

**EPA Request for Clarifications of the SAB Draft Peer Review Report on
Ethyl Tertiary Butyl Ether and *tert*-Butyl Alcohol (*tert*-Butanol)**

For March 22, 2018 Teleconference

EPA is seeking clarification on some recommendations provided in the Science Advisory Board Chemical Assessment Advisory Committee (SAB-CAAC) draft report, “Review of EPA’s Draft Assessments entitled Toxicological Review of Ethyl Tertiary Butyl Ether (ETBE) and Toxicological Review of *tert*-Butyl Alcohol (*tert*-Butanol).” For each area of clarification, text from the draft SAB-CAAC report is provided below, followed by EPA’s request for clarification.

Chemical Properties and Toxicokinetics

Draft report language

ETBE, page 2 lines 18-19: “The SAB finds the choice of the rate of metabolism of ETBE to be a reasonable dose metric; however, it is not recommended for extrapolation from inhalation to oral routes of administration of ETBE.”

Clarification

EPA is seeking clarification on whether the panel is suggesting that metabolic rate could be used for animal-human extrapolation within a route of exposure, and that choice of an alternate metric is based on the assumption that the alternate metric provides a more consistent dose-response evaluation.

Noncancer toxicity at other sites

Draft report language

ETBE, page 25 lines 28-30: “Since there are male reproductive effects on genetically susceptible mice, which mirror large human populations, at lower doses than other toxicities, the SAB recommends giving more emphasis to these results.”

Clarification

EPA is seeking clarification on what is meant by “giving more emphasis”? (Especially in the context of SAB’s agreement that noncancer toxicity at sites other than the kidney should not be used as the basis of reference values for ETBE and *tert*-Butanol.)

Draft report language

tert-Butanol, page 27 lines 24-28: “Maternal toxicity has effects on offspring development, particularly on neural and behavioral development, and female reproductive performance. Therefore, the LOAEL for lethargy and ataxia should be considered in the reference dose analysis. More specific information on metabolic and sedative actions of *tert*-Butanol on the exposed dam is needed since it impacts reproductive function and development of the offspring. Therefore, the LOAEL for lethargy and ataxia should be considered in the reference dose analysis.”

Clarification

EPA is seeking clarification on what manner of specific information regarding the metabolic and sedative actions of *tert*-Butanol on the exposed dams is requested. Is this a request for more research in this area (and if so could be considered a tier 3 recommendation)?

Draft report language

tert-Butanol, page 2 lines 44-45: In the Executive Summary, the SAB CAAC concludes that “The SAB agrees that noncancer toxicity at sites other than the kidney should not be used as the basis for deriving an oral reference dose (RfD) for *t*BA.”

Clarification

EPA is seeking clarification on how this advice can be interpreted with regards to the repeated tier 1 recommendation above that “the LOAEL for lethargy and ataxia should be considered in the reference dose analysis.”

Oral reference dose for noncancer outcomes

Draft report language

ETBE, page 28: The second and third bullets of Tier 1 recommendations for ETBE are very similar to the third and fourth bullets of Tier 3 recommendations for *tert*-Butanol, on page 29. “The tables within this section need to include units for completeness and interpretability; The EPA should consider a more integrated presentation of the current text, tables and graph; as is, it is difficult to track information and the text often requires much page-flipping.”

Clarification

EPA is seeking clarification on whether these recommendations were indeed seen as being a much higher priority for ETBE than for *tert*-Butanol. Or would the SAB CAAC consider these recommendations to be of similar tier for both assessments (and if so what would that tier be)?

Choice of dose metric

Draft report language

ETBE, Page 19 line 4: “The SAB notes that where EPA’s analysis question; is ETBE in blood versus in liver?”

Clarification

EPA is seeking clarification on the meaning of this statement.