

ETHYL CORPORATION
Health and Environment Department

CONTAINS NO CBI

R. L. Smith, Ph.D.
Chemical Technology
and Regulatory Affairs

2-PPS
January 11, 1991

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SHEQ-0191-0648 SUP

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Document Control Officer (TS-700)
Office of Toxic Substances
U.S. Environmental Protection Agency
401 N Street, SW
Washington, DC 20460

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EPA-OTS

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Attention: Section 8(e) Coordinator

Dear Sir:

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RE: SHEQ 1286-0648

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 male rats as well as the 26 male low dose and 37 male mid dose rats which died during the course of the study have been examined. Preliminary statistical analysis on the unaudited microscopic findings has been conducted.

A statistically significant increased incidence in hepatocellular carcinomas and hepatic proliferative lesions (eosinophilic and basophilic foci) was found in the high dose males as compared to control males. Many of the high dose rats had degenerative changes in the livers indicating a possible toxic effect on the liver.

A statistically significant increased incidence in follicular cell adenomas and follicular cell hypertrophy of the thyroid was found in the high dose males. One follicular cell carcinoma was present in a low dose male. Follicular cell hyperplasia and follicular cysts were increased in the thyroids of the mid and high dose males. Proliferative lesions of the thyroid can occur in animals with toxic severe liver damage.

The pancreas was identified as a target organ in previous subchronic studies. In the two year study, the pancreas of high dose males had an increase in multifocal acinar atrophy accompanied by interstitial fibrosis and fatty infiltration. Due to a reduction in the acinar glands, the evaluation of the quantity of islet cells was difficult but those islet cells present appeared to be normal. The incidence of islet cell tumors was comparable between the control and high dose male rats. Six high dose males had bilateral cataracts. Half of these rats had moderate to severe keratitis of the eyes and the relevance of treatment to these cataracts is unknown at this time.

The adrenals of the high dose males had a statistically significant increased incidence of multifocal medullary hyperplasia. However, many of the control rats had focal medullary hyperplasia. The combined incidence of medullary hyperplasia was fairly proportionate between the control and high dose male rats. The incidence of adrenal medullary tumors was not significantly different between the control and high dose males. There was a reversed trend in pituitary adenomas between the control and high dose male rats. The relevance of treatment to the multifocal medullary hyperplasia of the adrenal and the lower incidence of pituitary tumors in the high dose rats is questionable at this time.

Analysis of tissues from all female control and high dose rats and all 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.

Ethyl Corporation is taking action to inform our workers on the preliminary findings reported herein. We will be doing similar notifications to our customers.

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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