

201-15062

Anh Nguyen  
01/21/04 11:05 AM

To: NCIC HPV@EPA  
cc:  
Subject: Environmental Defense comments on Dimethyl 3,3'-thiobispropionate (CAS# 4131-74-2)

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Subject: Environmental Defense comments on Dimethyl 3,3'-thiobispropionate (CAS# 4131-74-2)

(Submitted via Internet 1/21/04 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, luciERG@msn.com and mark\_thomson@cromptoncorp.com)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for Dimethyl 3,3'-thiobispropionate (CAS# 4131-74-2).

The test plan and robust summary for dimethyl 3,3'-thiobispropionate (DTBP) was submitted by Crompton Corporation. This substance is used as an antioxidant in PVC systems. No information was provided on potential or actual environmental releases or concentrations in consumer products. Although release and exposure data are not required under the HPV program, they are helpful in the review process.

The sponsor proposes to use data from surrogate chemicals to fill most of the mammalian toxicity endpoints. However, inadequate evidence is presented to justify use of surrogate data, so we recommend that a combined repeat dose/reproductive/developmental study be conducted along with the studies already proposed by the sponsor on in vitro and in vivo genetic toxicity. If the sponsor provides additional data supporting the use of surrogates, we would be glad to review the revised test plan and robust summaries before the studies are conducted. Specific points are as follows:

1. The test plan proposes to use two surrogates: thiodipropionic acid (CAS# 111-17-1), a metabolite of some esters but apparently not of DTBP; and didodecyl thiopropionate (CAS# 123-28-4), an ester that is stated as having some structural similarities to DTBP. The chemical structures of the surrogates are not provided, however, either in the test plan or in the robust summaries.

2. The sponsor claims that the acid metabolites are formed in the stomach following oral administration of DTBP; however, no data on DTBP are provided to support this claim. In order to use CAS# 111-17-1 as a surrogate, the sponsor must show that it is formed rapidly and quantitatively in the gut following administration of DTBP. The only de-esterification data presented was for CAS# 123-28-4, and these data were only obtained from 4-day urine samples; a lot can happen in four days of importance to toxicological outcomes.

3. No data are provided to justify the use of CAS# 123-28-4 as a surrogate

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for DTBP. This is essential because the sponsor proposes to use this surrogate to satisfy requirements for the repeat dose, reproductive and developmental studies.

4. Aquatic toxicity endpoints are addressed using ECOSAR estimations of the toxicity of DTBP, and based on the estimated data, we agree that no further studies are needed, as DTBP appears to have low aquatic toxicity.

5. The heart appears to be the most sensitive target organ for toxicity caused by CAS# 123-28-4, as evidenced by myocarditis. No data are provided to determine if DTBP causes this effect as well.

6. The repeat dose and reproductive studies presented in the robust summaries on CAS# 123-28-4 appear to be the same study. No explanation is given for the results, which indicate that the NOEL for the repeat dose study was 350 mg/kg/day while the NOEL for the fertility study was 125 mg/kg/day.

Thank you for this opportunity to comment.

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