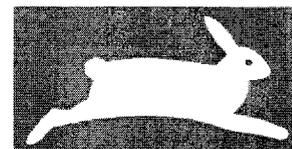


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**PETA**

PEOPLE FOR THE ETHICAL  
TREATMENT OF ANIMALS

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Michael O. Leavitt, Administrator  
U.S. Environmental Protection Agency  
Ariel Rios Bldg. (1101A)  
1200 Pennsylvania Ave., N.W.  
Washington, DC 20460

04 MAY -4 PM 12:07

Re: Comments on the HPV test plan for N-ethyl-N-(3-methylphenyl)-  
1,2-ethanediamine (EMPE)

Dear Administrator Leavitt:

The following comments on Eastman Chemical Company's test plan for EMPE (CAS no. 19248-13-6) are submitted on behalf of People for the Ethical Treatment of Animals, the Physicians Committee for Responsible Medicine, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These animal, health, and environmental protection organizations have a combined membership of more than ten million Americans.

Eastman's test plan states that no mammalian toxicity data are available for this chemical other than for acute toxicity and is proposing to conduct a combined developmental and reproductive toxicity study (OECD 421). This test will kill at least 675 animals, despite the fact that EMPE is both (i) a closed-system intermediate and (ii) a low-toxicity compound with rodent oral LD<sub>50</sub> values in the range of 200-800 mg/kg of bodyweight, and with little dermal toxicity even at the highest dose administered (summaries, pp. 20-21).

While Eastman test plans to date have been characterized by thoughtful toxicology, we are concerned that Eastman made no attempt to estimate the toxicity of EMPE from other aminotoluenes. Within the American Chemistry Council there is a body entitled the Monocyclic Aromatic Amines and Nitroaromatics Panel, and it is only logical to assume that the responsibility for the HPV test plan for EMPE lay with this Panel. On January 11, 2002, the Panel submitted an HPV test plan for a category of compounds termed the "monocyclic aromatic amines," and subsequently submitted a revised test plan on July 24, 2002. Since EMPE is a monocyclic aromatic amine, we are surprised that Eastman provides no explanation as to why EMPE was not included in that category. The monocyclic aromatic amines test plan does not specify the requirements for category membership, but does include the following statement:

"The aromatic amines all have a single amino group and are secondary or tertiary amines with methyl or ethyl substituents on the nitrogen atom. Some of these aromatic amines also have a methyl substituent on the aromatic ring" (p. 2).

EMPE fits this description, except that it has two amino groups. However, even if the Panel omitted EMPE for that reason, either the Panel or Eastman should have made some attempt to use the data from the other monocyclic aromatic amines for structure-activity analysis, especially as one of the compounds included in the category, N-ethyl m-toluidine, differs from EMPE solely in the absence of one amino group.

If Eastman insists on conducting the OECD 421 as planned, we request that it conduct the rodent embryonic stem cell test (EST). This *in vitro* embryotoxicity test method has been validated by the European Centre for the Validation of Alternative Methods (ECVAM), and the Centre's Scientific Advisory Committee has concluded that this test is ready to be considered for regulatory purposes (Genschow 2002). We have repeatedly provided validation and SOP references, and we have suggested that, in this screening-level program, a positive EST result should warrant the substance's treatment as a developmental toxicant/teratogen, and that no further testing should then be carried out, again, because the HPV program is a *screening level* program.

In addition, we have urged individual companies to consider the use of the EST in parallel, and several have agreed to do so in order to help build the database for industrial chemicals for eventual validation of the EST in the U.S. (please note that the cost of the EST is a fraction of the cost of the OECD 421). We hope to receive a positive response that Eastman will also run the EST for this substance. We would be happy to provide further information on a local laboratory that conducts this test commercially.

Thank you for the opportunity to comment on this test plan.

Sincerely,

Jessica Sandler  
Federal Agency Liaison

#### **Literature Cited**

Genschow E et al. The ECVAM international validation study on *in vitro* embryotoxicity tests: Results of the definitive phase and evaluation of prediction models. *Altern Lab Anim.* 30, 151-176 (2002).