

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 E 1/8/93
Registration Division (H75-05C)

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.
<u>iprodione: 3-(3,5-dichlorophenyl)-N-</u>	
<u>(1-methylethyl)-2,4-dioxo-1-imid-</u>	
<u>dazolidine carbamide</u>	<u>50.0</u>
Inert Ingredient(s):	<u>50.0</u>
Total	100.0%

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BACKGROUND

Rhône-Poulenc Ag Co. submitted acute oral, acute dermat, 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
Ravital WG Fungicide:

study	Classification	Category
acute oral LD ₅₀ > 5.0g/kg	Guideline	IV
acute dermal LD ₅₀ > 2.0g/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..."

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

3) Under Statement of Practical Treatment,

~~Wash with plenty of soap and water. Get medical attention.~~

"If on skin: ~~Wash with plenty of soap~~ 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) 10-2591 Reviewer: Woodrow
 MRID No.: 422264-07 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: Hazleton Sprague Dawley
 Test Material: ROVRAL WG Fungicide, granules
 Quality Assurance (40 CFR §160.12): yes (Q.A. & G.L.P.)

Conclusion:

- LD₅₀ (mg/kg): Males = > 5.0g/kg; Females = > 5.0g/kg; Combined = > 5.0g/kg
- The estimated LD₅₀ is > 5.0g/kg
- Tox. Category: IV. Classification: Guideline

Procedure (Deviations From §81-1): Animals acclimated to lab. condition at least 7 days. 5M+5F, ^{fasted} rats dosed by gavage with test material. Animals observed for clinical Results: signs and/or mortality frequently developing, and daily

Reported Mortality

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

Symptomology & Gross Necropsy Findings:

thereafter for 14 days. Body weights recorded days 0, 7 & 14.
All animals subjected to gross necropsy.
Clinical Signs: soft stool, staggered gait - females to 4 hrs post-dosing. M @ 1 hr day 2, 2 days audible breathing, hypoactivity, red stained face, dark stained face. females, days 1 & 2 - Dark-stained resorpted area. Audible breathing, hypoactivity.
Necropsy: No gross abnormalities.

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

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Product Manager: (21) 10-25-91
 MRID No.: 422264-08
 Testing Laboratory: Hazleton, Wt., Inc.
 Author(s): S.M. Glaze
 Species: Rabbit #2 White
 Sex: SM & Female Wt.: 2234-2664 g.
 Test Material: Revco 50WG, granules
 Quality Assurance (40 CFR §160.12): yes (P.A. & G.L.P.)

Reviewer: Wood 600
 Report Date: 3-26-92
 Report No. HDT 10603196

Summary:

- LD₅₀ (mg/kg): Males = _____; Females = _____; Combined = _____;
- The estimated LD₅₀ is 2.0 g/kg
- Tox. Category: III Classification: Guideline

Procedure (~~Deviations From §81-2~~): Animals acclimated at least

7 days. On day pre-test, rabbit backs shaved & electric clippers (10% body surface) 2.0 g/kg (thoroughly moistened before application & saline) applied to each animal back.

Results: 10 cm² gauze patch secured to top, to cover. Gauze overwrapped & seven wrap & elastoplast tape. Restraining collars

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

Symptomology & Gross Necropsy Findings:

applic. 24 hour exposure. Wrappings removed, backs washed in tap water. Body temp 37.1-37.4. Irritation scoring @ 30 min., Resp.: 3, 7 & 14. Animals stressed twice a day for 14 days. All animals subjected to gross necropsy: Irritation: (dermal) slight to moderate erythema & day 3. Necropsy: Survived to termination (9); no visible lesions. dead animal: Colon-multiple dark red areas on mucosa

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

Product Manager: (21) 10-25-91 Reviewer: Wooden
 MRID No.: 422264-04 Report Date: 3-26-92
 Testing Laboratory: Hazleton Wt, Inc. Report No. HW1 10603198
 Author(s): S.M. Glazay
 Species: Rabbit, NZ White
 Sex: 3m + 3f Weight: 2372-2730g.
 Source: not stated
 Dosage: 0.51 g/ml (gained to powder)
 Test Material: Rota 50 WG 7 bag granules
 Quality Assurance (40 CFR §160.12): yes (Q.A. + G.L.P.)

Summary:

Tox. Category: 11 Classification: Guideline

Procedure (~~Deviation from §81-4~~): Animals acclimated prior to test.
Exps chemical for defects, using sodium fluorescein dye, day before
test. Test material ground to fine powder pre-test. 0.51g (ml
equivalent) placed in excited lid, one eye, each rabbit. Lids
 Results: held together 1 second, not flicked or wiped. Treated eyes

Observations

	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea								
Opacity	0/6	4/6	6/6	5/6	5/6	2/6	0/6	
Iris	0/6	0/6	5/6	4/6	4/6	1/6	0/6	
Conjunctivae								
Redness	0/6	0/6	0/23	0/6	0/6	5/12	0/6	
Chemosis	0/12	0/23	0/6	5/6	5/6	3/6	0/6	
Discharge	0/13	0/6	0/12	1/6	1/6	0/6	0/6	

Comments: examined @ 1, 24, 48, 72 & 96 hrs, and day 7 & 14 post
treatment. Ocular Score.

Classing in 8-21 days - Category 11

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DATA REVIEW FOR SKIN IRRITATION TESTING

Product Manager: (21) 10-25-91
 MRID No.: 422264-01
 Testing Laboratory: Hazelton, WI, Inc.
 Author(s): Steven Glaza
 Species: Rabbit, Hra (N2W) SPF
 Age: adults
 Sex: 3M & 3F
 Weight: 2266, 2480 g
 Dosage: undiluted (1)
 Test Material: Ruvral 50 WG, granules
 Quality Assurance (40 CFR §160.121): yes (P.A. & G.L.P.)

Reviewer: (100 AL-4) 10131
 Report Date: 4-2-92
 Report No. HWI 10603197

Summary:

The Primary Irritation Index = 0.00

Toxicity Category: IV

Classification: Guideline

Procedure (Deviations From 101-57): Animals acclimated to lab.

conditions for at least 7 days. One day before treatment, hair was clipped from backs and flanks of each animal (G and GF sites). 0.5 mg test material, moistened in

0.9% saline, placed on each animal's back. Treated sites

Results: covered with 2.5 cm² gauze patch secured with tape,

loosely over wrapped with Saran Wrap, & secured with

Elcastoplast tape for a semi occlusive dressing.

After exposure, dressings removed, sites washed & scored for irritation according to the Organs system; at 4 hrs, 24, 48 & 72 hrs post patch removal.

Results: No irritation observed; at any of the

Special Comments: scoring points

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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: Wetzeltop Welschman Report No: HWI 10603199
 Author(s): Steven Glaza
 Species: Guinea Pig
 Sex: 28 males Weight: 350-448g.
 Source: Hba (DH) SPF
 Test Material: Revital 50 WG granules
 Positive Control Material: dibutyltin benzene (DNCB)
 Quality Assurance (40 CFR §160.12): yes (P.A. & G. L. B.)
 Method: Buehler

Summary:

1. This product is not a dermal sensitizer.
2. Classification: Guideline

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 & dissolved water, at concentrations of 25%, 50% & 75% w/w in water; & animal receiving two different concentrations of the test mat.
Test concentrations applied to Hill top chamber patches, placed on two shaved sites, covered & strip of dental dam & cover wrapped & taped. 6 hr exposure. Sites observed for erythema & edema at 24 & 48 hrs after patch removal. Based on screening results, test material induced @ 0.2g dose (moistened with dissolved water) for both induction, and for challenge.

Induction - Day of test, hair removed from back of each animal & clipped. Test material (0.2g moistened & dissolved water), placed on Hill top Chamber adhesive pad, pad placed on test site,

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10 animals
on rear left flank. Patch covered E Dental Lam
and cut wrapped E Elastoplast Tape. 6 hour exposure,
followed by patch removal. Positive Control animals
(4), received 50.3% W/V 2,4 dinitrochlorobenzene
(DNCB) in 80% Ethanol/deionized water administered
in same manner as for test group (0.4 ml dose).
Animals received 3 applications, (once/week for
3 weeks).

Challenge Two weeks following last induction
application, a challenge of 0.25g of test
material dissolved in 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 irritation and edema
at 24 and 48 hours following irritation screening,
induction and challenge. Body weights recorded
at weekly intervals.

Results:

Test animals - following (test animals), is a group of 24 x 48 hour readings for the three induction applications: (each No. represents average for 1 of 10 test animals)

	0.1	The values at left represented
<u>Induction</u>	0.1	to show that the induction
	0.1	response for test animals
	0.1	was (Bushler Scoring), or
	0.3	achieved an acceptable degree
	0.2	of irritation, although the
	0.1	tester could have easily
	0.3	intended using a more
	0.0	concentrated solution.
	0.0	

Challenge (test material) - no reading, at both 24 and 48 hour readings.

Naive Control animals - 0.00 scoring.

Positive Control: Guinea pigs were sensitive.

Conclusion: Test material did not sensitize guinea pigs.