

James S. Bus, Exponent, Inc., on behalf of LyondellBasell: Oral comments on the draft EPA Science Advisory Board report addressing the draft EPA IRIS Toxicological Reviews of Ethyl Tertiary Butyl Ether (ETBE) and *tert*-Butyl alcohol (tBA).

March 22, 2018

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Good morning. I am a toxicologist with Exponent, Incorporated and my comments today are offered on behalf of LyondellBasell.

I encourage SAB members to consider the brief written comments submitted by LyondellBasell, which provide further details of my oral summarization presented today.

First, and most importantly, LyondellBasell concurs with the clearly stated SAB Tier 1 conclusions that EPA should “refrain from conducting a quantitative analysis” of the cancer risks of both ETBE and tBA. However, in order to avoid future misinterpretation of this Tier 1 SAB conclusion, the SAB must clarify the conflicting conclusions that the oral slope factors are “scientifically supported” and “no consensus was reached regarding EPA’s calculation of an Inhalation Unit Risk for ETBE.”

Second, LyondellBasell recommends that SAB clarify its conclusion that acetaldehyde is a “plausible” contributor to ETBE genotoxicity and carcinogenicity. SAB has stated that the “preponderance of data” indicate ETBE and tBA are not genotoxic and that “the agency is encouraged to reduce emphasis on this mode of action in the final assessment.” In addition, worst-case occupational and consumer ETBE exposures associated with re-fueling operations are conservatively equivalent to acetaldehyde formed from consumption of 16% of 1 drop of beer, indicating this hypothesized mode of action lacks quantitative human exposure plausibility.

Third, the SAB did not reach a consensus on interpretation of the human relevance of the kidney toxicity endpoint, but nonetheless recommended sole use of this endpoint for derivation of an RfD and RfC. This recommendation non-transparently biases such values to an endpoint specifically regarded as highly controversial and uncertain, and thus should be expanded to include use of alternative endpoints for these non-cancer values.

Fourth, LyondellBasell agrees with the SAB conclusion that PBPK modeling is not necessary or appropriate to support inhalation-to-oral cross route risk extrapolation for ETBE in that a high quality drinking water study conducted at the limit of water solubility did not identify ETBE as a rat carcinogen. LyondellBasell also agrees with the SAB conclusion that the lack of a mouse PBPK model and other factors such as onset of nonlinear toxicokinetics indicates high-dose specific tBA mouse thyroid tumors are not suitable for derivation on an Inhalation Unit Risk.

Finally, the SAB is to be applauded for recommending that maternal systemic toxicity endpoints must be considered when evaluating developmental and reproductive toxicity outcomes.

Thank you.