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Anh Nguyen
05/18/2004 07:36 AM

To: NCIC HPV@EPA
CC:
Subject: Fw: Environmental Defense comments on
1H-Isoindole-1,3-(2H)-Dione,2-(Cyclohexylthio)- (CAS# 17796-82-6)

----- Forwarded by Anh Nguyen/DC/USEPA/US on 05/18/2004 07:36 AM -----



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cc: lucieryg@msn.com, kflorini@environmentaldefense.org, rdenison@environmentaldefense.org
Subject: Environmental Defense comments on
1H-Isoindole-1,3-(2H)-Dione,2-(Cyclohexylthio)- (CAS# 17796-82-6)

(Submitted via Internet 5/17/04 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucieryg@msn.com and anne_lehuray@americanchemistry.com)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for 1H-Isoindole-1,3-(2H)-Dione,2-(Cyclohexylthio)- (CAS# 17796-82-6).

The test plan and robust summaries for 1H-isoindole-1,3-(2H)-dione,2-(cyclohexylthio)-, abbreviated as CTP, were submitted by the Rubber and Plastics Additives Panel of the American Chemistry Council. The test plan is complete and well-organized, and the robust summaries contain sufficient detail to evaluate the adequacy of available studies in relation to requirements of the HPV program. The sponsor contends that available data are sufficient for all SIDS endpoints, so no new studies are proposed. We generally agree, although we do question some of the interpretations of the data made in the test plan.

CTP is used as a pre-vulcanization inhibitor for synthetic and natural rubber. According to the sponsor, there are no other commercial uses. CTP is used in the manufacture of large rubber articles such as tires, tubes, belts, hoses and other mechanical rubber products. The sponsor states that consumer exposure to CTP is virtually nil because the cyclohexyl portion of the molecule becomes polymer-bound during the rubber vulcanization process, releasing free phthalamide. While this should be the case during initial reaction, is it not to be expected that the cyclohexyl moiety will be released during abrasion, upon exposure to high temperatures or otherwise through long-term use of rubber compounds such as tires and belts? Also, does phthalamide pose an environmental or health risk? Some discussion of these points should be included in the test plan.

Other comments are as follows:

1. CTP is highly toxic to fish, with reported LC 50 values consistently < 1 mg/L for multiple species of fish. It appears considerably less toxic to aquatic invertebrates, and acute toxicity studies in rodents indicate a low level of acute toxicity. Does the sponsor have any information on the mechanism responsible for the unusually high toxicity to fish? Is it caused by CTP itself or by a degradation product? If a degradation product is responsible, is this product released from rubber compounds under varying uses and environmental conditions? This kind of information is needed to

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evaluate potential ecological concerns.

2. The sponsor states in the executive summary that CTP is of low concern for mammalian toxicity. This statement is contradicted by information presented in the robust summaries, which indicates that the NOEL for CTP in a 90-day inhalation study was 15 mg/m³ in female rats, and that all doses in male rats caused adverse effects, so a NOEL could not be derived from these studies. Adverse effects were observed in kidneys, in livers and in blood. This study does raise concerns that are further heightened by the irritancy and sensitizing properties of CTP, which are also reported in the robust summaries. We presume that the statement of low concern reflects the acute toxicity data without consideration of the repeat dose studies. In any event, it is clearly wrong and should be changed.

3. A 28-day inhalation study in rats indicated a NOEL of >563 mg/m³, while the 90-day inhalation study discussed in point 2 led to a NOEL of <15 mg/m³. Does the sponsor have an explanation for these very discordant findings?

4. The reported reproductive, developmental and genetic toxicity studies were well-conducted and they clearly meet the requirements of the HPV program.

Thank you for this opportunity to comment.

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