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**ETHYL CORPORATION**  
Health and Environment Department

R. L. Clark, Ph.D.  
Inorganic Toxicology  
and Respiratory Health

February 11, 1991

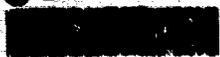
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*SHEQ-0291-0648 Final*

**CONFIDENTIAL - RETURN RECEIPT REQUEST - P 131 520 156**

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Office of Toxic Substances  
U.S. Environmental Protection Agency  
401 M Street, SW  
Washington, DC 20460

*88-870000015: PDCN.*  
EPA-OTS



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Attention: Section 8(e) Coordinator

Dear Sir:

*89-910000178: DEN.*

RE: SHEQ 1286-C 48

This is a follow-up to an 8(e) submission (SHEQ 1286-0648) Ethyl Corporation made in December 1986. Pursuant to the Agency's letter dated January 16, 1987, Ethyl Corporation is submitting additional preliminary results of a two-year bioassay on diethyltoluene diamine in Sprague Dawley rats.

The in-life phase of a two year oncogenicity study has been completed. Dose levels were 0, 10, 35 or 70 ppm in the diet. Each dose group was composed of 50 male and 50 female rats. Histopathological analysis of tissues is underway; tissues from the 50 control and 50 high dose female rats have been examined. Preliminary statistical analysis on the unaudited microscopic findings has been conducted.

The livers of the high dose females had a statistically significant increase in the incidence of hepatocellular adenomas and proliferative lesions (basophilic foci). One high dose female had a hepatocellular carcinoma in the liver; no hepatocellular carcinomas were present in the livers of the control females. The adrenals of the high dose females had a statistically significant increase in the incidence of multifocal cortical vacuolation. However, the incidence of tumors and hyperplastic changes in the adrenals was not significantly different between the control females and high dose females. The incidences of tumors and hyperplastic changes of the pituitary and thyroid glands were not significantly different between the control and high dose female rats. The pancreas of the high dose females had an increase in multifocal acinar atrophy but the incidence of interstitial fibrosis and fatty infiltration was not significantly increased in the high dose females as was observed in the high dose males. No cataracts were present in the eyes of the high dose females as was observed in the high dose males.

The mammary glands of the high dose females had statistically increased incidence of fibroadenomas. There was an increase in the

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number of tumors and tumor bearing animals (controls = 12 tumors in 12 females vs high dose = 43 tumors in 25 females). However, the incidence of mammary gland adenocarcinomas was higher in the control females than in the high dose females (controls = 12 tumors in 10 females vs high dose = 6 tumors in 4 females). The reported range for fibroadenomas in Charles River CD Sprague-Dawley rats is 14.5% to 58.1% and for adenocarcinomas is 0.0% to 16.0% (Charles River Monograph "Spontaneous Neoplastic Lesions in the Crl:CD BR Rat"). Since the incidence of malignant mammary gland tumors (adenocarcinomas) is high in the control females of this study, the relevance of the incidence of the fibroadenomas in the mammary gland of the high dose females is unknown at this time.

Analysis of tissues from mid and low dose females which died prior to terminal sacrifice is underway. In addition, selected tissues from all low and mid dose male and female terminally sacrificed rats will be examined. We will keep you informed of the results of the study.

If you have any questions, please call me at (504) 388-7608.

Sincerely,  
ETHYL CORPORATION

*R. L. Smith*

R. L. Smith, Ph.D.  
Director  
Toxicology and Regulatory Affairs

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