MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 2724-404

Zoecon RF-322 Ovicidal Pump Spray

FROM: William S. Woodrow WSW 7-8-91
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C) E 11/23/91

TO: P. Hutton / Linda Hollis (PM 18)
Insecticide - Rodenticide Branch
Registration Division (H75-05C)

APPLICANT: Zoecon Corp.
12200 Denton Dr.
Dallas, Texas 75234

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Methoprene	0.25%
Pyrethrins	0.18%
Piperonyl Butoxide, technical	0.36%
N-octyl bicycloheptene dicarboximide	0.60%
Inert Ingredient(s):	98.39%
Total	100.0%

BACKGROUND

The Zoecon Corp. submitted acute oral, acute dermal, primary eye and dermal, and dermal sensitization studies, to support registration of #2724-404; Zoecon RF-322 Ovicidal Pump Spray. MRID NOS. used were 418348-01 through 418348-05.

RECOMMENDATION

1) The acute toxicity studies submitted by Zoecon are acceptable to RSB/PRS.
2) The Registrant must submit an acute inhalation toxicity study, generated using Zoecon RF-322 ovicidal pump spray.
3) Current RF-322 acute toxicity profile:

acute oral		Tox Category	classification
acute oral	> 5100 mg/kg	IV	Guideline
acute dermal	> 20.1 g/kg	IV	Guideline
eye irrit.	redness (1/10 thru 10 d.) opacity through 7 days (1/10)	II	Guideline
skin irrit.	No irritation	IV	Guideline
dermal sen.	Did sensitize guinea p.		Guideline

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LABELING

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

2) Change the Precautionary Statements as follows:

"Causes substantial but temporary eye injury. Do not get in eyes or on clothing. Wear goggles, face shield, or safety glasses. Wash thoroughly with soap and water after handling. Remove clothing and wash before reuse."

3) The Statement of Practical treatment is acceptable.

4) The statement regarding sensitization is acceptable.

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

Product Manager: (18) 1-24-91
Reviewer: ~~M. Waller~~ Woodrow
MRID No.: 418348-01
Report Date: 7-3-91
Testing Facility: Bio/Dynamics, Inc.
Report No. 5900-90
Author(s): D. L. Blazey
Species: Rat - Sprague Dawley
Age: approx. 7 weeks
Observation Days (Post Exposure): (14); other ( )
Weight: 265-293, F 240-269g
Source: Charles River Labs., Kingston, N.Y.
Test Material: RE-322 (Ovitrol w/ thawt (R-11) Batch # 6013, liquid
Quality Assurance (40 CFR §160.12): yes (G.L.P.

Conclusion:

1. LD_{50} (mg/kg): Males = ——; Females = ——; Combined = ——
2. The estimated LD_{50} is > 5100 mg/kg
3. Tox. Category: IV. Classification: Guideline

Procedure (~~Deviations From §81-1~~): Animals equilibrated 13 days prior to test; animals fasted overnight, prior to test. 5M & 5F rats each were dosed @ 5.1g/kg by Gavage. Animals observed 1, 2, 4 hrs post-dosing, daily to 14 days. All animals subjected to necropsy. Bodyweights recorded days 0, 7 & 14.

Results:

Reported Mortality

DOSAGE (g./kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
5,100 mg/kg	1/5	0/5	1/10

Symptomology & Gross Necropsy Findings:

One male found dead at 21 hours, no other mortality. All survivors gained weight.

Clinical: ~~irregular gait, nasal, oral, anal discharge~~, hypopnea, hypoactivity, piloerection.

Necropsy: No gross abnormalities for survivors (1 found). Dead animal showed changes in the lungs and intestine.

DATA REVIEW FOR ACUT DERMAL TOXICITY TESTING (§ -2)

Product Manager: (18) 1-24-91 Reviewer: Woodrow
MRID No.: 418348-02 Report Date: 7-7-91
Testing Laboratory: Bio/Dynamics, Inc. Report No. 5901-90
Author(s): D. L. Blaszcak
Species: Rabbit, NZ white
Sex: 10M:10F Wt.: M 2.0-2.4, F 2.1-2.5 kg
Test Material: RF-322 - Ovitrol without R-11, liquid.
Quality Assurance (40 CFR §160.12): yes (Q.A. & G.L.P.)

Summary:

1. LD_{50} (mg/kg): Males = ; Females = ; Combined = ;
2. The estimated LD_{50} is > 20.1 g/kg ,
3. Tox. Category: IV . Classification: Guideline

Procedure (~~Deviations From §81-2~~): Animals acclimated 15 or 17 days" 24 hrs prior to dosing, hairs from animal backs removed by clipping (dorsal & lateral surfaces). Two groups of 5M & 5F rabbits each separately dosed with test material - spread directly to dorsal skin (10% of body surface). Gauze wrapped around the animal & gauze covered with pieces of impervious Elastoplast - Animals fitted with collars.

Results:

Reported Mortality

DOSAGE (g /kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
2.1 g / kg	0/5	0/5	0/10
20.1 g / kg	0/5	4/5	4/10

~~Symptomology & Gross Necropsy Findings:~~

24 hours skin contact. (Wrappings removed, sites wiped. Animals observed for toxic signs/mortality 2x daily to 14 days. Body wts recorded days 0, 7 & 14. All animals subjected to necropsy.

Clinical: 2/5 males in high dose group exhibited necrosis & dk tan eschar, which persisted. Day of dosing: irregular gait, tremors, hyperpnea, tearyes, hypoactivity.

Post mortem: Presence of dermal lesions.

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

Product Manager: (18) 1-24-91
MRID No.: 418348-03
Testing Laboratory: Bio/dynamics, inc.
Author(s): D. L. Blaszczak
Species: Rabbit, NZ white
Sex: 5M/4F Weight: not given
Source: Hazleton Res. Animals, PA
Dosage: 0.1ml
Test Material: RF-322 (control without R-11 & liquid)
Quality Assurance (40 CFR §160.12): yes (Q.A. & G.L.P.)

Reviewer: Woodrow
Report Date: 7-8-91
Report No. 5903-90

Summary:

Tox. Category: II Classification: Guideline

Procedure ~~(Deviation From §81-4)~~: 24hrs prior to dosing, all animal eyes examined for defects, using fluorescein. 0.1ml into-cul-de-sac into lower conjunctival sac, right eye of 5M and 4 female rabbits. Treated eyes held together gently post-dosing. 6 eyes remained unwashed; 3 treated eyes washed 1 minute w/ water.

Results: Eyes observed for irritation & scored according to what appears

Observations (number "positive"/number tested)

Unwashed eyes only →

	Hour	Days						
	1	1	2	3	4	7	10 ~~14~~	~~21~~
Cornea Opacity	6/6	6/6	4/6	3/6		1/6	0/10	
Iris	4/6	3/6	3/6	2/6		0/6	0/6	
Conjunctivae Redness	6/6	5/6	6/6	6/6		5/6	1/6	
Chemosis	6/6	6/6	3/6	2/6		0/6	0/6	
Discharge	6/6	6/6	6/6	2/6		0/6	0/6	

~~Comments~~: To be a modified Draize scale.

Results: Corneal opacity (1/6) through 7 days, absent by 10 days. Conjunctival redness (1/10) through Day 10.

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

1-24-91

Product Manager: (18)
MRID No.: 418348-04
Testing Laboratory: Bio/dynamics, Inc.
Author(s): D.L. Blaszcak
Species: Rabbit, N.Z. White
Age: At least 8 weeks.
Sex : 3M & 3F
Weight: not stated
Dosage: 0.5ml
Test Material: RF-322-Orvitrol Without R-11, liquid, Batch: 6013
Quality Assurance (40 CFR §160.12): yes (Q.A. & G.L.P.)

Reviewer. ~~R. Walker~~ Woodrow
Report Date: 7-8-91
Report No. 5902-90

Summary:

The Primary Irritation Index = P.I. Index = 0.00

Toxicity Category: IV

Classification: Guideline

Procedure ~~(Deviations From §81-5)~~: Animals acclimated at least 36 days. 24 hrs prior to test, backs of 3M & 3F rabbits clipped free of hair. 0.5ml test mat. applied beneath 1" sq. gauze on test site, secured c tape. Gauze then wrapped around animal, followed by tape, to provide semi-occlusive dressing. Animals

Results: restrained with fitted collars. 4 hour exposure. wrapping removed, sites wiped, scored for irritation; scale similar to Draize system @ 30-60 min, 24, 48 & 72 hours

Results: NO irritation (in any animal, at any scoring interval.

Special Comments:

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

Product Manager: (18) 1-24-91 Reviewer: Woodrow ~~Mr Waller~~
MRID No.: 418348-06 Report Date: 7-8-91
Testing Laboratory: Biodynamics, Inc. Report No. 5904-91
Author(s): D.L. Blaszcak
Species: Guinea Pig; Hartley
Sex: M/F Weight: M 314-347, F 300-337g
Source: Hazleton Res. Grounds, PA
Test Material: RF-322, - Outrol Without R-11
Positive Control Material: Dinitrochlorobenzene (DNCB)
Quality Assurance (40 CFR §160.12): yes (Q.A. #

Method: Modified Buehler - closed patch

Summary:
1. This product (is) / is not a dermal sensitizer.
2. Classification: Guideline

Procedure (~~Deviation From §81-6~~): Test Protocol:

Quoted:

Group	material tested	# animals	Concentration induction	challenge
1A	DNCB (+control)	5M&5F	0.3%	0.3%
~~1B~~ Results:	DNCB (irritation cont.	5M&5F	-	0.3%
11A	RF-322	20 (10M, 10F)	100%	100%
11B	RF-322 (irritation Cont.)	5M/5F	-	100%

Unquote

Animals acclimated 9 days. A range finding study was conducted "in order to select a slightly irritating concentration for topical induction". 100%, 50%, 25% & 10% evaluated. V/V test material in distilled water - using 0.3ml volumes in Hilltop Chambers. Chambers occluded with elastic adhesive; entire torso then wrapped - elastic adhesive - 6 hour skin contact. Materials removed, sites wiped, observations for irritation made at 24 & 48 hours. Undiluted used in main test for both induction and challenge.

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the positive control material:
a. induction: 0.05 g DNCB + 80% EtOH q.s. to 10 ml → 0.005 g/ml (0.5% W/V) mixture.
b. 0.03 g. DNCB + acetone q.s. to 10 ml sodium → 0.003 g/ml (0.3% W/V) mixture.

Test and control materials - 0.3 ml in Hill top chamber directly on test site (right side mid-line. Chamber covered by overlapping, impermeable plastic, secured by elastic bandage. 6 hour contact. (wrapping/chamber removed), site wiped. This procedure repeated once/week, to total 3 exposures.
Challenge: Fourteen days after last induction exposure, challenges made. The same test and control materials placed on the same sites used for induction. A second (virgin) site also challenged. 6 hours skin contact. Distilled water control also challenged.
Results: Desired evaluations made about 24 & 48 hours after 1st induction. Challenge also scored at 24 & 48 hrs after dosing:
Group 1A (DNCB) 0.3% conc. 24 hrs: 2/scores of 1.0, 7/@ 2.0, 1/@ 3.0 score. 48 hrs. 5 an. @ 1.0, 3 @ 2.0 and 2 animals @ 3.0. (Challenge score)

Group I B (DNCB irritation control) 0.3% conc. 3 animals ≈ 0.5 scores. 48 hrs, 3 animals ≈ 0.5,

Challenge:

Group II A RF-322 100% conc. 24 hours: 6 animals @ 0.5, 8 animals @ 1.0, and 1 animal @ 2.0 score:

Group II B RF-322 (irritation control) : No irritation scoring.

Conclusions: 1) The DNCB positive control material did sensitize guinea pigs

2) The RF-322 test material did sensitize guinea pigs, and therefore could be considered a dermal sensitizer.

613 N-octyl bicycloheptene dicarboximide
670 piperonyl butoxide
715 pyrethrins

Chem No. 028AAA methoprene File Last Updated _____ Current Date 7-8-91

#/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX. Cat.	CORE Grade/ Doc. No.
acute oral LD_{50}, Rat Bio/Dynamics, Inc. 5900-90 1-24-91	RF-322 control without R-11	418348-01	LD_{50} > 5100 mg/kg	IV	Guideline
acute dermal LD_{50}, rabbit Bio/dynamics, inc. # 5901-90 1-24-91	"	418348-02	LD_{50} > 20.1 g/kg	IV	Guideline
eye irritation, rabbit Biodynamics, Inc. # 5903-90 1-24-91	"	418348-03	Corneal opacity third day 1 (1/6), conjunctival redness third day 10 (1/6)	II	Guideline
skin irritation, rabbit Bio/dynamics, inc. # 5902-90 1-24-91	"	418348-04	No irritation. P.I. Index = 0.00	IV	Guideline
dermal sensitization, guinea pigs. Bio/dynamics. # 5904-90	"	418348-05	Test material did sensitize guinea pigs	-	Guidelines