

Response to EPA's Comments on Reproductive Toxicity

EPA assumes that these two recommendations are directed at reproductive studies/endpoints brought forward for dose-response and discussed in Chapter 2 of the draft assessment. EPA notes that the consideration of reproductive toxicity studies and endpoints for POD/BMD analyses and the RfD derivation are discussed on pp. 2-4 and 2-5 of the draft assessment. Can the SAB clarify which additional ovarian and testicular effects/studies should be considered?

The SAB recommends that follicular counts be added for females. For male studies, the SAB recommends adding the recovery time after treatment prior to whatever endpoint is measured since the testis is proliferative and new rounds of spermatogenesis could change the outcome. The SAB also recommends the EPA add the new biologically relevant endpoint of germline mutagenesis, since BaP is a mutagen. The SAB recommends that the life stage at which the animals are exposed to BaP and the life stage at which endpoints are measured be added since the testis matures after birth. The abundance of BaP lesions incurred by germ cells is another relevant measure for male and female studies.

Also, could the SAB expand on the recommendation regarding the studies or parts of studies brought forward for dose-response analysis?

The SAB found a lack of explanation for why certain studies were brought forward and others were not, e.g. uterine hyperplasia/inflammation in the Gao et al study was not included. The EPA draft document does mention effects on the ovary but little attention is paid to the actual mode of action (decreases follicle pool) and there is a disconnect with linking this to the calculation of a point of departure. We recommend that EPA should either include these, or provide appropriate justification as to why that they are not suitable for RfD determination (e.g. they support the mode of action, but given in experimental design limitation- appropriateness of the route of administration, short exposure duration they are not suitable for generation of an RfD).