Comments to SAB PAH Mixtures Review Panel
Review of "Development of a Relative Potency Factor (RPF) Approach for Polycyclic Aromatic Hydrocarbon (PAH) Mixtures

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Good morning, and thank you for the opportunity to provide comments today. I am Annette Rohr, an environmental health scientist and board-certified toxicologist, and am speaking on behalf of the Electric Power Research Institute. I hope the SAB PAH Mixtures Review Panel has had a chance to review our full written comments.

I would like to highlight several major comments today; again, additional detail regarding each of these is provided in our submitted comments.

First, we have concerns regarding the weight of evidence evaluation performed by EPA in the document. It appears that this evaluation was not performed in accordance with the Weight of Evidence Narrative required in EPA's 2005 Guidelines for Carcinogen Risk Assessment for assessing the human carcinogenic potential of agents. EPA did not utilize a weight of evidence approach to determine if a given PAH was "carcinogenic to humans," "likely to be carcinogenic to humans," "suggestive evidence of carcinogenic potential," or "not likely to be carcinogenic to humans." The analysis was restricted to determining if the substance was positive in an assay in which benzo(a)pyrene was tested, so EPA determined if the weight of evidence was adequate to conclude that a substance tested positive in one short term system. More importantly, EPA considered a single positive result to be adequate weight of evidence to conclude that the substance should be included in the Relative Potency Factor (RPF) scheme. Ten RPFs are based on a single positive result and some of these were accompanied by negative results. One stand-alone positive result in a tumorigenicity test or one positive plus one or more negative results provides an inadequate weight of evidence that a PAH should be included in any RPF scheme. In conclusion, EPA's weight of evidence analysis was scientifically inadequate.

Second, EPA has derived RPFs for many PAHs based on an outdated and scientifically unjustifiable Cancer Slope Factor (CSF) for benzo[a]pyrene (BaP). There was no discussion in the report regarding the need to update the CSF for BaP despite the fact that a guideline-compliant two-year feeding study in mice (performed at the National Center for Toxicological Research) has been available for such purpose for more than ten years (Beland and Culp, 1996; Culp et al., 1998).

Third, EPA has issued a proposed set of RPFs without performing any validation exercises to determine if they are predictive of the tumorigenicity of real world mixtures. A perfect study for such a validation exercise is the two-year dietary study performed on

two well-characterized coal tar samples, funded by EPRI and conducted at NCTR. Using the study data, actual tumorigenicity and predicted carcinogenic potency of the mixtures were compared, and the RPF approach was found to overestimate the true carcinogenic potencies of the coal tar mixtures using either current or proposed RPFs. When the proposed RPFs were used, the overestimation of risk increased from 2 to 3-fold to 14 to 21-fold. I encourage SAB members to review pages 19-25 of our comments, which outline the details of the original study as well as this validation exercise.

Fourth, EPA did not adequately assess the data quality of the studies used for RPF derivation. With studies performed 30-40 years ago, there is a real issue with regard to the identity and purity of the test article. In many of these old studies, PAHs were purified by paper or column chromatography and then identified by melting point or ultraviolet absorption spectroscopy. While these were state of the art methods of the day, there is great uncertainty with regard to both the identity and purity of the material that was tested and then attributed to a specific chemical structure. In some cases no information is provided about the test chemical except to say that it was provided by a named person. An ancillary comment here is that many old studies carry considerable weight because they are the source of more than one, and in some cases, many RPFs. For instance, the Hoffmann and Wynder (1966) study is the sole basis for five RPFs. Such studies should be scrutinized to a greater degree because of their overall importance in the entire scheme.

Thank you very much.