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Subject: Environmental Defense comments on 2,5-Dihydrothiophene 1,1-Dioxide (Sulfolene) (CAS# 77-99-2)

(Submitted via Internet 8/17/04 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierrg@msn.com and Santav@cpchem.com)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for 2,5-Dihydrothiophene 1,1-Dioxide (Sulfolene) (CAS# 77-99-2).

The test plan and robust summaries for Sulfolene were submitted by Chevron Phillips Chemical Company. Sulfolene is produced from a reaction with 1,3-butadiene and sulfur dioxide and, according to the test plan, has a wide array of uses as an industrial solvent and in the production of Sulfolane. Sulfolane, in turn, has numerous commercial applications involving plasticizers, fractionation of wood tars and tall oil, textile finishing and medicinal applications. However, no information is provided on environmental releases, the opportunities for human exposure or the presence of Sulfolene or Sulfolane in consumer products.

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The sponsor contends that existing data are adequate to meet HPV requirements. This contention relies on the use of surrogate data from Sulfolane studies. However, there are several problems with the use of the Sulfolane data. The greatest concern is that Sulfolene has a double bond in the aromatic ring not present in Sulfolane. This could create significant differences in the metabolism and toxicology between the two agents. The sponsor partially addresses this issue, but full metabolic profiles are not presented. We also note that there appear to be significant differences in the results from the acute inhalation studies between Sulfolene and Sulfolane. Moreover, there appear to be significant differences in target organ toxicity, biodegradation rates and aquatic toxicity.

For the above reasons, we do not agree that Sulfolane can be used as a surrogate for Sulfolene. Therefore, we recommend that the sponsor conduct a combined reproductive/developmental study on Sulfolene, as there are no existing data on these endpoints. Existing experimental data and model estimations are adequate to meet HPV requirements for all other endpoints.

Other comments are as follows:

1. The repeat dose study on Sulfolene was conducted by the NCI as part of the cancer bioassay program. However, the robust summaries do not provide information on the histological methods used or the tissues examined. This information needs to be provided in the revised submission. We note that the histological methods for the Sulfolane repeat dose study are well-described in the robust summaries. If Sulfolane is used as a surrogate, then the presentation of data needs to be consistent between the two substances so that reliable comparisons can be made.

2. The test substances used in the various studies on Sulfolene contain varying amounts of isopropyl alcohol (0-7%). Does isopropyl alcohol influence toxic responses in any of the studies?

3. The sponsor indicates in the test plan that Sulfolene is biodegradable under real world conditions even though the models predict that it is resistant to degradation. What is the evidence from real world situations that support this contention?

Thank you for this opportunity to comment.

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