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

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OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Bayleton: Company Response to 6(a)(2) Data

Project No: 2-0490
Tox. Chem. No.: 862AA
Record No.: S407095

TO: Cynthia Giles-Parker, PM 22
Registration Division (H7505C)

THRU: Roger Gardner, Section Head
Review Section 1
Toxicology Branch
Health Effects Division (H7509C)

FROM: Nguyen Bich Thoa, Ph.D
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Toxicology Branch I
Health Effects Division (H7509C)

Registrant: Mobay Corp. Agricultural Chemicals Division,
Kansas City, MO 64120-0013

ACTIONS REQUESTED:

Review a Supplemental Submission to EPA MRID 414462-01. This is an Addendum in which corrections for two deficiencies observed by TBI in a developmental study (EPA MRID 414462-01) entitled: Teratology Study in the Rabbit with MEB 6447 (Triadimefon) were provided.

CONCLUSIONS:

TBI is satisfied with the corrections provided by the Registrant. The study entitled "Teratology Study in the Rabbit with MEB 6447 (Triadimefon)" (MRID 414462-01) can now be considered to have satisfied the toxicological requirements for a developmental study (83-3) in rabbits and is upgraded from core Supplementary to core Minimum.

134

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BACKGROUND:

A developmental study of Bayleton in rabbits (MRID 414462-01) was reviewed and classified by TBI as core Supplementary, upgradable to core Minimum upon the Registrant satisfactory responses to the following two deficiencies:

1. The expiration date of the Triadimefon batch used in this study was 06/18/88 (pp 38 of report). The dates of artificial insemination (gestation day 0) were from 05/31/88 to 06/03/88 (5 rabbits/dose group/day; pp 153 of report) and the last dosing day (day 18) was from 06/18/88 to 06/21/88. According to these dates, only 5 animals/dose group would have received good test material for the entire dosing period (day 6-18). The remaining animals were given out of date test material, for 1-3 days. The Registrant is required to clarify this matter since 1-3 days of misdosing might have severe impact on the integrity of a developmental toxicity study. The Registrant may provide information demonstrating that the test material was stable up to 06/21/88.

2. Except for extra ribs, the litter incidence increases were not statistically evaluated. The Registrant is requested to submit statistical evaluations of the following litter incidence increases: external alteration of the tail (HDT group),incomplete ossification of the pelvic pubes and the anterior and posterior phalanges, and irregular spinous process formation (MDT and HDT), and malformations of the arches and centra of the caudal vertebrae, incomplete/non ossification of the 1st, 2nd, 5th sternebrae, posterior talus, and posterior phalanges (HDT). Potential teratogenic effects should be evaluated on both a fetal and litter bases.

The Registrant's responses are as follows:

1. "When it was realized that the expiration date would expire prior to the completion of the dosing period, the test material was reanalyzed. As a result of the analysis, the expiration date was expanded to 17 November 1988. The new expiration date was documented in Section 1 of this addendum".(See attached copy)

2. "Litter incidence data with statistical analysis are provided for all fetal findings in Section 2 of this addendum" (See attached copy). "This analysis may be summarized as follows:

a. The finding, external alteration of the tail, observed in 2 litters in the 120 mg/kg group was not found to be statistically significant.

b. Incomplete ossification of the pelvic pubes and the posterior phalanges was found to be statistically significant ($p \leq 0.01$) on a litter basis for the 120 mg/kg group; however, on a litter basis, incomplete ossification of the anterior phalanges was not found to be statistically significant.

2

c. On a litter basis, irregular spinous process was statistically significant ($p \leq 0.05$ or 0.01) for both the 50 and 120 mg/kg groups.

d. On a litter basis malformations of the arches and centra of the caudal vertebrae were not statistically different from the control group.

e. On a litter basis, there was a statistically significant increase in incomplete ossification of the 1st and 2nd sternebrae, and incomplete/non ossification of the posterior phalanges. On a litter basis, nonossification of the 5th sternebrae and incomplete ossification of the talus was not found to be statistically significantly different from the control group.

TBI considers the responses adequate. The study entitled "Teratology Study in the Rabbit with MEB 6447 (Triadimefon)" (MRID 414462-01) can now be considered to have satisfied the toxicological requirements for a developmental study (83-3) in rabbits. The study may be upgraded from core Supplementary to core Minimum.

A copy of Section 1 (Expiration date for MEB 6447 Batch Number 203 780 190) and Section 2 (Litter incidence data with statistical analysis for all fetal findings) of the Addendum are attached.

RID 5711-93

TRIADIMEFON TOX REVIEWS

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