2-27-79

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: February 27, 1979

SUBJECT: EUP for evaluation of Ridomil-2E for black shank control on tobacco. Caswell #[redacted]

FROM: William Woodrow, Ph.D
Toxicology Branch/HED/TS-769

TO: Mr. Henry Jacoby
Product Manager#24

THRU: Dr. Lamar Dale, Acting Chief William D. Butler for LB. Dale.
Toxicology Branch/HED/TS-769

Registration No.
100-EUP-62
63

Ciba-Geigy Corp.
Agricultural Division
P.O. Box 11422
Greensoboro, N.C. 27409

Recommendations - Conclusions

1. A tolerance for Ridomil-2E used on tobacco is not necessary, according to the Guidelines for Registering Pesticides in the U.S.

2. A request for an Experimental Use Permit for Ridomil-2E used to control tobacco black shank can be toxicologically supported.

3. Acceptable toxicology studies were submitted:

   A. Using the product formulation (containing ethylene dichloride)

      a. Acute Oral Toxicity, Rats
         Toxicity Category III, Core-Minimum Data

      b. Acute Dermal Toxicity, Rabbits
         Toxicity Category III, Core-Minimum Data

      c. Primary Eye Irritation, Rabbits
         Toxicity Category I, Core-Guidelines Data

      d. Primary Skin Irritation, Rabbits
         Toxicity Category IV, Core-Guidelines Data

   B. Using the technical grade active ingredient

      Teratology Study, Rats
      Core-Minimum Data

1
170

4. Prior to registration, additional required information using the new product formulation shall include but not be limited to: acute rat oral LD50, acute rabbit dermal LD50, acute eye irritation, acute dermal irritation, and a acute inhalation LC50 (if applicable).

   A subacute smoke inhalation study, especially if it can be determined that residues remain on cure tobacco.

BACKGROUND INFORMATION

On June 30, 1978, Ciba-Geigy submitted a request for an experimental use permit for Ridomil-2E fungicide to control tobacco black shank. A review of the toxicology data in this submission was performed by W. Woodrow, Nov. 27, 1978. P.M.#24 was informed in this review that the Ridomil-2E formulation contained ethylene dichloride, which is presently on the pre-RPAR review compound list. A recommendation stated that a crop destruct request should accompany an EUP grant for the formulation containing ethylene dichloride, and that the crop destruct request could be withdrawn, provided ethylene dichloride was removed from the formulation.

On January 9, 1979, Ciba-Geigy submitted a change of formulation for Ridomil-2E, which eliminated ethylene dichloride and certain of the other inert compounds. The new formulation included inert solvent and emulsifier materials:

Ridomil-2E formulation containing ethylene dichloride

Active Ingredient	% by wt.
CGA-48988 technical, (90% a.i.) [(N-(2,6-dimethyl-phenyl)-N-(methoxyacetyl)-alanine ester]	27.8
Inert Ingredients	
[redacted]	
	100.0

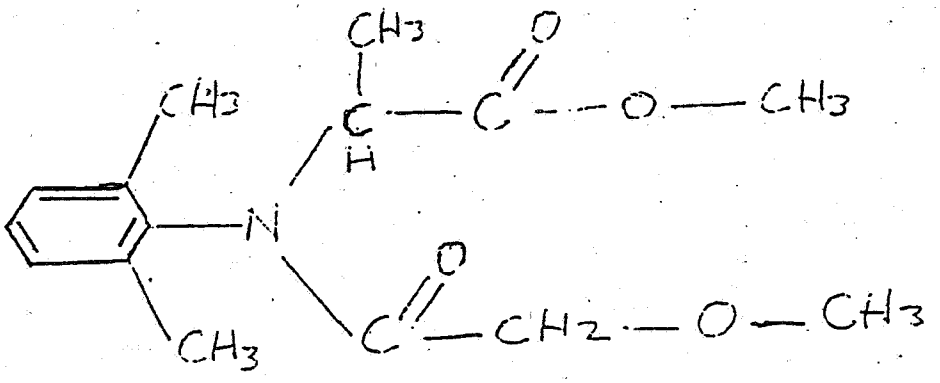
INERT INGREDIENT INFORMATION IS NOT INCLUDED

Ridomil-2E formulation submitted January 9, 1979, that eliminated ethylene dichloride

Active Ingredient	% by wt.
CGA-48988 technical, (90% a.i.) [(N-(2,6-dimethylphenyl)-N-(methoxyacetyl)-alanine ester]	27.9
Inert Ingredients INERT INGREDIENT INFORMATION IS NOT INCLUDED	[redacted]
	100.0

Ciba-Geigy submitted acute toxicity data for the Ridomil-2E formulation that contained [redacted] and a teratology study that evaluated the technical active ingredient.

Structural formula (active ingredient)



Review of Data

A. Studies using the product formulation:

Ridomil-2E - EPA ACC. No. 234429

a. Acute Oral Toxicity, Rats. Performed by Hazelton Labs. American, May 30, 1978, submitted by Ciba-Geigy. Project No. 438-148.

5M & 5F rats/dose level treated with 312.5, 625, 1250, 2500, or 5000 mg/kg. Animals observed daily through 14 days post treatment. Necropsies performed on all animals dying and sacrificed.

Results: Combined acute oral LD_{50} = 1889.48 mg/kg (95% C.L. 1427.8 to 250014 mg/kg).

Acute oral LD_{50} males = 2341.9 mg/kg (95% C.L. of 1550.9 to 3536.4 mg/kg).

Acute oral LD_{50} females = 1520.4 mg/kg (95% C.L. of 1010.2 to 2288.1 mg/kg).

Toxicity Category III

Classification - Core-Minimum Data. Untreated control animals not included.

b. Acute Dermal Toxicity, Rabbits. Performed by Hazelton Labs. American, May 30, 1978, submitted by Ciba-Geigy. Project No. 483-149.

Two rabbits/sex/each of 4 dose levels; one rabbit/sex abraded skin 625, 1250, 2500, or 5000 mg/kg applied under wrap maintained 24 hours. Observed 14 days. Dermal responses observed for surviving animals at 1, 3, 7, 10, and 14 days according to Draize.

Results: Acute dermal LD_{50} = 3571.5 mg/kg (95% C.L. of 1518.1to 8402.6 mg/kg).

Toxicity Category III

Classification - Core-Minimum Data. Should have used 4 animals/sex/dose. Untreated controls not included.

c. Primary Eye Irritation Study. Performed by Hazelton Labs. American, May 19, 1978, submitted by Ciba-Geigy. Project No. 483-150.

0.1 ml test material instilled 1 eye each of 9 rats. 3 treated eyes washed 30 seconds post instillation, remaining unwashed. Examined at 24, 48 and 72 hours, 7 days, 10 & 14 days if persistent injury at day 7.

4

173

Results - Unwashed eyes - Slight corneal opacity in three rabbits to day 7. Conjunctival irritation through 48 hours all rabbits through day 7 in 4 rabbits. Washed eyes - Corneal opacity in one rabbit at 24 hours; at 24 & 48 hours in a second rabbit, conjunctival irritation persisting through 48 & 72 hours. Corneal opacity and conjunctival irritation through 7 days in a third rabbit.

Toxicity Category: I

Classification: Core-Guidelines Data

d. Primary Skin Irritation Study. Performed by Hazelton Labs. American, May 24, 1978, submitted by Ciba-Geigy. Project No. 483-151.

0.5 ml undiluted material placed on one intact and one abraded skin site each of 6 rabbits, sites occluded 24 hours.

Results - Very slight erythema for all animals at 24 hours. Slight edema 2 rabbits at 24 hours. No dermal irritation at 72 hours. Primary irritation score = 0.5. A very slight irritation agent.

Toxicity Category: IV

Classification: Core-Guidelines Data

B. Teratology study using product Technical Chemical. Performed by Ciba-Geigy Basle, Switzerland, February 7, 1978, submitted by Ciba-Geigy. Expt. No. 227716. EPA ACC. No. 234428.

20, 60 & 120 mg/kg b. wt. administered by intubation to groups of 25 rat dams from day 6 through 15 of pregnancies. A fourth group of 25 pregnant dams served as vehicle controls.

Results - No maternal mortality. Higher doses (60 & 120 mg/kg) did elicit toxic effects in dams; diminished food consumption, wt. gain depression, during 1st 15 days of treatment.

Ratios of implantations and resorptions were comparable in treatment and control groups. Sex ratios of live fetuses from treatment groups unchanged from vehicle control group. No malformations in fetuses, av. wt. of fetuses from treated groups not significantly changed from control fetuses.

No deviations in 20 or 60 mg/kg treatment group fetuses from controls examined by a slicing technique; 95% con. L. A slightly increased number of incompletely ossified 5th sternbrae occurred in fetuses from dams treated with 120 mg/kg; this finding not considered significant.

5

174

No dams aborted, no corpus luteae. Fetal resorptions: 0.3, 60 mg/kg; 0.7120 mg/kg; 0.0, 20 mg/kg and untreated controls.

Classification - Core-Minimum Data. No positive control chemical evaluation was included.

TOX/HED:th:RD Initial :2-27-79

dar 2/27/79 cc Lambert 5/20/79