CASWELL FILE

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

Rekasable

NOV 26 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Trichlorfon - Data Requirements Noted in Registration Standard

Caswell No. 385

FROM: Irving Mauer, Ph.D. Geneticist
Toxicology Branch
Hazard Evaluation Division (TS-769)

TO: Wm. Miller/G. Otakie
Product Manager #16
Registration Division (TS-767)

THRU: Jane E. Harris, Ph.D.
Section Head, Toxicology Branch
Hazard Evaluation Division (TS-769)

Registrant: Mobay

Action Requested:

Respond to letter from registrant dated July 17, 1985, commenting upon certain data requirements noted in the Trichlorfon Registration Standard (Toxicology Chapter, transmitted March 13, 1984; R.S. dated June 30, 1984).

TB Response (Point-by-point to attached)

(81-3) Acute Inhalation Toxicity: This study was reviewed by TB (dated 6/27/85) under Accession No. 256446, and classified CORE-MINIMUM (Tox. Cat. II)

(82-1) 90-Day Feeding Study in the Rat: Provided that a chronic (2-year) rat feeding study is submitted, TB recommends granting the waiver of this requirement for a subchronic rat feeding study.

4 pages

(82-1) 90-Day Feeding Study in the Dog: TB has received, but not yet reviewed, an interim report on a dietary trichlorfon monkey study, entitled: "Report No. 90237 (Trichlorfon Monkey Study - Ninety-Six Month Interim Report)", submitted July 17, 1985, under Accession No. 258816. Data provided in this submission should be adequate to determine subchronic effects and a NOEL for the required non-rodent species, and TB recommends granting this waiver for a subchronic dog study.

(82-3) 90-Day Dermal Rabbit: The 90-day dermal requirement is waived if as agreed, it is replaced with a 21-day dermal study.

(82-4) 90-Day Inhalation Rat: TB agrees that the 90-day inhalation study can be waived because repeated inhalation exposure at toxic levels would not be expected. Moreover, TB has already reviewed a three-week inhalation study in rats (under Accession No. 256446, and transmitted 9/27/85). This study was judged CORE MINIMUM DATA, and demonstrated NOEL's for cholinesterase inhibition = 12.7 mg/m^3 and for systemic effect = 35.5 mg/m^3.

(83-1) Chronic Toxicity in the Rat and Dog: TB notes the difficulties encountered with ingredient stability in both the older rat chronic (designated by the registrant as "Mobay Report No. 840099") and mouse oncogenicity studies.

> [NB - Our records show that portions of a study with the same report number, 84009, were previously submitted (2/28/83) to the Agency, but as a "Two-Generation, Two-Year Feeding Study of Trichlorfon in the Rat," under Accession No. 256477. Since only a summary was provided, this report was judged CORE-INVALID (memo: Mauer to Otakie, 6/27/85.]

Toxicology Branch defers to RD consideration on the registrant's request for an extension of time to submit a new rat chronic study.

As indicated above, TB has received the progress report on the 10-year Rhesus feeding study (Interim, #90237), but has not yet completed a review. TB agrees that this long-term Rhesus monkey study could substitute for the non-rodent (dog) long-term study, but defers to RD consideration of the registrant's request for an extension of time to submit a final report on this study.

(83-2) Oncogenicity in the Rat and Mouse: TB notes that the scheduled rat chronic mentioned above (83-1) will use a combined chronic toxicity/oncogenicity protocol to satisfy both requirements.

TB defers to RD with respect to the registrant's request for an extension of time to submit its mouse oncogenicity study.

(83-3) Teratogenicity in the Rat and Rabbit: Both studies mentioned by the registrant (Mobay #69298, #69299, submitted under Accession No. 244915) have been reviewed by TB, and the following recorded (Document No. 002912):

Teratology-Rat: CORE-MINIMUM - (Bayer # 8400; Mobay #69298)

Teratogenic NOEL
> 100 mg/kg/day (HDT)
Maternal NOEL
> 100 mg/kg/day (HDT)
Fetal Toxic NOEL
> 100 mg/kg/day (HDT)

However, because of the absence of maternal or fetotoxicity at the highest dose tested, a new rat teratology study is required.

Teratology-Rabbit: CORE-MINIMUM - (Bayer # 8430; Mobay #69299)

Teratogenic NOEL
> 45 mg/kg/day (HDT)
Maternal NOEL
= 15 mg/kg/day (HDT)
Maternal LEL = 45 mg/kg
(decreased weight gain)
Fetal Toxic NOEL = 15 mg/kg
Fetal Toxic LEL = 45 mg/kg
(two litters aborted)

(84-2) Chromosomal Aberration: Both studies mentioned by the registrant (Mobay #68925, 68783, both submitted under Accession #257819) have been reviewed by TB, and the following recorded (Document No. 004561):

Dominant Lethal-Mice: (Bayer #8745; Mobay # 68925)	UNACCEPTABLE -	Reported as negative, but insufficient dosage administered (only dose tested = 250 mg/kg, inducing no clinical effects or effects on fertility), and no positive controls.
Micronucleus Test-Mice: (Bayer #8505; Mobay #68783)	INCONCLUSIVE-	Because no clinical or cytotoxicity noted at the HDT (250 mg/kg).

OPP:HED:TOX:I.MAUER:sb 11/~~19~~25/85 X77395