8-30-91
CASWELL FILE

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

AUG 30 1991

MEMORANDUM

AUG 3 1991

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: One-year dog feeding study with acephate technical: 6(a)(2) notice.

Tox. Chem. No.: 002A
Case No.: 026102
Submission No.: S388160
Chemical No.: 103301
ID No.: 062499-00023
HED Project No.: 1-0449

FROM: Krystyna K. Locke, Toxicologist Krystyna K. Locke 5/1/91
Section I, Toxicology Branch I
Health Effects Division (H7509C)

TO: Marilyn A. Mautz, PM/RM Team No. 16
Insecticide/Rodenticide Branch
Registration Division (H7505C)

THRU: Roger Gardner, Section Head Roger Gardner 8-29-91 KB 8/30/91
Section I, Toxicology Branch I
Health Effects Division (H7509C)

Toxicology Branch I (TB-I)/HED acknowledges the receipt of a FIFRA 6(a)(2) notice from the registrants, Chevron Chemical Company/Valent USA Corporation (Attachment I). The registrants reported that brain cholinesterase (ChE) activity was inhibited 16%, relative to the control value, in the low-dose male dogs, in a one-year feeding study. This inhibition was statistically significant, but the degree of significance (p value) was not reported. Brain ChE activity in the female dogs, and plasma and erythrocyte ChE activities in both sexes were not statistically significantly inhibited in the low-dose group. A comment was also made that the individual and group mean ChE data were submitted with the 6(a)(2) notice, but these data were missing.

The one-year dog feeding study was conducted for the registrants by Hazleton Laboratories America, to satisfy California SB-950 data requirements. The doses of acephate administered (in diet) were 0, 10, 120 and 800 ppm*. Brain ChE activity

*Using the conversion factor of 1 ppm = 0.025 mg/kg of body weight, these values correspond to 0, 0.25, 3.0 and 20 mg/kg, respectively.

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was determined only at the termination of the study, whereas plasma and erythrocyte ChE activities were determined before the initiation of the study and at test weeks 4, 13, 26 and 52.

TB-I/HED has also recently received the full, final report on this study (No.: HWA 2107-165; dated January 25, 1991; MRID No.: 418120-01). Although not requested in the Registration Standard for acephate, this study will be evaluated and included in the TB data baseline for acephate. Special attention will be fiven to the ChE values in the low-dose group and the effect of these values, if any, on the existing RfD for acephate. In the currently available 2-year dog feeding study (valid IBT study No. C8732, dated 12/28/72), ChE activities in brain, plasma and erythrocytes were not inhibited in both sexes at 30 ppm of acephate.

Findings reported in the 6(a)(2) notice do not affect the existing OPP/EPA RfD for acephate which is 0.004 mg/kg of body weight/day. This value is based on the LEL for brain ChE inhibition (2 ppm or 0.12 mg/kg), observed in a special 90-day rat feeding (ChE) study and UF/SF of 30.

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Attachment I

1333 North California Blvd
Suite 600
P.O. Box 8025
Walnut Creek CA 94596-8025
(415) 256 2700

VALENT

December 18, 1990

ACEPHATE:
ONE-YEAR DOG STUDY
FIFRA 6(a)(2)
REPORTABLE FINDING
ORTHENE Technical
EPA Reg. No.: 62499-23

VIA EXPRESS MAIL - RETURN RECEIPT
Article No: B036277614

Mr. William H. Miller
Product Management Team 16
Document Processing Desk
Office of Pesticide Programs - H7505C
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202

Dear Mr. Miller:

Valent USA Corporation has recently received preliminary clinical chemistry data from a new one-year chronic oral toxicity study in dogs with acephate technical. This study is being performed at Hazleton Laboratories America, Inc. under sponsorship of Chevron Chemical Company to satisfy California SB-950 data requirements. Five dogs per sex per dose were fed acephate technical in the diet for 52 weeks over a wide dose range of 0, 10, 120 and 800 ppm. Determination of plasma and erythrocyte cholinesterase activity were made at -3, -2, -1, 4, 13, 26, and 52 weeks. Brain cholinesterase activity was determined at terminal sacrifice.

The data indicate that a statistically significant, 16 percent, depression of brain cholinesterase activity was observed at terminal sacrifice for male dogs at 10 ppm, the lowest dose tested. There was no statistically significant difference in brain cholinesterase activity for females at this dose level. There was no statistically significant depression of plasma cholinesterase activity for either sex at any dose level or interval. A no-observed-effect level (NOEL) of 10 ppm was observed for erythrocyte cholinesterase in both sexes. A copy of the individual and group mean data for these cholinesterase parameters is attached.

The existing two-year dog study on file with the Agency [MRID 00001498] had established a brain cholinesterase NOEL of 30 ppm. The finding of statistically significant depression in males at 10 ppm is a new finding which we are reporting under FIFRA 6(a)(2). The toxicological significance of this finding has not been determined

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since no clinical signs of toxicity were observed at any level over a wide dose range. Further, NOELs were established for brain cholinesterase in females at 10 ppm, for plasma cholinesterase in both sexes at 800 ppm and, for erythrocyte cholinesterase in both sexes at 10 ppm.

The final report for this study will be submitted for the Agency's review in early February, 1991. We will communicate further with the Agency once the study has been reported and we have had a chance to assess the toxicological significance of this new finding.

Please contact me at (415) 256-2763 or John Finegan in our Washington D.C. office at (202) 472-8762 if you have any questions or require additional information.

Sincerely,

John F. Flanagan
Manager,
Registration and
Regulatory Affairs

RAZ/slf

cc. Chevron Chemical Company