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

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DEC 2 0 1993

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: TEBUPIRIMPHOS (previously **Phostebupirim**, MAT 7484) - Developmental Toxicity Study in Rabbits - Addenda to the Original Report - **6(a)(2)**

DP Barcode: D196472 **Case:** 030678
Submission: S452373 **PC Code:** 129086
MRID No.: 429819-01 **Identification No.:** 003125-URR
Action: 101 RESB NC-FOOD/FEED USE

FROM: Alan C. Levy, Ph.D., Toxicologist Alan C. Levy 12-16-93
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Health Effects Division (H7509C)

TO: Robert Forrest/Marilyn Mautz, PM 14
Registration Division (H7505C)

THRU: Jess Rowland, M.S., Acting Section Head 12/16/93.
Review Section IV, Toxicology Branch II
Health Effects Division (H7509C)

and

Marcia van Gemert, Ph.D., Branch Chief
Toxicology Branch II
Health Effects Division (H7509C)

REQUEST: Review the addenda submitted by the Registrant regarding the rabbit developmental toxicity study with TEBUPIRIMPHOS.

Registrant: Miles Agriculture Division, Kansas City, MO

BACKGROUND:

The original developmental toxicity study in rabbits (MRID No. 420054-55) was reviewed by the Agency January 5, 1993 (HED Document No. 009954). This study was Core Classified as MINIMUM.

A transmittal letter (10/13/93) referred to four addenda to the above study. [Addendum A accompanied the original study; Addenda B, C and D accompanied the transmittal letter]. Addendum B provided additional information on maternal effects, a historical control database and a reevaluation of several fetal parameters. Addendum C provided additional maternal clinical findings omitted from the original report. Addendum D provided corrections for recording errors.

The transmittal letter indicated that on 8/26/92 an addendum to report 99812 (MRID No. 420054-55) was submitted to the Agency as a possible 6(a)(2). At that time, only a German version of the addendum was available. A translation of this addendum is Report No. 99812-1 and is referred to as Addendum B.

EVALUATION OF THE ADDENDA

The only aspect of the addenda which had an effect upon the study, were changes in the developmental NOEL and LEL. The transmittal letter stated, "No information in the enclosed Addenda significantly alters any conclusions made in the original report, except Addenda B which concludes that there was an increase in resorptions and preimplantation loss in the 0.3 mg/kg dose group. This results in a NOEL for fetotoxcity of 0.1 mg/kg (NOEL in the original report was 0.3 mg/kg)." The CONCLUSIONS presented in the Data Evaluation Report (DER) stated," The 0.3 mg/kg dose had a suggested effect on pregnant rabbits as evidenced by possible lower uterine weights, decreased number of live fetuses/litter and the higher number of resorptions/group as well as the number of litters with at least one resorption."

The following table presents data from Addendum B as well as from the DER.

A COMPARISON OF THE CESAREAN SECTION DATA FROM THE DATA EVALUATION REPORT VERSUS THE RECENTLY RECEIVED ADDENDUM

Parameter mg/kg/day =	0	0.03	0.1	0.3
Live fetuses (mean/group)	6.0a 5.6b	5.3 4.9	6.5 6.1	4.5* 4.0
Resorptions (mean/litter)	0.4 0.4	1.1 1.1	1.1 1.1	1.6*** 1.6
Weight of live fetuses (g)	41 41	40 41	41 42	43** 44

Statistical Significance: * = $p<0.05$; ** = $p<0.01$; *** = $p<0.001$
a = Data from Addendum B.
b = Data from the Data Evaluation Report (HED Document No. 009954).

CONCLUSIONS:

Based on the data provided in this submission, the No Observed Effect Level (NOEL) for developmental toxcity (fetotoxicity) is established at 0.1 mg/kg/day rather than the NOEL in the original report which was 0.3 mg/kg/day. The developmental Lowest Observed Effect Level (LOEL) is established at 0.3 mg/kg/day rather than the LOEL in the original report which was "not attained, >0.3 mg/kg/day." The new LOEL is based on an increase in resorptions and fetal body weights.

2