Primary Comments

- Confusion regarding $\alpha_2\mu$ -globulin:
 - p.ES-1, lines 30-32: "Mode of action analysis determined that male rat kidney effects were not mediated by $\alpha_2\mu$ -globulin, and these effects are concluded to be relevant for human health hazard assessment."
 - p.ES-2, lines 16-18: "Mode of action analysis determined that male rat kidney effects were not mediated by $\alpha_2\mu$ -globulin, and these effects are concluded to be relevant for human health hazard assessment."
 - p.ES-5, lines 17-20: "Because the available data supports the occurrence of at least two of the subsequent steps in the pathological sequence, these data are sufficient to conclude that $\alpha_2\mu$ -globulin nephropathy is occurring in the kidney of male rats following *tert*-butanol exposure. Thus, the noncancer lesions associated with $\alpha_2\mu$ -globulin nephropathy are not considered relevant to humans."
- Table 2-6: please demarcate which rows (candidate values) are based off of a subchronic inhalation study or route-to-route extrapolation from a chronic drinking water study.

Comments on Charge to the SAB

- Follow-up to question 3e: Has EPA presented sufficient justification for deriving an oral slope factor and an inhalation unit risk when the cancer descriptor of "suggestive evidence" was concluded?