

**[Draft Response – August 27, 2015 prepared by Annette Bunge]**

**Regarding exclusion of the Nesnow et al. (1983) and Levin et al. (1977) studies in the analysis of the dermal slope factor.**

On page 5 of the document “Clarifications/Comments for the SAB Draft Peer Review Report on Benzo[a]pyrene: Public Teleconference, August 21, 2015”, EPA provided the following response to the SAB recommendation that EPA add Nesnow et al. (1983) and Levin et al. (1977) studies to Table 2-11.

*EPA notes that the intent of table 2-11 was to capture the studies considered most appropriate for dose-response analysis and derivation of a cancer slope factor for lifetime dermal exposure. Based on several criteria (see p. 2-39 of the draft assessment), ten studies were incorporated into table 2-11 and several others were excluded. One of the major criterion was duration of exposure, in which the Agency focused on studies of approximately 2-years duration (i.e., lifetime). As noted in the draft assessment, less-than-lifetime studies “would tend to underestimate lifetime risk by overlooking the potential*

The SAB recommendations regarding Nesnow et al. (1983) and Levin et al. (197) studies to Table 2-11 were based on the criteria for considering studies listed in the September 2014 draft of the IRIS toxicological review of BaP. Specifically, the text on p. 2-39 (lines 24-35) provided three reasons that studies were not considered in the dose-response analysis and listing in Table 2-11: (1) insufficient information to estimate the doses applied; (2) bioassays with minimal dose-response information (e.g., only one dose level or dose levels inducing a 90-100% incidence in dose response); or (3) studies that were < 1 year. The studies by Nesnow et al. 1983 and Levin et al. 1977 were listed as excluded because they were conducted for < 1 year. By this criteria, the Nesnow et al., 1983 study of 60 weeks should not be excluded. In the case of the Levin et al., 1977 study, the SAB judged the 50 week duration to be so close one-year to make its exclusion questionable. There is no mention in the IRIS review document that studies consider for dose response were limited to those of approximately 2-years duration. This is new information.

A different set of criteria are listed in the Supplemental Materials (p. D-62, lines 5-12), which states that studies were excluded from the dose-response analysis because: (1) they included only one BaP dose level or all dose levels considered induced 90-100% incidence of tumors; (2) they used a 1-time/week or 1-time/2 weeks exposure protocol, “which is less useful for extrapolating to daily human exposure; or (3) they used a vehicle demonstrate to interact with or enhance BaP carcinogenicity. Thus, the Supplemental Materials states that Nesnow et al. 1983 study was excluded because the dosing was 1-time/week, and the Levin et al., 1977 study was excluded because dosing was 1-time every 2 weeks. Note that Levin et al., 1977 administered BaP doses at 1x/week for the three lower doses and 2x/week for the highest dose.

The SAB questioned the requirement that applications of BaP be more frequent than 1-time/week (listed in the Supplemental Materials), because it “is less useful for extrapolating to daily human exposure”. Dermal absorption measurements of BaP are consistent with nearly complete absorption of BaP into the skin for all the dosing regimens considered. Also, the daily human exposure doses used in risk assessment studies are almost always daily averages of exposures that occur on a less than daily basis. If the results of applying BaP once/week differ from applications of 2-times or more per week, then continuous daily exposure, which has been assumed in the analysis for the dermal slope factor is

inappropriate; i.e., there would be data indicating that dose-rate effects cannot be ignored (see lines 12-13, p. 2-41).

The addition of these two studies to Table 2-11, with comments regarding the dosing frequency and duration, is appropriate.