Data has file

Shaughnessy No.: 109801

Date Out of EAB: JUN 24 1988

To: Lois Rossi
Product Manager #21
Herbicide- Fungicide Branch
Registration Division (TS-767C)

From: Emil Regelman, Supervisory Chemist
Review Section #3
Exposure Assessment Branch
Hazard Evaluation Division (TS-769C)

Thru: Paul F. Schuda, Ph.D., Chief
Exposure Assessment Branch
Hazard Evaluation Division (TS-769C)

Attached, please find the EAB review of...

Reg./File # : 359-685

Common Name: Iprodione

Type Product : Fungicide

Product Name : Rovral, Glycophene

Company Name : Rhone-Poulenc Ag Company

Purpose : Review additional data submitted in response to deficiencies cited in EAB review #6818, 7/30/87.

Date Received: 2/24/88

Action Code(s): 336

Date Completed: 6/24/88

EAB #(s) : 80464

Monitoring study submitted: ____

Total Reviewing Time: 3.0 days

Monitoring study voluntarily: ____

Deferrals to: ____ Ecological Effects Branch

____ Residue Chemistry Branch

____ Toxicology Branch

1. CHEMICAL: Common name(s):

Iprodione

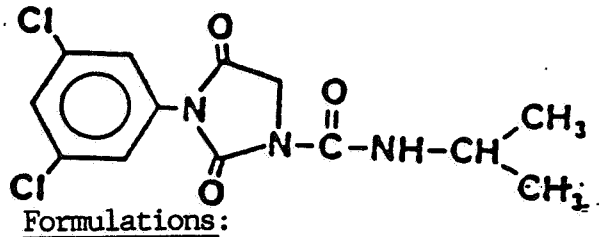
Chemical name:

3-(3,5-Dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide.

Other name(s):

Rovral, RP-26019, Glycophene

Structure:



Formulations:

50% WP

Physical/Chemical properties:

Molecular formula:	$C_{13}H_{13}Cl_2N_3O_3$.
Molecular weight:	329.5
Physical state:	White, odorless, non-hydroscopic crystal.
Solubility:	Soluble in acetone and benzene. Almost insoluble in water (13 mg/L).

2. TEST MATERIAL:

N/A.

3. STUDY/ACTION TYPE:

Review registrant's rebuttal of data gaps identified in EAB review #6818, 7/30/87, for anaerobic aquatic metabolism (§162-3), aerobic aquatic metabolism (§162-4), aquatic field (sediment) dissipation (§164-2), and accumulation of iprodione in crayfish (§165-4).

4. STUDY IDENTIFICATION:

Gemma, A., G. Heinzelmann, and J. Wargo. 1986. Iprodione aquatic field dissipation and field irrigated crop study. Submitted by Rhone-Poulenc, Inc., Monmouth Junction, NJ. MRID #00162218.

Mcallister, W. A., B. Bunch, and J. Burnett. 1986. Bioconcentration and depuration of [^{14}C]-iprodione by crayfish (Procambarus Simulans, Faxon) under static uptake conditions with a treated soil substrate. Report No. 33438. Unpublished study prepared by Analytical Bio-Chemistry Laboratories Inc., Monmouth Junction, NJ. MRID #00162221.

Thomas, R. D. 1983. Aquatic metabolism of [^{14}C]-RP-26019. Borriston Project No. 32201. Unpublished study prepared by Borriston Laboratories, Temple Hills, MD and submitted by Rhone-Poulenc, Chemical Co., Monmouth Junction, NJ. MRID #00162219.

Thomas, R. D. 1983. Anaerobic aquatic metabolism of [^{14}C]- RP-26019. Prepared by Borriston Laboratories, Inc., Temple Hills, MD, and submitted by Rhone-Poulenc, Inc., Monmouth Junction, NJ. MRID #00162220.

5. REVIEWED BY:

Padma Datta, Ph.D.
Chemist
Review Section #3
EAB/HED/OPP

Signature: PR Datta

Date: 6/24/88

6. APPROVED BY:

Emil Regelman
Supervisory Chemist
Review Section #3
EAB/HED/OPP

Signature: E Regelman

Date: JUN 24 1988

7. CONCLUSIONS:

The additional information submitted by Rhone-Poulenc in response to deficiencies cited in EAB review #6818, 7/30/87, for the anaerobic aquatic (§162-3) and aerobic aquatic (§162-4) metabolism studies; and, the aquatic field dissipation study (§164-2) are inadequate. (For details, see the Discussion section below).

8. RECOMMENDATION:

RD should advice Rhone-Poulenc to: (1) repeat the aerobic aquatic (§162-3) and anaerobic aquatic (§162-4) metabolism studies for a duration of a year (365 days); and, (2) answer the questions raised in EAB review #6818, 7/30/87, re the aquatic field dissipation studies in LA and AR rice fields (§164-2).

9. BACKGROUND:

On 1/25/88 Rhone-Poulenc submitted additional information in response to deficiencies cited in EAB review #6818, 7/30/87.

10. DISCUSSION OF INDIVIDUAL TESTS OR STUDIES:

§162-3: Anaerobic Aquatic Metabolism of Iprodione (^{14}C-RP-26019) MRID #00162220

On 8/22/86, the registrant reported half-lives for iprodione in water and sediment of 6.4 days and 126 days, respectively, using log DPM vs log time plot of the data from Table 6 (attached).

On 5/27/87, EAB/HED computed the half-lives of iprodione in water and sediment to be 13.7 days (r^2 = 0.756) and 35.1 days (r^2 = 0.337), respectively. EAB also stated that the data in Table 6 did not fit the residue decline curves of iprodione (RP-26019); (refer to EAB review #6818, 7/30/87). The apparent problem is either the registrant's failure to justify computing half-life using second order (log/log) kinetics or poor quality data.

On 1/25/88, the registrant submitted additional information in response to deficiencies cited in EAB #6818, 7/30/87. The registrant reported half-lives for iprodione in water and sediment to be 7.1 days and 100 days, respectively.

The discrepancy of regression analysis half-lives of iprodione in water between EAB (13.7 days) and Rhone-Poulenc (7.1 days) and iprodione in sediment between EAB (35.1 days) and the registrant (100 days) remains unresolved for the following reasons:

1. No rationale for the linear regression analysis method used was provided by the registrant.

2. The data may be of such poor quality that a new study may have to be conducted.

On 7/30/87, EAB concluded that the laboratory study (duration, 184 days) submitted 8/22/86 showed that the concentration of degradate RP-30228 was increasing at termination (184 day post-treatment). Therefore, the formation and decline of degradate(s) in water and in sediment could not be established. Also, there are insufficient data points in Table 6 to construct residue decline curves of parent and degradates.

In response, the registrant agreed that the concentration of RP-30228 was increasing at 184 days in the laboratory study but pointed out that 1) degradate RP-30228 rapidly degrades under field conditions as evident in the soil field dissipation study (§164-2); 2) iprodione (RP-26019) isomerizes to RP-30228 with $t_{1/2}$ = 6-7 days in water and $t_{1/2}$ = 3-4 months in sediment; and, 3) the resulting RP-30288 would be absorbed into the sediment and an insignificant amount of parent iprodione would remain in water.

EAB can not accept the above pertinent data to validate this anaerobic aquatic metabolism study (§162-3) because the registrant quoted these data from an unacceptable field dissipation study (§164-2). Furthermore, the registrant did not provide a) a reasonable explanation re the discrepancy in half-lives between the anaerobic aquatic metabolism study and the soil field dissipation study (§164-2); and, b) identities of degradates >10% in sediment.

EAB cannot accept this anaerobic aquatic metabolism study (§162-3). Rhone-Poulenc should be advised to conduct a new study.

§162-4: Aerobic Aquatic Metabolism of Iprodione (^{14}C-RP-26019) MRID #162219

On 8/22/86, Rhone-Poulenc (registrant) submitted an aerobic aquatic metabolism study (§162-3) conducted in unfiltered water (without soil) obtained from a rice field in Mississippi.

EAB rejected this study because: 1) no soil was used; 2) degradates >10% were neither separated (TLC, cochromatographed) nor identified; 3) material balances were incomplete (range varied from 16.3% to 84.9% ; four out of seven studies had material balances $\leq$ 62% or lower); and, 4) no supporting data re low % recovery from fortified samples were reported.

On 1/25/88, the registrant responded by stating: 1) that the study was conducted in unfiltered natural water instead of a water-plus-sediment medium to obtain more information on the behavior of iprodione in water; 2) sufficient data are available on a soil/water system from other studies; 3) the calculated half-life was found to be 2.9 days in water, compared to 6-7 days in the water phase of the anaerobic aquatic metabolism study; 4) in both studies (aquatic aerobic and anaerobic metabolism) the formation of degradates never exceeded 10% of the applied [^{14}C] activity; and, 5) consideration of the results of other studies (for example, crayfish metabolism and aquatic field dissipation) would validate the results of this study. EAB cannot accept these statements without supporting data.

EAB cannot accept the data submitted in support of the aerobic aquatic metabolism data requirement of iprodione because aerobic aquatic studies must be conducted in a water-plus-sediment medium to determine the impact of iprodione in water or sediment during the dispersal of iprodione in an aquatic environment (rice fields) and to compare the rates and formation of degradate(s) with those measured during the anaerobic aquatic metabolism study (§162-4). Therefore, a new study must be conducted consistent with Subdivision N of the Pesticides Assessment Guidelines, and Rhone- Poulenc should be so informed.

§164-2: Iprodione Aquatic Field Dissipation and Field Irrigated Crop Study MRID #00162218.

On 8/22/86, Rhone-Poulenc submitted an aquatic soil field dissipation study.

EAB found this study unacceptable for the following reasons: 1) the initial concentrations of iprodione in water varied widely between replicate plots, ranging from 0.02 to 0.70 ppm in the AR plots and 0.11 to 0.63 ppm in the LA plots; 2) degradate RP-30288 comprised up to 50% of total residues in the AR plots immediately post-treatment; and, 3) residue decline curves of parent and degradates were not provided. (For details, see EAB review #6818, 7/30/87).

On 1/25/88, the registrant provided additional information, including residue decline curves using the averages of concentrations measured for iprodione and RP-30228 (Table 1) in the two plots in LA and the two plots in AR re aquatic field dissipation studies (§164-2).

The registrant explained that the inconsistency of the initial concentrations (range from 0.02 to 0.70 ppm in AR plots and 0.11 to 0.63 ppm in LA plots) is due to the non-equilibrium in large plot size (600 square meters in area) and increased interception of iprodione by foliage cover.

EAB rejected the above explanations because: 1) the ranges have very large variation; and, 2) the average concentrations in water and in soil sediment are not adequate to construct accurate residue decline curves for aquatic field dissipation studies (§164-2).

The registrant concurs that the exact reason is not known re the concentration of isomer RP-30228 equal to 50% of total residues measured in the AR plot immediately after treatment. Since the above data resulted from a sample taken immediately after treatment (within one hour), the registrant's explanation that iprodione hydrolyzes and rearranges to isomer RP-30228 within a day is not acceptable to EAB.

In summary, the additional information submitted on 1/25/88 was inadequate to resolve the issues raised in EAB review #6818, 7/30/87. Therefore, the aquatic field dissipation study (§164-2) does not fulfill the data requirement to support registration of iprodione (Rovral 50% WP) on rice under 40 CFR §158.130.

§165-4: Bioconcentration and Depuration of ^{14}C-Iprodione by Crayfish Under Uptake Condition with a Treated Soil Substrate. MRID #00162221.

The crayfish accumulation data are ancillary information to the fish accumulation study (§165-4), whose data requirement is satisfied. Rhone-Poulenc's claims to the similar types and amounts of residues in fish, water and soil sediment are a moot point and are not relevant to deficiencies found in the aquatic anaerobic (§162-3) and aerobic (§162-4) metabolism studies.

11. COMPLETION OF ONE-LINER:

N/A.

12. CBI APPENDIX:

All data reviewed are considered Company-confidential by the registrant and must be treated as such.

FIN 5721-93

Iprodione EF Reviews

Page 1 is not included in this copy.

Pages _____ through _____ are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

✓ FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.
