UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: ~~March 21,1979~~ 3-30-79

SUBJECT: The Request to register

~~FROM~~ I. Technical CGA-48988 (Ridomil), EPA #100-ANR for formulation use

~~TO~~ II. Formulation CGA48988, 5W, EPA #100-ANN Caswell No. 375 C

From: Chan S-L Ph.D. Tox/HED Chan S-L 3/30/79

To: Mr. H. Jacoby PM/RD

Thru: Acting Deputy Chief, Tox/HED William M. Butler

I. The request to register technical CGA-48988 for formulation use.

The physical, chemical and certain toxicological properties of the technical material havebeen recently reviewed by Dr. W. Woodrow, (see reviews on 8G2121 dated 11/27/78 and on EPA #100-EUP-62 dated 11/8/78). This chemical is seen to be not readily respirable. All toxicological studies that are needed to support this registration have been evaluated as acceptable by Dr. Woodrow. These studies are briefly summarized below:

1. The Acute Oral LD_{50} for Rats = 669 mg/kg
   Toxicity Category III,
   Classification - Core Guidelines Data

2. The Acute Dermal LD_{50} for Rabbits > 6 gm/kg
   Toxicity Category III,
   Classification - Core Minimum Data

3. The Rabbit Skin Irritation Index = 0.1/8
   Toxicity Category IV,
   Classification - Core Guidelines Data

4. The Rabbit Eye Irritation Index = 9.5/110
   Toxicity Category II,
   Classification - Core Guidelines Data

5. The Rat Teratology Study
   Not teratogenic to 120 mg/kg
   Classification - Core Minimum Data

6. The Salmonella Mutagenicity Study
   Mutagenic potential - Negative in TA 1535, TA 1537, TA 98 and TA 100 with and without microsomal activation
   Classification - Core Guidelines Data

7. The Mouse Dominant Lethal Study
   Mutagenic potential - Negative
   Classification - Core Minimum Data

Conclusion: The registration of technical CGA-48988 can be toxicologically supported. The precautionary statement should however be modified to read as follow:

Warning

Causes eye irritation. Harmful if swallowed. Do not get in eyes or on clothing. Wash thoroughly after handling. Remove contaminated clothing and wash before reuse. In case of contact, flush eyes or skin with plenty of water. Get immediate medical attention. If swallowed, drink promptly a large quantity of milk, egg whites gelatin solution, or if these are not available drink a large amount of water and induce vomitting. Get medical attention.

II. The request to register CGA-48988 5W

This product is a systemic fungicide in the form of a wettable powder. It is intended for the control of certain diseases of ornamentals and non-bearing citrus. It may be applied to container, bench or bedgrow ornamentals in greenhouses or outdoor nurseries. It is applied as a soil drench or soil mix on ornamentals or as a foliar spray on azaleas. Depending on the way it is applied and the extent of the disease, repeat application may be made after a varying period of 6 to 20 weeks.

In support of this application for registration, acute toxicity data on the formulated product have been submitted (in ac. no. 235064). These studies are evaluated as follow:

1. The rat acute oral LD_{50} study; by Hazleton Labs., 5/30/78.

   Procedure: Dose levels of 625, 1250, 2500, 5000 and 10,000 mg/kg of the material were given by oral intubation to 5M + 5F/ group of fasted albino rats. Treated animals were observed for 14 days. All dead animals and animals remaining at the end of the study were necropsied.

Results:	10,000 mg/kg>LD_{50}>5000 mg/kg.
Toxic signs:	tremors and convulsion before death.
Necropsy:	pale liver and yellowish fluid in the stomach.
Tox. Evaluation:	LD_{50} > 5000 mg/kg
Tox. Cat. =	IV, Classification: Core minimum data.

2. The rabbit acute dermal LD_{50} study; by Hazleton Labs., 5/30/78

   Procedure: Dose levles of 5000, 6310, 7940 and 10,000 mg/kg of the material were applied to 2M + 2F rabbits/group in a 24 hr.

occlusive test. The sites of application for half the no. of animals/sex were abraded. Animals were observed daily for 14 days. Necropsies were performed on all dead animals and animals remaining at the end of study.

Results: LD_{50} > 10,000 mg/kg
Dermal responses: minor erythema reversed before day 3.
Toxic signs: depression, anorexia and soft feces.
Necropsy: unremarkable
Tox. Evaluation: LD_{50} > 10,000 mg/kg
Tox. Cat. = III, Classification: Core minimum data.

3. The rabbit eye irritation study; by Hazelton Labs., 5/19/78.

Procedure: 100 mg of the material was instilled into the right eyes of 9 rabbits. 30 seconds after treatment, 3 eyes were washed for 1 minute. All treated eyes were examined at 24, 48, 72 hr. and at 7, 10, and 14 days after treatment.

Results: Unwashed eyes: moderate corneal opacity and conjunctival redness with 5 recovered and 1 persisting by day 7. All injuries were reversed by day 10. One rabbit was found dead on day 7, apparently not treatment related.

Washed eyes: no irritation
Tox. Evaluation: corneal opacity, fully reversed by day 10.
Tox. Cat. = II, Classification: Core minimum data.

4. The rabbit primary skin irritation study; by Hazelton Labs. 5/24/78.

Procedure: 0.5 gm/site of the material was applied to an abraded and an intact site on each of 6 rabbits in a 24 hr. occluded test. Skin reactions were scored at 24 and 72 hr. post application.

Results: no irritation was observed on any site.
Tox. Evaluation: the treatment produced no skin irritation.
Tox. Cat. = IV, Classification: Core minimum data.

5. The rat acute inhalation LC_{50} study; by Hazelton Labs; 6/20/78.

Procedure: 6 male and 6 female rats were exposed for 4 hr. in separate inhalation chambers to an average concentration of 2.97 mg/L of the material as a dust. The dust concentration was determined by gravimetric filter samples taken at hourly intervals. The mass median diameter of the airborne particles was determined as 3μ. Treated animals were separated by sex, kept in separate cages and observed for 14 days. Dead animals and remaining animals sacrificed at the end of study were necropsied.

Results:	LC_{50} >2.97 mg/L (no mortality).
Toxic signs:	labored breathing during exposure, normal appearance subsequently.
Necropsy:	no useful information in the absence of control animals.
Tox Evaluation:	LC_{50} > 2.97 mg/kg,
Tox Cat. =	III, Classification: Core mimimum data, on account of low toxicity.

Other toxicological studies useful to support this registration have been recently accepted by tox. branch, see reviews by Dr. W. Woodrow on 8G-2121 dated 11/27/78 and on EPA #100-EUP-62 dated 11/8/78. These studies are listed below:

1. The rat teratology study.
2. The Ames test.
3. The mouse dominant lethal study.

Conclusion: The registration of this product can be toxicologically supported.

3/27/79
4/18/79

[6560-01-M]

ENVIRONMENTAL PROTECTION AGENCY

[FRL 1058-7; OPP-30160]

PESTICIDE PROGRAMS

Receipt of Application To Register Pesticide Product Containing New Active Ingredient

Ciba-Geigy Corp., Agricultural Div., PO Box 11422, Greensboro, NC 27409, has submitted to the Environmental Protection Agency (EPA) an application to register the pesticide product CGA-48988 TECHNICAL (EPA File Symbol 100-ANR) containing 90% of the active ingredient *N*-(2,6-dimethylphenyl)-*N*-(methoxyacetyl) alanine methyl ester which has not been included in any previously registered pesticide products. The applicant proposes that this product be used as a technical chemical for formulating fungicides.

Notice of receipt of this application does not indicate a decision by the Agency on the application. Interested persons are invited to submit written comments on this application to the Federal Register Section, Program Support Division (TS-757), Office of Pesticide Programs, EPA, Rm. 401, East Tower, 401 M St., SW, Washington DC 20460. The comments must be received on or before March 15, 1979, and should bear a notation indicating the EPA File Symbol "100-ANR." Comments received within the specified time period will be considered before a final decision is made; comments received after the specified time period will be considered only to the extent possible without delaying processing of the application. Specific questions concerning this application and the data submitted should be directed to Product Manager (PM) 21, Registration Division (TS-767), Office of Pesticide Programs, at the above address or by telephone at 202/755-2562. The label furnished by Ciba-Geigy Corp., as well as all written comments filed pursuant to this notice, will be available for public inspection in the office of the Federal Register Section from 8:30 a.m. to 4:00 p.m. Monday through Friday.

Notice of approval or denial of this application to register CGA-48988 TECHNICAL will be announced in the FEDERAL REGISTER. Except for such material protected by Section 10 of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) as amended in 1972, 1975, and 1978 (92 Stat. 819; 7 U.S.C. 136), the test data and other information submitted in support of registration as well as other scientific information deemed relevant to the registration decision may be made available after approval under the provisions of the Freedom of Information Act. The procedures for requesting such data will be given in the FEDERAL REGISTER if an application is approved.

Dated: February 1, 1979.

DOUGLAS D. CAMPT,
Acting Director,
Registration Division.

[FR Doc. 79-4648 Filed 2-12-79; 8:45 am]

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