Scientific Review Panel on Toxic Air Contaminants
c/o Jim Behrmann, Panel Liaison,
California Air Resources Board,
1001 I Street, 2nd Floor,
P.O. Box 2815,
Sacramento, CA 95812

March 2, 2017

Dear Chairman Kleinmann and Members of the Scientific Review Panel,

After reviewing the presentation from OEHHA and transcript from your December 13th, 2016, meeting on the proposed cancer risk factor for TBAC, it is apparent that there was confusion about the regulatory status of TBAC and TBA in California and some of the toxicological data presented. As OEHHA stated in response to Panel Member Blanc's question (p. 159, lines 11-14), the proposed cancer unit risk factor is *not* a revision of a previously established risk factor for a Prop 65 or Hot Spots-listed carcinogen. Neither the SRP nor the Cancer Identification Committee (CIC) has previously reviewed either chemical except in the context of MTBE, another chemical that metabolizes to TBA. Now, OEHHA is asking the SRP for only the second time ever, to sanction a cancer risk factor for a chemical that has not been determined to be a carcinogen by any authoritative agency. We urge the Panel to reconsider the evidence presented in our November 14th letter and the following additional comments.

In 1998, the Cancer Identification Committe was asked to review the toxicological database on MTBE and concluded, as other international agencies have, that MTBE cannot be classified as a human carcinogen and and should not be added to the Prop 65 list of carcinogens. Nonetheless, in 1999, the SRP reviewed the same data and added MTBE to the list of Air Toxics as a carcinogen. To date, MTBE remains the ONLY chemical out of 150 that is listed as a Hot Spots carcinogen but has not been listed on Prop 65 by the CIC, see Figure 1. MTBE also has the lowest calculated cancer risk factor of any chemical on the Hot Spots list. Furthermore, no authoritative body has concluded that MTBE, TBA, or TBAC are potential or known human carcinogens including the authors of the National Toxicology Program's 2-year TBA drinking water study, California's CIC, the US Environmental Protection Agency (EPA), or the International Agency for Research for Cancer (IARC).

In addition, a Pathology Working Group (PWG) of 5 kidney pathologists led by Dr. Gordon Hard reviewed the 1995 NTP kidney pathology slides (Hard et al., 2011) and arrived at the following conclusion:

> "*There was unanimous agreement among the members of this independent PWG that both a2u-g nephropathy and CPN exacerbation* ***were the only causative factors*** *(emphasis added) in the development of renal tubule tumors observed in male rats exposed to TBA in drinking water. As neither of these modes of action have human counterparts, the PWG concluded that TBA-related renal changes in rats could not be extrapolated for human health risk assessment, and were unlikely to pose any risk for humans*."

OEHHA's proposed cancer slope factor for TBAC is based solely on their speculation that TBA, the primary metabolite of both TBAC and MTBE, is a genotoxic human carcinogen which is contrary to the

LyondellBasell
One Houston Center, Suite 700
1221 McKinney Street
Houston, TX 77010

Tel +1 713-309-2000
lyondellbasell.com

weight of the genotoxicity evidence. This opinion also runs counter to that of several independent panels of toxicologists including California's Cancer Identification Committee. SRP validation of OEHHA's cancer risk factor calculation for TBAC would amount to a tacit endorsement that TBA is a genotoxic human carcinogen based on the male rat kidney tumors observed in the 1995 TBA drinking study, and would contradict a previous determination by the CIC for MTBE. If TBA or TBAC were added to the Hot Spots Air Toxics list as carcinogens, they would be the ***only*** ones on the list, besides MTBE, that are not also listed as carcinogens on Prop 65 and have not been classified a carcinogens by anybody OEHHA considers authoritative.

OEHHA's conclusions are also not supported by multiple weight of evidence reviews of TBA or TBAC as follows:

1. The weight of the scientific evidence supports the conclusion that neither TBA nor TBAC is genotoxic. (Felton 2014, Cruzan & Kilpatrick 2010, Bus et. al. 2015, McGregor 2010)
2. The male rat kidney tumors from which the cancer risk factor was estimated were only caused by modes of action, α-2u-globulin nephropathy and exacerbation of chronic progressive nephropathy (CPN), that do not exist in humans. (Hard et.al. 2011)
3. The estimated risk factor incorrectly assumes a non-threshold cancer mechanism that is relevant to humans.

A related procedural comment concerns Panel Member Blanc's question on transcript page 165, lines 13-25, and is tied directly to history of the TBAC draft document under review by the SRP. The reason OEHHA developed an *interim* risk factor for TBAC based on the 1995 TBA chronic study was because Arco Chemical requested that CARB grant a VOC exemption for TBAC based on its negligible ozone forming potential. As mentioned earlier, the *interim* cancer risk factors developed by OEHHA in 1999 and 2000 for TBA and TBAC were never sanctioned by CIC or reviewed by the SRP, but nonetheless have been used by CARB and a few air quality districts to deny the VOC exemption of TBAC in California for the past 13 years. Because of this use of an unsanctioned and unofficial risk factor to deny the VOC exemption, Lyondell requested a formal evaluation of the risk factors in 2011 and a peer review by the State's qualified experts, i.e., the CIC or SRP. OEHHA not only failed to engage the CIC in resolving the scientific adequacy of the interim cancer risk factor assumptions, but also took four years to independently complete the reevaluation and a full year to respond to our comments, leaving us with two weeks to respond, and the SRP less than a month to review the extensive literature and form an opinion on the merits of the OEHHA case.

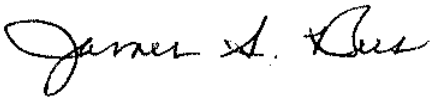
Understandably, some members of the panel questioned why a chemical with minimal exposure and hazards should take precedence over far more toxic and prevalent chemicals in current use. We agree and are concerned that OEHHA has not allotted adequate time for meaningful independent review and public comment and is now asking the SRP to make a determination of carcinogenicity that is normally the purview of the CIC. Given the little amount of time you were afforded to understand the history, to review the literature, and to form an independent opinion on the science, we urge you to reexamine the relevant facts on TBA and TBAC cancer evaluations and genotoxicity, as well as the detailed comments on the toxicology provided in our first letter and the references described above.

We are confident that, given adequate time to review the evidence, you will arrive at the same conclusion as numerous other independent authorities and experts, which is that neither TBA nor TBAC poses a cancer risk to humans. The controversy over the carcinogenicity of TBA, and TBAC has lingered in California for almost 20 years and both regulators and the regulated community have

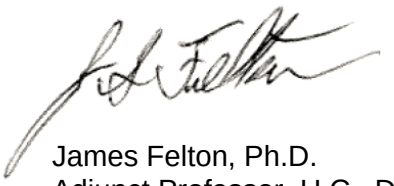
the right to expect a fair, thorough, and independent review and ruling by the State's Qualified Experts.

We thank you again for the time you will take to review these comments and the information provided.

Respectfully,

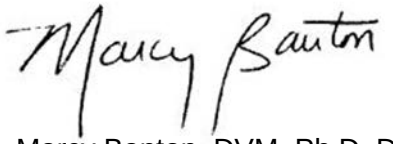


James S. Bus Ph.D., DABT, Fellow ATS
Senior Managing Scientist
Center for Toxicology and Mechanistic Biology
E[x]ponent®



James Felton, Ph.D.
Adjunct Professor, U.C., Davis School of Veterinary Medicine

Daniel B. Pourreau, Ph.D.
Technical Service Manager
LyondellBasell



Marcy Banton, DVM, Ph.D. DABVT
Senior Manager, Toxicology
LyondellBasell

Figure 1: Cancer Unit Risk Factors for Prop 65 Carcinogens on the Air Toxics list, and those proposed by OEHHA for MTBE, TBA, and TBAC.