



Aug 21, 2015

Comments submitted to the SAB CAAC via email to Diana Wong

Public statement from Nancy Beck, PhD, DABT, on behalf of the American Chemistry Council, to the Scientific Advisory Board Chemical Assessment Advisory Committee (CAAC) for the review of the Draft Benzo[a]pyrene (BaP) IRIS Assessment.

Good Afternoon.

I am providing remarks today on behalf of the American Chemistry Council (ACC). We have read your draft report on the IRIS Benzo[a]pyrene (BaP) Assessment and want to thank you all again for the time and energy you are putting into this review. It is clear that each of you is taking your responsibilities seriously and we recognize the considerable effort that has gone into conducting this review. Not only is it important to get the BaP science correct, but as this is one of the first semi-revised IRIS assessments you are reviewing, your comments on the structure, approach and methodologies used in this assessment will have precedent setting implications for many other IRIS assessments.

There are many recommendations in the draft report that ACC supports and due to the time constraints I will not point them out. Thus my comments today will focus on areas where public input may help to improve the clarity of your recommendations and therefore help to strengthen the final IRIS assessment.

- 1) **The quality of individual studies should be objectively evaluated and transparently presented.** In multiple places the draft report appropriately points out that EPA either did not consistently address the quality of the studies or the agency did not appropriately consider the quality of studies (including the endpoints evaluated in the studies) when conducting dose-response modelling. Having clear criteria by which to evaluate study quality is an integral part of systematic review approaches. While EPA is working to implement these approaches in future assessments, based on the draft report and observations during your review, it would be beneficial if this CAAC report recommended that EPA clearly evaluate each critical study for its overall quality using transparently described and objective criteria. Due to the importance of IRIS values and their varied uses for regulatory determinations, studies must meet a sufficient quality standard for use in dose-response modelling. Simply saying a study

was the “best available” does not guarantee the necessary level of study quality. Once studies are all objectively and transparently evaluated, we recommend that the study quality rating be clearly noted in summary tables such as tables 2-1 and 2-1 in the draft IRIS assessment. This clarity and transparency will not only assist EPA assessors, but will also go a long way to helping peer reviewers and stakeholders understand the importance of study quality in IRIS assessments. We encourage the CAAC to make this recommendation to improve the draft BaP assessment.

- 2) **The mode of action for forestomach tumors should matter when applying the EPA’s supplemental guidance.** We appreciate the consideration the draft report gives to the presence and relevance of forestomach tumors. The EPA draft assessment and your draft report support the notion that the forestomach tumors arise from a hyperplasia of squamous epithelial cells. This is not a mutagenic mode of action. We note that these tumors drive the oral slope factor (see table 2-7). While we are not disputing the fact that BaP may have a mutagenic mode of action, the forestomach tumors, seen after exposure via gavage and diet, which drive the oral slope factor, *may not necessarily occur via a mutagenic mode of action*. Thus we ask you to consider whether the application of age-dependent adjustment factors (ADAFs) is appropriate for this value.<sup>1</sup> While EPA’s *Supplemental Guidance for Assessing Susceptibility from Early Life Exposures to Carcinogens* (U.S. EPA, 2005b) provides general guidance on when to apply the ADAFs, this guidance must be used in the context of the best available scientific information and what is known about the relevant mode of action. In this case the relevant mode of action, for the forestomach tumors, does not appear to be mutagenic.
- 3) **Comments on the confidence of the RfD and RfC values would be useful.** In 2013, when EPA first took comment on the charge questions for this review, ACC suggested that a charge question be added to evaluate EPA’s confidence ratings for the non-cancer values. We reiterated this request to you in March 2015.<sup>2</sup> As the draft report does express some serious concerns about EPA’s non-cancer values, and the quality of the data supporting them, it would be extremely useful if the CAAC would provide clear recommendations to EPA regarding what the quality rating of these derivations should be, based on the available data. For instance, for the RfC, EPA has used the maximal value of uncertainty factors (3000), yet EPA has stated that the overall confidence in the RfC determination is low-to-medium. ACC

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<sup>1</sup> The EPA supplemental guidance, at page vi states: “Therefore, the Supplemental Guidance has no binding effect on EPA or on any regulated entity. Where EPA does use the approaches in the Supplemental Guidance in developing risk assessments, it will be because EPA has decided in the context of that risk assessment that the approaches from the Supplemental Guidance are suitable and appropriate. This judgment will be tested through peer review, and the risk assessment will be modified to use different approaches if appropriate.” Available at: [http://www.epa.gov/ttnatw01/childrens\\_supplement\\_final.pdf](http://www.epa.gov/ttnatw01/childrens_supplement_final.pdf).

<sup>2</sup> See ACC comments available at: [http://yosemite.epa.gov/sab/sabproduct.nsf/F06F2E035E6AB06185257DFD007AA896/\\$File/ACC+letter+to+BaP+CAAC+03032015+docx.pdf](http://yosemite.epa.gov/sab/sabproduct.nsf/F06F2E035E6AB06185257DFD007AA896/$File/ACC+letter+to+BaP+CAAC+03032015+docx.pdf).

disagrees with this characterization and we therefore suggested that a charge question be provided to peer reviewers to address this and other differences regarding the strength of evidence of the non-cancer values. While EPA did not provide such a charge question, your comments on the confidence in the RfD and RfC derivations would be extremely helpful to stakeholders.

Thank you again for the time and energy you have put into this important review. There are many areas in the draft report where your comments are extremely helpful and will be very useful as EPA works to finalize the BaP IRIS assessment. Your efforts are greatly appreciated. I would be happy to answer any questions.