THE ADMINISTRATOR OF THE ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

AUG 31 2016

Peter S. Thorne, Ph.D.
Chairman
Science Advisory
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460

Dear Dr. Thorne:

Thank you for your April 5, 2016, letter providing the Science Advisory Board review panel's comments on the U.S. Environmental Protection Agency's draft Integrated Risk Information System Toxicological Review of Benzo[a]pyrene, referred to as BaP, that was released for external peer review in September 2014.

The EPA appreciates the panel's thorough review and thoughtful recommendations. We are pleased that the SAB agreed with key decisions in the draft assessment, including the following:

- the classification of BaP as carcinogenic to humans by all routes of exposure;
- the conclusion that the available mechanistic data supports a mutagenic mode of action for BaP-induced tumors and the proposed use of age-dependent adjustment factors;
- the conclusion that developmental neurotoxicity, developmental toxicity, male and female reproductive toxicity and immune toxicity are human hazards of BaP exposure;
- that developmental effects, in particular neurodevelopmental endpoints, are the appropriate basis for deriving an RfD for BaP;
- that the appropriate studies and models were included for dose-response analysis for the oral slope factor for cancer;
- that an appropriate study and models were selected for derivation of the inhalation unit risk for cancer; and
- that skin tumors in mice are relevant to humans based on evidence of a similar mode of action and can be used to derive a dermal slope factor for human skin cancer.

Your letter also included several recommendations from the SAB that will enhance the clarity of the EPA's assessment and strengthen the scientific basis for its conclusions. The EPA will carefully consider the SAB report and make revisions to the assessment that will address these recommendations. Some of the key SAB recommendations that we will address include:

- further evaluation and clarification of the noncancer hazard conclusions regarding cardiovascular toxicity, adult neurotoxicity and forestomach toxicity in rodents;
- expanding the justification for the critical endpoint selected for the basis of the reference dose for neurodevelopmental effects considering the overall picture of supporting neurodevelopmental effects and endpoints;

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- additional consideration of cervical effects as potential critical endpoints;
- increasing the comprehensiveness of the dose-response relationship for the endpoint used as the basis of the reference concentration (decreased fetal survival) through benchmark dose modeling and consideration of two additional studies;
- consideration of derivation of an oral slope factor incorporating all appropriate studies (rather than solely on a single-sex mouse study);
- clarifying the rationale for the use of allometric scaling in the derivation of the BaP oral slope factor; and
- further discussion of key assumptions used in the derivation of the inhalation unit risk.

As you are aware, the September 2014 draft BaP assessment included an approach for estimating the risk of skin cancer following dermal exposure. The EPA appreciates the SAB's commendation of this effort. Some of the key SAB recommendations for improving the scientific basis of the proposed dermal slope factor, which we will address as we move forward, include:

- exploring combining results from several mouse skin tumor bioassays;
- further consideration of cross-species scaling, taking into consideration differences between mouse and human skin such as thickness and metabolic rates in the target tissue; and
- modeling skin-cancer risk as a function of absorbed dose rather than applied dose.

The EPA is working expeditiously to respond to these recommendations and to finalize the assessment as quickly as possible.

In the meantime, I want to reiterate my gratitude for the thoughtful review by the SAB and the panel. Your contributions are extremely valuable to ensuring that the EPA uses best available science in finalizing this important health assessment.

Sincerely,

Gina McCarthy

THE ADMINISTRATOR OF THE ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

AUG 31 2016

Elaine M. Faustman, Ph.D.
Chairwoman
Chemical Assessment Advisory Committee Augmented for the Review
of the Draft IRIS Benzo[a]pyrene Assessment
Science Advisory Board
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460

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Gina McCarthy