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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Prometon, EPA I.D. No. 100-544, Caswell No. ~~362~~, 96
Accession Nos. ~~250917~~, ~~250918~~ 259108

FROM: Dr. Jane E. Harris JEH 11/6/85
Section Head, Review Section VI
Toxicology Branch
Hazard Evaluation Division (TS-769C)

TO: Robert J. Taylor
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Registration Division (TS-767C)

Applicant: Ciba-Geigy Corp.
Greensboro, NC

Submission Purpose:

Review registrant's comments on Toxicology Branch's previous evaluation of two teratology studies and a 90-day rat study.

RECOMMENDATION:

In response to the registrant's critique of a previous Toxicology Branch review of March 26, 1984, on Prometon of rat and rabbit teratology studies and a 90-day rat feeding study, the Toxicology Branch concurs with the registrant's comments and thereby recommends the following amendments:

1. Argus Research Labs: #203-003, EPA Accession No. 250917.

No additional information is required from the registrant concerning the rat teratology study which is still core classified:

Minimum with
Maternal Toxicity LEL = 360 mg/kg/day
(decreased weight gain)

Fetotoxicity NOEL ≥ 360 mg/kg/day (HDT)
Teratogencity NOEL ≥ 360 mg/kg/day (HDT)
Maternal Toxicity NOEL = 120 mg/kg/day

Levels Tested: 36, 120 and 360 mg/kg/day by gavage on days 6 through 15 of gestation.

It is also acknowledged that Prometon Technical (98% ai) was used in this study rather than the 80% ai.

2. Argus Research Labs: #203-002. EPA Accession No. 250917.

The submission of the composition of Prometon Technical as 98% ai permits the upgrading of the rabbit teratology study to a core classification of Minimum. Toxicology Branch also concurs with the registrant in assessing the absence of any alteration in implantation efficiency at the high dose in comparison with controls and the initiating of treatment on day 6, suggestive of a absence of any treatment-related effect on the pregnancy rate. Thus, the lower pregnancy rate at the HDT is more likely attributable to biological variation than to treatment with Prometon. The following conclusions of the rabbit teratology study are proposed:

Teratogenicity NOEL ≥ 24.5 mg/kg/day (HDT)
Maternal Toxicity LEL = 24.5 mg/kg/day (decreased weight gain)
Maternal Toxicity NOEL = 3.5 mg/kg/day
Fetotoxicity NOEL ≥ 24.5 mg/kg/day (HDT)
Levels Tested 0, 0.5, 3.5, and 24.5 mg/kg/day on days 6 through 18 of gestation

3. Food and Drug Research Labs: #6805. EPA Accession Nos. 250917, 250918.

Presentation of the Prometon Technical as 98 percent ai permits the upgrading of the 90-day feeding study in the rat to a core classification of Minimum. The Toxicology Branch also concurs with the registrant that the minimal increase in absolute kidney weights in females at the high dose level is of no toxicological significance considering the absence of any change in the relative kidney to body weight ratios. Moreover, the failure to demonstrate any significant alterations in clinical blood chemistries or urinalysis or renal histology support a NOEL of 300 ppm, the highest dose tested in the 90-day rat study.

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