

NTP Comments on Draft IRIS Toxicological Review of Tetrahydrofuran

The draft IRIS Toxicological Review of tetrahydrofuran (THF) is well prepared document and has all the relevant toxicology information. The RfC derivation based on NTP subchronic rather than chronic studies is well justified and clearly explained. The uncertainty factors used in derivation of RfC are appropriate.

We do have some issues that were also raised by the external reviewers as well as by some public commentators on the selection of critical studies for derivation of RfD. None of the oral toxicity studies in the literature have clearly identified target organ toxicity for THF. Decreases in the pup body weight gains in the F1 and F2 and delayed eye openings in the two-generation BASF reproductive studies were selected as critical effects to derive RfD by EPA. Our reproductive toxicologists consider these effects as marginal at best. The delayed eye opening is most likely related to slightly decreased body weight gains in the high dose pups. Overall, we consider the effects as equivocal and are concerned as to the selection of these as critical toxicity endpoints. We suggest EPA should consider not deriving RfD based on the fact that none of the oral toxicology studies in the literature are defensible for the risk assessment purposes.

Overall, we commend EPA; this is an excellent documentation of toxicology information on tetrahydrofuran.

Submitted by:

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