

## **Comments to SAB Chemical Assessment Advisory Committee Augmented for the Review of Benzo(a)pyrene IRIS Assessment**

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Good afternoon, and thank you for the opportunity to provide comments today. I am Dr. Annette Rohr, an environmental health scientist and board-certified toxicologist, and I am speaking on behalf of the Electric Power Research Institute.

In my time today, I want to highlight a scientific issue that EPRI included in our comment document on the public comment draft of the IRIS assessment, which is that of differing mutational signatures in human skin tumors versus experimental mouse skin PAH-induced skin tumors. During the IRIS meeting in December 2013, IRIS staff requested additional information regarding this issue, which was prepared and transmitted to IRIS staff as an addendum to EPRI's comments on February 25, 2014. This 22-page addendum reviewed 62 papers related to genetic signatures. However, in the current draft of the IRIS assessment for peer review, EPA does not acknowledge receipt of this addendum, nor of the information contained within it.

Overall, the literature search provided evidence that human skin tumors are largely a result of UV light exposure, not of PAH exposure. More specifically, the literature shows that:

1. The majority of human nonmelanoma skin cancers have p53 mutations caused by UV light, typically C to T or CC to TT transitions at specific dipyrimidine sites.
2. In mouse skin photocarcinogenesis experiments, UV-induced mouse skin tumors have the same genetic signature as human basal cell carcinomas and squamous cell carcinomas.
3. On the other hand, mouse skin tumors induced by 7,12-dimethyl benz(a)anthracene (DMBA), BaP, and other PAHs have high rates of mutations in the *H-ras* proto-oncogene, and have different mutational signatures, most frequently A to T or G to T transversions in specific codons.
4. There is very little evidence that PAH-induced mouse skin tumors contain p53 mutations.
5. There is very little evidence that UV-induced mouse skin tumors, or human skin tumors, contain *H-ras* mutations.

Thus, the literature review strongly suggests that human skin tumors have a unique mutational signature attributed to UV exposure, which agrees with the signature of mouse

skin tumors induced by UV light, and that mouse skin tumors induced by PAHs contain a distinct and separate mutational signature, which is not seen in human skin tumors.

In written comments that will be submitted to the docket shortly, EPRI will include the 22-page addendum on this topic, and we hope that this information will be considered by the Panel.

Thank you for your time and for the opportunity to provide input into the IRIS process.