Comments on Benzo[a]pyrene risk assessment documents from NIEHS/NTP

The toxicological review for benzo[a]pyrene was read with attention to clarity, flow, thoroughness, and scientific soundness. Overall, the document was well-written and provided an excellent review of the available literature. The mechanistic section (4.5) and dose-response assessment (5) were particularly strong. The rationale for study selection and uncertainty factors were clear and well-justified.

The one area that seemed to have a disproportionate emphasis was the metabolism section (3.3). There was minimal discussion of the ultimate carcinogen (benzo[a]pyrene 7,8 dihydrodiol 9,10 epoxide) and a great deal of emphasis on specific enzymes and their roles in contributing to phase I activation or detoxification reactions. This gave the impression that BPDE could be important, but its role in carcinogenicity was not confirmed, which is contrary to the section on mechanisms (4.5.2). A more robust discussion of the evidence supporting BPDE as the ultimate carcinogen and mention of the importance of the bay region in PAH carcinogenicity, in general, could be informative in this section.

In reading the oral reference dose section, it was interesting to see that ovarian weight was the critical endpoint for calculating the RfD. It would be informative to include a minimal amount of information on whether this ovotoxicity is seen with other related compounds or mixtures of PAHs.

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