**CASWELL FILE**

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUN 28 1990

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

Chemical (Caswell) No.: 346
RD Record No.: 260,700
HED Project No.: 0-0837

MEMORANDUM

SUBJECT: Deet - Screening of Data submitted for in-depth review of a List A chemcal

EPA ID No. 080301-5

TO: Jane Mitchell, PM Team 74
Reregistration Branch
Special Review and Reregistration Division (H7508C)

FROM: Victor Miller, Science Analysis and Coordination Branch, Health Effects Division (H7509C) V. M.

THROUGH: Esther Saito, Acting Section Head, Science Administration, Science Analysis and Coordination Branch Esther Saito

and

Reto Engler, Ph.D., Chief
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

Registrant: Hartz Mountain Corporation

All the studies received for review were forwarded directly to the primary reviewer because of the recent history of neurotoxicity reported to be associated with this chemical. At this time none have been rejected because of poor design.

MRID Nos. 41344101, 40979001 (a 90-day dose-range finding study in hamsters and a two-generation reproduction study in rats respectively) have been reviewed (see attached Doc. # 007833). MRID Nos. 40573401, 40573501, 40704001, and 40704002 [domestic animal safety studlies] have been reviewed (see attached list of one-liners).

The three mutagenicity studies (MRID Nos. 41344801, 41344401, 41344301) are at present at Dynamac and we are awaiting the outcome of the review process. According to the memo from Wang Phang to Donna Williams dated March 23, 1990 (see attached Doc. No. 007833), the mouse oncogenicity study (MRID No. 41351501) and the rat teratology study (MRID No. 41351401) will be reviewed at a later date.

As an outcome of the Data Call-In Notice for Deet issued 9/1/88, mutagenicity and domestic animal safety studies were received as referred to above. At the present time the following studies are awaited: metabolism, dermal absorption in the mature rat and neurotoxicity. No further data call-ins are anticipated.

346

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007833

OFFICE OF
PESTICIDES AND
TOXIC SUBSTANCES

MAR 23 1990

**MEMORANDUM**

SUBJECT: DEET: Review of a two-generation reproduction in rats and a 90-day dose-range finding study in hamsters

Caswell No. 346 HED Project NO. 0-0837
MRID No. 413441-01 (90-day Hamster study)
409790-01 (2-generation reproduction in rats)
EPA Record No. 260700

TO: Donna Williams, PM Team (17)
Special Review and Re-registration Division (H5705C)

FROM: Whang Phang, Ph.D. Whang Phang 3/16/90
Pharmacologist
HFAS/Tox. Branch II/ HED (H5709C)

THROUGH: K. Clark Swentzel, Section Head K. Clark Swentzel 3/16/90
and
Marcia van Gemert, Ph.D. Marcia van Gemert 3/19/90
Branch Chief
HFAS/Tox. Branch II/ HED (H5709C)

Toxicology Branch II has been requested to review a 2-generation reproduction study in rats, a 90-day dose-range finding study in hamsters, a mouse oncogenicity study, and a rat teratology study on Deet by Special Review and Re-registration Division. These studies were listed under the same Data Review Record. The 2-generation reproduction study in rats was previously reviewed and transmitted to P. Hutton/J. Tavano, PM Team 17, on Dec 13, 1989 (Tox. Doc. No. 007645). The results from the 90-day dose-range finding study in hamsters are to be used for selecting the appropriate test animals and dose levels for a chronic feeding study. To facilitate the initiation of the long term study, the 90-day feeding study in hamster has been reviewed first while the mouse oncogenicity and the rat teratology studies will be reviewed in a later date. The data evaluation reports of the two evaluated studies are attached, and the conclusions are as follows:

1). 2-generation reproduction study in rats: The study was evaluated by Dynamac Corp.. The HFAS/Tox. Branch II does not agree with certain scientific judgments made by Dynamac. This reviewer has prepared an addendum reflecting the

scientific opinions of the Branch. The addendum is attached to the data evaluation report of this study.

Groups of rats (28/sex/dose) received DEET at dietary concentrations of 0, 500, 2000, and 5000 ppm for two consecutive generations. Based upon the results presented in the study, the NOEL for parental toxicity could not be established, and the LOEL was 500 ppm which was the lowest tested dose. The 500 ppm males showed signs of kidney effects which included mottling, inflam- presence of hyaline droplets, granular cast formation, and tubular regeneration.

No reproductive or developmental toxicity was found, and the NOEL for reproductive toxicity was 5000 ppm (highest tested dose).

This study satisfies the data requirements for a 2-generation reproduction study (Guideline No. 83-4) and is classifies as core minimum.

2). 90-day dose-range finding study in hamsters: Groups of hamsters (15/sex/dose) received 0, 1,000, 5,000, 10,000, and 15,000 ppm of DEET (technical grade) in the diet for 90 days. Compound-related effects were seen in animals which received 5,000 ppm DEET or above. At 5,000 ppm in males, there was a consistent drop in food consumption and body weight. The decrease in body and food consumption was more marked in 10,000 and 15,000 ppm males and females. The increase in the incidence of gross pathologic and histologic changes in testes and epididymides were found in 10,000 and 15,000 ppm males. The gross pathologic changes were small testes and epididymides, and microscopically these changes were degeneration of the testes and cellular debris in the epididymal tubules. At 15,000 ppm, there were deaths in both males and females. Based upon these observations, the NOEL was 1,000 ppm; LEL, 5,000 ppm.

The results of the study clearly demonstrated that the renal lesion seen in the DEET treated male rats was not found in the hamsters which received DEET up to 15,000 ppm. This study satisfies data requirements for a 90-day feeding study in rodent (Guideline No. 82-1) and is classified as core minimum.