1-8-93

010131

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 264-LEU
Rovral WG Brand Fungicide

FROM: William S. Woodrow WSW 4-2-92
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C)
E 1/8/93

TO: S. Lewis / Robert Rose (PM 21)
Fungicide - Herbicide Branch
Registration Division (H75-05C)

APPLICANT: Rhone-Poulenc Ag Co.
P.O. Box 12014, 2 T.W.
Alexander Drive.
Research Triangle Park, NC 27709

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
iprodione: 3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboximide	50.0
Inert Ingredient(s):	50.0
Total	100.0%

BACKGROUND

Rhône-Poulenc Ag Co. submilled acute oral, acute dermal, eye and skin irritation and dermal sensitization studies to support registration of Rovral WG Fungicide (EPA Reg. No. 264-LEU). MRID NOS. used were 422264-01, -07, -08, -09, and 422264-11.

RECOMMENDATION

1) The acute toxicity studies submitted by Rhône Poulenc are acceptable, and were graded Core Guideline Data.

2) The registrant must submit an inhalation toxicity study. The Rovral WG Fungicide must be ground to a fine powder, and administered to laboratory animals via an aerosol, for an exposure period of four hours, as described in the Pesticide Assessment Guidelines, Subdivision F Hazard Evaluation, Nov., 1984.

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3) Current acute toxicity profile for Rabral WG Fungicide:

study	Classification for Category
acute oral LD50 > 5.0 g/kg Guideline	IV
acute dermal LD50 > 2.0 g/kg Guideline	III
eye irritation - Clearing in 8 - 21 days Guideline	II
skin irritation - NO irritation Guideline	IV
dermal sensitization - not a sensitizer Guideline	—

P.M. Note: Upon receipt of the requested acute inhalation toxicity study, Precautionary Labeling may require revision.

LABELING

1) Change the signal word from CAUTION to read "WARNING".

2) Change the Precautionary Statements to read as follows:

"Causes substantial but temporary eye injury. Harmful if absorbed through skin. Avoid contact with eyes, skin or clothing. Wash thoroughly with soap and

water after handling. Wear (goggles, face shield, or safety glasses). Remove contaminated clothing and wash before reuse."

3) Under Statement of Practical Treatment, ~~[illegible]~~

"If on skin: ~~[illegible]~~ Wash with plenty of soap and water. Get medical attention." E

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DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§81-1)

Product Manager: (21) 10-25-91 Reviewer: Woodrow ~~Mr Walker~~
MRID No.: 422264-67 Report Date: 3-26-92
Testing Facility: Hazleton, WI., inc. Report No. HWI 10603195
Author(s): S.M. Glaza
Species: Rat, Sprague Dawley
Age: young adult Observation Days (Post Exposure): (14) other ( )
Weight: 216-296g
Source: Harlan Sprague Dawley
Test Material: ROVRAL WG Fungicide, granules
Quality Assurance (40 CFR §160.12): yes (Q.A. + G.L.P.)

Conclusion:

1. LD_{50} (mg/kg): Males = > 5.0 g/kg ; Females = > 5.0 g/kg ; Combined = ~~[illegible]~~
2. The estimated LD_{50} is > 5.0 g/kg.
3. Tox. Category: IV. Classification: Guideline.

Procedure (~~Deviations From §81-1~~): Animals acclimated to lab. conditions at least 7 days. 5M & 5F, fasted, rats dosed by gavage with test material. Animals observed for clinical

Results: signs and/or mortality frequently descriptions, and daily

Reported Mortality

DOSAGE (g /kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
5.0 g/kg	0/5	0/5	0/10

Symptomology & Gross Necropsy Findings:

thereafter for 14 days. Body weights recorded days 0, 7 & 14. All animals subject to gross necropsy.

Clinical Signs: Soft stool, staggered gait - females to 4 hrs post dosing. 1M @ 1 hr. day, 2 days audible breathing, hyperactivity, reddened face, dark stained face. females, days 1 & 2 - Dark-stained encrusted eyes. Audible breathing, hyperactivity.

Necropsy: No gross abnormalities.

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DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2)

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Product Manager: (21) 10-25-91
Reviewer: ~~W. Weller~~ Woodrow
MRID No.: 422264-08
Report Date: 3-26-92
Testing Laboratory: Hazleton, Wt., Inc.
Report No. HWI 1060196
Author(s): S.M. Glaza
Species: Rabbit; NZW White
Sex: 5M/5 female Wt.: 2234-2664 g.
Test Material: Rovral 50WG, granules
Quality Assurance (40 CFR §160.12): yes (G.A. + G.L.P.)

Summary:

1. LD_{50} (mg/kg): Males = ~~—~~; Females = ~~—~~; Combined = ~~—~~;
2. The estimated LD_{50} is > 2.0 g/kg
3. Tox. Category: III. Classification: Guideline

Procedure (~~Deviations From §81-2~~): Animals acclimated at least 7 days. One day pre-test, rabbit backs shaved & electric clipper (10% body surface) & 2.0 g/kg (thoroughly moistened before application & saline) applied to each animal back. 10 cm^2 gauze patch secured & tape to cover. Gauze overwrapped & Saran wrap & elastoplast tape. Restraining collars

Results: Reported Mortality

DOSAGE (g /kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
2.0 g/kg	1/5	0/5	1/10

Symptomology & Gross Necropsy Findings:

applied. 24 hours exposure - wrappings removed, backs washed & tap water. Body wt. days 0, 7 & 14. Dilation clearing @ 30 min., days 3, 7 & 14. Animals observed twice a day for 14 days. All animals subjected to gross necropsy. Irritation: (dermal) slight to moderate erythema & day 3. Necropsy: Survived to termination (a), no visible lesions. dead animal: Colon-multiple dark red areas on mucosa

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7 DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: (21) 10-25-91 Reviewer: Woodlow
MRID No.: 422264-09 Report Date: 3-26-92
Testing Laboratory: Huzleton WI, Inc. Report No. HWI 10603198
Author(s): S. M. Glaza
Species: Rabbit, NZ White
Sex: 3M 3F Weight: 2372 - 2730g.
Source: not stated
Dosage: 0.61g/M (ground to powder)
Test Material: Rovral 50 WG gray granules
Quality Assurance (40 CFR §160.12)? yes (Q.A. & G.L.P.)

Summary:

Tox. Category: II Classification: Guideline

Procedure ~~(Deviation From §81-4):~~ Animals acclimated prior to test. Eyes examined for defects, using Sodium fluorescein dye, day before test. Test material ground to fine powder pre-test. 0.61g (.1ml equivalent) placed in everted lid, one eye, each rabbit. Lids held together 1 second, not flushed or rinsed. Treated eyes

Observations (number "positive"/number tested)

	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea Opacity	0/6	6/6 1	6/6 1	5/6 1	5/6 1-2	2/6 1	0/6	
Iris	6/6 1	6/6 1	5/6 1	4/6 1	4/6 1	1/6 1	0/6	
Conjunctivae Redness	6/6 2	6/6 3	6/6 2-3	6/6 3	6/6 2	5/6 1-2	0/6	
Chemosis	6/6 1-2	6/6 2-3	6/6 1	5/6 1	5/6 1	3/6 1	0/6	
Discharge	6/6 1-3	6/6 3	6/6 1-2	1/6 1	1/6 1	0/6	0/6	

~~Comments:~~ examined @ 1, 24, 48, 72 & 96 hrs, and days 7 & 14 post treatment. Draize Score.

Clearing in 8-21 days — Category II

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: e DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5)

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Product Manager: (21) 10-25-91
MRID No.: 422264-01
Testing Laboratory: Wazleton, WI, Inc.
Author(s): Steven Glaza
Species: Rabbit, Hra:(NZW) SPF
Age: adults
Sex: 3M & 3F
Weight: 2266, 2480 g
Dosage: undiluted (0.5 g)
Test Material: Rovral 50WG, granules
Quality Assurance (40 CFR §160.12): yes (G.L. & G.L.P.)

Reviewer: Woodruff
Report Date: 4-2-92
Report No. HWI 106 03197

Summary:

The Primary Irritation Index = 0.00

Toxicity Category: IV

Classification: Guideline

Procedure (~~Deviations From §81-5~~): Animals acclimated to lab. conditions for at least 7 days. On day before treatment, hair was clipped from backs and flanks of each animal (6 M & 6 F rabbits). 0.5 mg. test material, moistened ≈ 0.9% Saline, placed on each animals back. Treated sites covered with 2.5 cm² gauze patch secured ≈ tape, loosly overwrapped ≈ Saran Wrap & secured ≈ ELastoplast tape for a semi occlusive dressing. 4 hrs exposure, wrappings removed, sites washed & scored for irritation according to the Draize system; at 4 hrs, 24, 48 & 72 hrs post patch removal.

Results: No irritation observed, at any of the scoring periods.

Special Comments:

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DATA REVIEW FOR SKIN SENSITIZATION TESTING (§81-6)

Product Manager: (21) 10-25-91 Reviewer: Woodrow
MRID No.: 422264-11 Report Date: 4-2-92
Testing Laboratory: Appleton, Wisconsin Report No.: HWI 106031-99
Author(s): Steven Glaza
Species: Guinea Pigs
Sex: 28 males Weight: 350-448g.
Source: Hsa (DH) SPF
Test Material: Rovral 50 WG, granules
Positive Control Material: dinitrochlorobenzene (DNCB)
Quality Assurance (40 CFR §160.12): yes (Q.A. & G.L.P.)

Method: Buehler

Summary:
1. This product is / is not a dermal sensitizer.
2. Classification: Guidelines

Procedure ~~(Deviation From §81-6):~~ Animals acclimated for at least 7 days, prior to test. Pre-test screen to "determine the irritation threshold of the animal", was conducted. 4 g.p. used: ~~Results:~~ 0.2g, moistened w/ deionized water, at concentrations of 25%, 50% & 75% w/v in water; 2 chamber receiving two different concentrations of the test mat. Test concentrations applied to Hill top chamber patches, placed on two shaved sites, covered w/ strip of dental dam & wrap (wrapped w/ tape. Gauze opposite. Sites observed for erythema & edema at 24 & 48 hrs after patch removal. Based on screening results, test material induced @ 0.2g dose (moistened with deionized water) — for both induction, and for challenge.

Induction - Day of test, hair removed from back of each animal w/ clippers - test material (0.2g moistened w/ deionized water), placed on Hill top Chamber adhesive pad, pad placed on test site,

10 animals

on each left flank. Patch covered w dental dam and overwrapped w Elastoplast tape. 6 hour exposure, followed by patch removal. Positive control animals (4), received [0.3% W/V 2,4 dinitrochlorobenzene (DNCB) in 80% Ethanol/deionized water] administered in same manner as for test group (0.4ml dose). Animals received 3 applications, (once/week for 3 weeks).

Challenge: Two weeks following last induction application, a challenge of 0.2% of test material micronized w deionized water was administered to right rear flank of test group animals. Also 10 naive (untreated) animals, received a test material challenge dose in same manner as test group. Positive control material administered at a concentration of 0.1% W/V in acetone.

Application sites scored for erythema and edema at 24 and 48 hours following induction scoring, induction and challenge. Body weights recorded at weekly intervals.

Results:

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Test animals — following (test animals), is average of 24 & 48 hour readings for the three inductions of readiness: (each N.O. represents average for 10 test animals)

0.1	The values at left are presented
Induction 0.1	to show that the induction
0.1	response for test animals
0.1	was (Buehler Scoring), or
0.3	achieved an acceptable degree
0.2	of initiation, although the
0.1	tester could have easily
0.3	induced using a more
0.0	concentrated solution.
0.0	

Challenge (test material) — no scoring, at both 24 and 48 hour readings.

Naive Control animals — 0.00 scoring.

Positive Control: Guinea pigs were sensitized.

Conclusion: test material did not sensitize guinea pigs.

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