Pavement Coatings Technology Council

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October 2, 2014

Dr. Diana Wong, Designated Federal Officer
U.S. Environmental Protection Agency
Science Advisory Board Staff Office

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Dear Dr. Wong,

Subject: Invitation for Public Comment on the List of Candidates for the EPA Science Advisory Board Chemical Assessment Advisory Committee Augmented for Benzo[a]pyrene Review (List of Candidates), September 10, 2014

On behalf of the Pavement Coatings Technology Council (PCTC), thank you for the opportunity to comment on the subject List of Candidates posted to the Environmental Protection Agency (EPA) Science Advisory Board (SAB) web site. That 72 distinguished scientists are willing to participate as members of the Benzo[a]pyrene (BaP) augmented Chemical Assessment Advisory Committee (CAAC) panel speaks to the importance of the BaP assessment. The task the BaP panel will be asked to undertake will differ in many ways from previous reviews of Integrated Risk Information System (IRIS) assessments. Thus, the focus of our comments is not on recommending individual candidates, but rather on the importance of identifying candidates with "the necessary domains of knowledge, the relevant scientific perspectives (which, among other factors, can be influenced by work history and affiliation), and the collective breadth of experience to adequately address the general charge" to effectively undertake the BaP review.

THE SAB BAP PANEL MAY BE THE FIRST IRIS PEER REVIEW OF A SUBSTANCE WITH A SUBSTANTIAL BODY OF HUMAN EXPOSURE DATA FROM THE MEDICAL LITERATURE

EPA is in the process of improving its IRIS assessment process, as recommended by National Academy of Science panels. One of the IRIS enhancements is increased transparency and stakeholder involvement early in the process. The BaP assessment is one of the last IRIS cases proceeding without benefit of the early transparency enhancements, and provides a case study in why process changes were needed. The draft BaP assessment was subject to both internal EPA review and subsequent intra-agency review prior to release as a public review draft. In all these drafts, the hazard assessment was based on many incorrectly cited and anecdotal reports of adverse effects of human exposures to materials containing high PAH concentrations, such as coal tar and coal tar derived substances while discounting or ignoring the substantial body of literature concerning medicinal uses of coal tar and coal tar derived pharmaceuticals. Public

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comments included a thorough re-examination of the exposure information cited in the draft as well as a comprehensive review of studies of pharmacological uses of coal tar.

The draft IRIS hazard assessment identified the PAH surrogate BaP as a potent dermal carcinogen without considering the robust body of human exposure studies that resulted in the U.S. Food and Drug Administration (FDA) classification of coal tar[1] as "Generally Recognized as Safe and Effective" (GRASE) for use as an active ingredient in over-the-counter medications to treat common skin disorders such as psoriasis.[2]

Reviewers will be asked to address topics that are specific to the BaP assessment, as well as broad policy issues. The topics might include:

- An evaluation of the evidence regarding human dermal carcinogenicity and overall human hazard assessment of BaP (and the PAHs in general, for which BaP is EPA's index compound), in light of the substantial evidence of clinical studies and other reports in the medical literature;
- An evaluation of species differences and the relevance of rodent data to human dose-response assessment in the case of BaP; and
- Methods used by the IRIS program to evaluate dermal dose-response and to quantitate dermal cancer slope factors.

In the context of IRIS assessments, BaP is unusual in having such well-developed human exposure studies, and such clear indications of differences in responses between humans and test species. The BaP assessment is also precedent setting in that, for the first time, EPA proposes a dermal dose-response assessment, and, even more precedent setting, uses a substance abundantly present in FDA-approved skin medicines. The challenge the SAB office faces, then, is to assemble an augmented CAAC panel with appropriate expertise that will result in a thorough and dynamic peer review of the issues presented by the BaP assessment.

RECOMMENDATIONS CONCERNING THE LIST OF CANDIDATES IN LIGHT OF ANTICIPATED PEER REVIEW ISSUES

PCTC respectfully offers the following recommendations concerning the list of candidates for SAB's augmented CAAC review panel for BaP.

1. A number of the listed candidates are current members of the SAB's CAAC, included to foster continuity across peer reviews of IRIS assessment. PCTC commends EPA and the

[1] 21 CFR 358.703, Definitions: **(a)** *Coal tar.* The tar used for medicinal purposes that is obtained as a byproduct during the destructive distillation of bituminous coal at temperatures in the range of 900 °C to 1,100 °C. It may be further processed using either extraction with alcohol and suitable dispersing agents and maceration times or fractional distillation with or without the use of suitable organic solvents.
[2] 21 CFR 358.710 - Active ingredients for the control of dandruff, seborrheic dermatitis, or psoriasis.

SAB for instituting this measure, which will not only promote consistency but will also foster a broader awareness within the SAB and among CAAC members of overarching issues provoked by the BaP review. If EPA must choose among the candidate members for assignment to the augmented CAAC BaP review panel, we urge EPA to primarily consider those candidate members with experience with pharmacological data, species differences and dermal toxicology.

2. Several of the listed candidates served as members of the SAB's peer review panel for the IRIS program's *Development of a Relative Potency Factor (RPF) Approach for Polycyclic Aromatic Hydrocarbon (PAH) Mixtures (External Review Draft)* document. PCTC commends EPA and the SAB for encouraging continuity with the RPF panel, as BaP is used in EPA's RPF approach as the index compound for the PAHs. One of the recommendations of the RPF panel was that EPA fund testing of representative PAH-containing mixtures by the National Toxicology Program (NTP) with a view to future improvements in PAH risk assessments. Thus, participants in the RPF panel are well aware of many of the issues that they will be asked to review in peer reviewing the BaP assessment. Once again, if EPA must choose among candidates who also participated in the RPF panel, we again urge that the choice be made keeping in mind some of the broad philosophical questions that pertain to the draft BaP assessment.

3. The draft hazard assessment relied on many incorrectly cited and anecdotal reports of adverse effects associated with exposure to PAH-containing substances. Public comments challenged the draft hazard assessment. The BaP panel will be asked to review the hazard assessment. To ensure appropriate consideration of associations between exposures to BaP- and BaP equivalent-containing compounds and reports of adverse effects, as well as studies of patients published in the medical/pharmacological literature, the panel should include several epidemiologists. The List of Candidates includes a number of well qualified epidemiologists. Preparation of the public comments on the draft hazard assessment was a time consuming exercise involving review of the materials cited in the draft as well as uncited materials. A well conducted SAB panel review is not likely to require less effort. For this reason, we recommend that EPA consider including three or four epidemiologists on the panel.

4. Classification of coal tar as GRASE for use in over-the-counter skin medications by FDA and similar international government agencies means there are millions of people worldwide who intentionally slather themselves every day with lotions, creams and ointments that contain high concentrations of BaP and BaP equivalents (i.e., other PAHs). Including scientists with an understanding of FDA drug approval and classification processes could prove crucial to the BaP panel's peer review. Two of the candidates are identified as current or former researchers at FDA's National Center for Toxicological

Research (NCTR). Because an FDA perspective seems crucial to the work of the BaP peer review panel, we recommend inclusion of both.

5. In the draft BaP assessment EPA, for the first time, developed methods to quantitate dermal cancer slope factors. For this reason, and because of the FDA-approved uses of coal tar as a dermal medication, it is vital that the BaP panel include scientists with expertise in dermal toxicology. The biosketches of three candidates indicate such expertise. Because there may be different perspectives on EPA's approach to dermal carcinogenicity, we recommend including all three on the panel.

6. An issue that routinely presents in assessing hazards and dose-response evaluations in risk assessments involving BaP and BaP equivalents is bioavailability. The biosketches of four candidates indicate significant research focus on PAH bioavailibility. We recommend selection of at least two of the candidates with expertise in bioavailability on the panel.

7. A number of the scientists on the candidate list are distinguished inhalation toxicologists. There are little available inhalation data in animal models for BaP *per se*. The inhalation data that do exist are for inhalant mixtures that may contain PAHs, such as tobacco or marijuana smoke or some airborne particulate matter. Thus, in making choices among candidates with different areas of expertise, we again urge EPA to consider the questions that the BaP panel will be asked to address. While inhalation is an important pathway for some PAH mixtures, application of BaP toxicity factors and equivalents to mixtures was one of the charges of the RPF panel (see #2, above) and not likely to play as prominent a role in reviewing the IRIS assessment of BaP *per se*. PCTC therefore recommends that EPA consider inclusion of an inhalation toxicologist on the panel as a lower priority.

8. Despite the inclusion of 72 eminent scientists on the List of Candidates, we are disappointed that none of the candidates are identified as having an expertise in:

    a. The incidence of cancer among users of coal tar pharmaceuticals; or

    b. Studies of species differences, such as xenograft studies (in which human skin has been grafted onto mice, which are then exposed to PAH compounds) or genetic characteristics of tumors in different species.

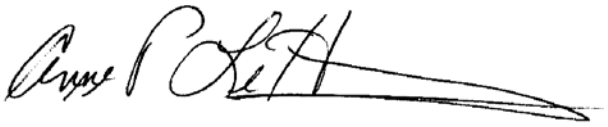
    To be as prepared as possible for the issues to be reviewed, we urge the SAB to consider further expanding the list of potential candidates to include scientists with additional pharmaceutical and interspecies expertise.

9. Finally, we are disappointed that only one of the 72 candidates is affiliated with an industry toxicology and risk assessment department. Too often, government organized review panels are composed predominantly of academic and research organization

scientists with considerable expertise on a sometimes very narrow issue associated with chemical hazard and risk assessment. We hope that industry scientists have not been discouraged by the drumbeat of anti-industry rhetoric from some in the activist community. In the case of BaP and the PAHs, many industry scientists have the requisite expertise and experience to peer review EPA's IRIS assessment without any possible conflict of interest - the universe of companies that use or make products containing BaP and the PAHs is readily identifiable. To promote balance of points of view as well as to punctuate the principle that science should be evaluated on its merits, not sources of funding or anti-industry bias, we urge the SAB to select the sole industry-affiliated scientist as a member of the BaP peer review panel.

Thank you for your consideration. Please feel free to contact me at alehuray@pavementcouncil.org or at (703) 299-8470.

Yours truly,



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