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Subject: Environmental Defense comments on Dimethyl 1,4-Cyclohexanedicarboxylate (CAS# 94-60-0)

(Submitted via Internet 10/31/03 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, MTC@mchsi.com, and deyo@eastman.com)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for Dimethyl 1,4-Cyclohexanedicarboxylate (CAS# 94-60-0).

The Eastman Chemical Company, in response to the High Production (HPV) Challenge, has submitted a Robust Summary/Test Plan to describe available data and testing needs for dimethyl 1,4-cyclohexanedicarboxylate (CAS# 94-60-0). On review of this document, we find several statements, assumptions and oversights that we feel make this Robust Summary/Test Plan unacceptable to meet the needs of the EPA HPV Challenge for this chemical. Our two major objections to this Robust Summary/Test Plan are as follows.

First, according to the Test Plan this chemical is "used primarily as an industrial intermediate in the manufacture of various types of polymers and resins". Based on this statement, the sponsor claims that "exposure to the environment and general public is essentially non-existent". Given that no information is provided regarding other uses, transport and measures taken to limit possible release of this chemical into the environment, we cannot accept the sponsor's assertion that exposure to the environment and general public are in fact "essentially non-existent". Description only of its "primary" use is not sufficient to document that other uses do not result in human or environmental exposure. For example, it is mentioned in the Test Plan that a polyester synthesized from this chemical is used as an adhesive in food packaging. No data are provided to indicate that no monomer remains in this polymer. These and other possible sources of human and environmental exposure need to be addressed. Also, industrial hygiene measures used to limit worker exposure should be discussed.

Second, the use of data from a chemical analog, 1,4-cyclohexanedicarboxylic acid, is not appropriate to assess the toxicity of dimethyl 1,4-cyclohexanedicarboxylate to humans. Whereas we agree that metabolism of dimethyl 1,4-cyclohexanedicarboxylate would likely yield 1,4-cyclohexanedicarboxylic acid, as described in the Test Plan, the latter chemical is not in fact the metabolite of most concern; methanol is the metabolite of most concern. If metabolism proceeds as described in the Test Plan, then approximately 32% of dimethyl 1,4-cyclohexanedicarboxylate metabolizes to methanol. Methanol has of course been the subject of considerable study. It is well-established that humans are much more sensitive to intoxication by methanol than are rodents. Humans are estimated to be as much as ten times more sensitive to intoxication by methanol than are rodents (IPCS 1997). Thus, many scientists familiar with methanol and/or chemicals metabolized to methanol do not consider data developed using rodents to be adequate to assess human health risks. In

the toxicity studies cited for dimethyl 1,4-cyclohexanedicarboxylate, there is little doubt that doses of the chemical easily tolerated by rats would be lethal to humans. Therefore, we do not consider data developed for dimethyl 1,4-cyclohexanedicarboxylate using rodents to be appropriate for assessment of risks to human health.

In rejecting data developed for dimethyl 1,4-cyclohexanedicarboxylate using rodents, we do not suggest or request additional animal studies unless the sponsor also intends to conduct metabolism studies of this compound to determine the relative amounts of each metabolite formed. Rather, we request that the Robust Summary/Test Plan for dimethyl 1,4-cyclohexanedicarboxylate be completely revised to emphasize the likely metabolism of this compound to methanol and to discuss in some depth the very ample data for methanol toxicity in primates and its significance for human exposure to this chemical.

Reference:
IPCS IpoCS?Environmental Health Criteria 196. ? Methanol ISBN 92 401571969 ISSN 0250-863X. Geneva: WHO, 1997.

Thank you for this opportunity to comment.

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