

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 2724-404  
Zocon RF-322 Ovicidal Pump Spray

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

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

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

FORMULATION FROM LABEL:

<u>Active Ingredient(s):</u>	<u>% by wt.</u>
<u>Methoprene</u>	<u>0.25%</u>
<u>Permethrin</u>	<u>0.18%</u>
<u>Piperonyl Butoxide, technical</u>	<u>0.36%</u>
<u>N-octyl bicycloheptene dicarbamide</u>	<u>0.60%</u>
<u>Inert Ingredient(s):</u> . . . . .	<u>98.39%</u>
Total	100.0%

## BACKGROUND

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

## RECOMMENDATION

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

<u>acute oral</u>		<u>Tox Category</u>	<u>classification</u>
acute oral	> 5100 mg/kg	IV	guideline
acute dermal	> 20.1 g/kg	IV	guideline
eye irrit.	redness (via thulod.) opacity through 7 days (V <sub>10</sub> )	II	guideline
skin irrit.	No irritation	IV	guideline
dermal sen.	Did sensitize guinea p.		guideline

## LABELING

- 1) Change the signal word from CAUTION to read, "WARNING".
- 2) Change the Precautionary Statements as follows =

"Causes substantiated 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.

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

Product Manager: (18) 1-24-91 Reviewer: Wooten  
 MRID No.: 418348-01 Report Date: 7-3-91  
 Testing Facility: Bio/Dynamics, Inc. Report No. 5900-90  
 Author(s): D.L. Blaszyk  
 Species: Rat - Sprague Dawley  
 Age: Approx. 9 weeks Observation Days (Post Exposure): (14); other ( )  
 Weight: 265-263, F 240-260g  
 Source: Charles River Labs., Kingston, N.Y.  
 Test Material: RF-322 (Ovitrol without R-11) Batch # 6013, liquid  
 Quality Assurance (40 CFR §160.12): yes (Q.A. + G.L.P.)

Conclusion:

- LD50 (mg/kg): Males = \_\_\_\_\_; Females = \_\_\_\_\_; Combined = \_\_\_\_\_
- The estimated LD50 is > 5100 mg/kg
- Tox. Category: IV. Classification: Guideline

Procedure (~~Deviations From §81-1~~): Animals acclimated 13 days prior to test; animals fasted overnight, prior to test. 5M and 5F rats each were dosed @ 5.1g/kg by gavage. Animals observed 2, 4 hrs post-dosing, daily to 4 days. All animals subjected to necropsy. Body weights recorded daily. Reported Mortality 0/7 + 4.

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 animal found dead at 21 hours, no other mortality.  
All survivors gained weight.  
Clinical: irregular gait, nasal, oral, ocular discharge, hypopnea, hyperactivity, prostration.  
Necropsy: No gross abnormalities for survivors (found). Dead animal showed changes in the lungs and intestine.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (S -2)

Product Manager: (18) 1-24-91  
 MRID No.: 418348-02  
 Testing Laboratory: Bio/Dynamics, Inc.  
 Author(s): D.L. Blaszcak  
 Species: Rabbit, N2 white  
 Sex: 10M, 10F  
 Test Material: RF-322 - Ovitrol without R-11, liquid  
 Quality Assurance (40 CFR §160.12): yes (Q.A. & G.L.P.)

Reviewer: Woodhead  
 Report Date: 7-3-91  
 Report No. 5901-90

Summary:

- LD50 (mg/kg): Males = \_\_\_\_\_; Females = \_\_\_\_\_; Combined = \_\_\_\_\_;
- The estimated LD50 is > 20.1 g/kg
- Tox. Category: IV. Classification: Guideline

Procedure (~~Deviations From §81-27~~): Animals acclimated 15 or 17 days "24 hrs prior to dosing) hair 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 (60% of

Results: body surface). Group wrapped around the animal & group covered with pieces of impervious Elastoplast - Animals fitted with collars.  
 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. Wrapping removed, sites wiped. All animals observed for toxic signs mortality 2x daily to 4 days. Body weights recorded days 0, 7 & 14. All animals subjected to necropsy.

Clinical: 2/5 males in high dose group exhibited necrosis & a caudal eschar, which progressed. Day of dosing: irregular gait, tremors, hypopnea, red eyes, hypoactivity.

Post mortem: Presence of dermal lesions.

DATA REVIEW FOR A RTE 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 x 4f  
 Weight: not given  
 Source: Hazelton Res. Animals, PA  
 Dosage: 0.1ml  
 Test Material: RF-322 (control without R-11 liquid)  
 Quality Assurance (40 CFR §160.12): yes (P.A. & G.L.P.)

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

Summary:

Tox. Category: II Classification: Guideline

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

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

Observations

	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	10	21
Unwashed eyes only →								
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 Dosing schedule  
 Results: Corneal opacity (1/6) through 7 days, absent by 10 days. Conjunctival redness (1/10) through Day 10.

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

Product Manager: (18) 1-24-91 Reviewer: ~~Walter~~ Woodrow  
MRID No.: 418348-04 Report Date: 7-8-91  
Testing Laboratory: Bio/dynamics, Inc. Report No. 5902-90  
Author(s): O.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-Ovitol Without R-11, liquid, Batch: 6013  
Quality Assurance (40 CFR §160.12): yes (Q.A. & G.L.P.)

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, bodies of 3M & 3F rabbits clipped free of hair. 0.5ml test mat. applied beneath 1" sq. gauze on test site, secured w/ tape. Gauze then wrapped around animal, followed by tape, to provide semi-occlusive dressing. Animals

Results: restrained with fitted collars. 4 hour exposure. Wrappings 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:

DATA REVIEW FOR SKIN SENSITIZATION TESTING (§81-0)

Woodrow

Product Manager: (18) - 1-24-91

Reviewer: M. Waller

MRID No.: 418348-06

Report Date: 7-8-91

Testing Laboratory: Biodynamics, Inc.

Report No. 5904-90

Author(s): D. L. Blaszcak

Species: Guinea Pig; Hartley

Sex: = M & F

Weight: M 314-397, F 300-337g

Source: Hazelton Res. animals, PA

Test Material: RF-322, - control without R-11

Positive Control Material: Dimitro Chlorobenzene (DNCB)

Quality Assurance (40 CFR §160.12): yes (Q.A. #)

Method: Modified Burdick - closed patch

Summary:

- This product (is) is not a dermal sensitizer.
- Classification: Guinea

Procedure (Deviation From §81-6): Test protocol:

Results:

Group	Material Tested	# animals	Induction	Challenge
IA	DNCB (+control)	5M & 5F	0.0%	0.37%
IB	DNCB (irritation cont.)	5M & 5F	-	0.37%
IIA	RF-322	20 (10M, 10F)	100%	100%
IIB	RF-322	5M & 5F	-	100%

(Irritation Conts.)

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% evaluations; 1/4 test material in test water - using 0.3ml volumes in Hartley 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.



The positive control material:

a. induction: 0.05 g DNCB + 80% EtOH q.s. to 10ml  
 → 0.005 g/ml (0.5% w/v) mixture.

b. 0.03 g DNCB + acetone q.s. to 10ml volume →  
 0.003 g/ml (0.3% w/v) mixture.

Test and + control material - 0.3ml in Willtz  
 chamber directly on test site right side mid-  
 line. Chamber covered & over lapping, impermeable  
 plastic secured by elastic bandage. 6 hour contact.  
 Wrapping/chamber removed, site wiped. This  
 procedure repeated once/week, to total 3 exposures.  
Challenge: Facetion drop after last induction  
 exposure, challenges made. The same test and  
 control material placed on the same sites used  
 for induction. A second (higher) site also challenged.  
 6 hours skin contacts. Induction control also  
 challenged.

Results: Dermal evaluations made about 24 & 48  
 hours after 1st induction. Challenge also scored  
 at 24 & 48 hrs after dosing.

Group 1A (DNCB) 0.3% conc. 24hrs: 2/scores & 3.0,  
 7/2.0, 1/3.0 score. 48hrs. 5 animals 1.0, 3/2.0, and  
 2 animals 3.0. (Challenge score.)

Group 1B (DNCB, irritation control) 0.3% conc. 3 animals @ 0.5 doses, 48 hrs, 3 animals @ 0.5,

Challenge:

Group 11A RF-322 100% conc. 24 hours: 6 animals @ 0.5, 8 animals @ 1.0, and 1 animal @ 2.0 conc.

Group 11B RF-322 (irritation control) in Na irritation scoring.

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

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

613 N-octyl bicycloheptene dicarboximide  
 670 pipetonyl butoxide

715 pyrethroids

Chem No. 528AAA metheptene

File Last Updated \_\_\_\_\_

Current Date 2-8-91

Lab/Study #/Date	Material	EPA Accession No.	LD50, LO50, PIS, NOEL, LEL	Results	TOX. CONC. GRADE/ Cat. Doc. No.
acute oral LD50, Rat Bio/dynamics, Inc. # 5900-90 1-24-91	RF-322 control without R-11	418348 -01	LD50 > 5100 mg/kg		IV Guide- line
acute dermal LD50, rabbit Bio/dynamics, Inc. # 5901-90 1-24-91	"	418348 -02	LD50 > 20.1 g/kg		IV Guide- line
eye irritation, rabbit Bio/dynamics, Inc. # 5903-90 1-24-91	"	418348 -03	Corneal opacity third day → (1/6), conjunctival tenderness third day (0 1/6)		II Guide- line
skin irritation, rabbits Bio/dynamics, Inc. # 5902-90 1-24-91	"	418348 -04	No irritation. P.I. Irritation = 0.00		IV Guide- line
inhalation sensitization, guinea pig. Bio/dynamics. # 5904-90	"	418348 -05	Test material <u>did</u> sensitize guinea pigs		- Guide- line