UNITED STATES ENVIRONMENTAL PROTECTION AGENCY 11/8/78 67

DATE: November 8, 1978

SUBJECT: EUP proposed for evaluation of Ridomil 2E for black shank control on tobacco. Caswell#375C

FROM: Dr. Woodrow, Ph.D (WSW)
Toxicology Branch/HED

TO: Dr. E. Wilson
Product Manager#21

Registration Number: 100-EUP-62

Ciba-Geigy Corp.
Agricultural Division
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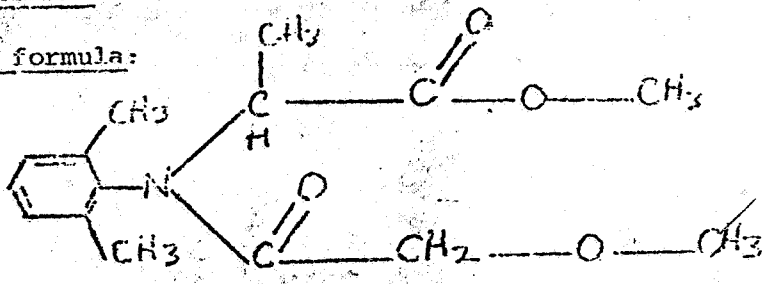
Formulation:

Active Ingredient N-(2,6-dimethylphenyl)-N-(methoxyacetyl)-alanine ester	25.06%
Inert Ingredient	74.08%

Structural formula:



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. [redacted]

INERT INGREDIENT INFORMATION IS NOT INCLUDED

3. Toxicology studies using the product formulation:

   a. Acute oral toxicity study with rats is acceptable (Project No. 483-148).
   b. Acute dermal toxicity study with rabbits is acceptable (Project No. 483-149).
   c. Primary eye irritation study with rabbits is acceptable (Project No. 483-150).
   d. Primary skin irritation study with rabbits is acceptable (Project No. 483-151).

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4. The teratology study using technical grade product with rats is acceptable (Expt. No. 227716).

5. Prior to registration additional required information shall include but not be limited to:

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

Review of Data

A. Studies using the product formulation:

   Ridomil 2E - EPA ACC. No. 234429

a. Acute Oral Toxicity, Rats. Performed by Hazelton Labs. America, 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. of 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 30m 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 1518.1 to 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.

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: II

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. 22771. EPA ACC No. 234428.

20, 60 of 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; dimivied 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 [illegible] treatment group fetuses from controls [illegible]

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number of incompletely ossified 5th sternbrae occurred in fetuses from dams treated with 120 mg/kg; this finding not considered significant.

No dams aborted, no corpora lutea. Fetal resorptione: 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.

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