MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 27244 - 404
Zoscon RF-322 Oxicidal Pump Spray

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

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

APPLICANT: Zoscon Corp.
12700 Denon Dr.
Dallas, Texas 75234

FORMULATION FROM LABEL:

Active Ingredient(s):

- Methoprene 0.25%
- Butothion 0.18%
- Propoxyl Butoxide, technical 0.36%
- N-Isopropyl bicycloheptene dicarboximide 0.60%

Inert Ingredient(s): .................................................

Total 98.79% 100.0%
BACKGROUND

The Zocon Corp. submitted acute oral, acute dermal, primary eye and dermal and dermal sensitization studies to support registration of *2,3,5-*trichloro-4-carboxybenzoic acid (2,3,5-TCA) in Zocon RF-322 Ovicideal Pump Spray. MRVP NOS. used were 418-348-01 through 418-348-05.

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 Ovicideal pump spray.
3) Current RF-322 acute toxicity profile:

<table>
<thead>
<tr>
<th>Route</th>
<th>Toxicity</th>
<th>Toxic Category</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>5100 mg/kg</td>
<td>IV</td>
<td>Guideline</td>
</tr>
<tr>
<td>Dermal</td>
<td>20.1 g/kg</td>
<td>IV</td>
<td>Guideline</td>
</tr>
<tr>
<td>Eye</td>
<td>Redness (via instillation)</td>
<td>II</td>
<td>Guideline</td>
</tr>
<tr>
<td>Skin irritation</td>
<td>No irritation</td>
<td>IV</td>
<td>Guideline</td>
</tr>
<tr>
<td>Dermal sensitization</td>
<td>Did not sensitize guinea pigs</td>
<td></td>
<td>Guideline</td>
</tr>
</tbody>
</table>
LABELING

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

Product Manager: (12) 1-24-91
MRID No.: 413348-01
Author(s): D.L. Blaine
Species: Rat, Sprague-Dawley
Age: 4-6 weeks
Source: Charles River Labs, Kingston, N.Y.
Test Material: AE-322 (Control without (R) Batch # 6013, Liquid

Conclusion:
1. LD50 (mg/kg): Males = ; Combined = ; Females =
2. The estimated LD50 is > 5000 mg/kg
3. Tox. Category: IV. Classification: Guideline

Procedure (Deviation From §81-1): Mammals equilibrated 13 days prior
to test. Mammals fasted overnight prior to test. 5,000 mg/kg 2/6 each
were dosed by gastric intubation. Mammals observed 24 hrs post-

Results: dose, daily to 4 days. All animals subjected to necropy. Body weights recorded daily 07/4.

<table>
<thead>
<tr>
<th>DOSAGE (g/kg)</th>
<th>(NUMBER KILLED/NUMBER TESTED)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5,000 mg/kg</td>
<td>Males 0 0 0 0 0</td>
</tr>
</tbody>
</table>

Symptomology & Gross Necropsy Findings:

All animals found dead at 21 hours, no other mortality.

Gross: no gross abnormalities noted. Deed
animal showed changes in the lungs and intestines.
DATA REVIEW FOR ACUT DERMA LTOXICITY TESTING (§ -2)

Product Manager: [18] 1-24-91
Reviewer: [Woodward]
MRID No.: 418-348-02
MRID No.: 5201-98
Testing Laboratory: Bionynamics, Inc.
Report Date: 7-3-91
Author(s): D. L. Blaszak
Species: Rabbit, NZ white
Sex: MALE
Test Material: PF-322 - Control without R-11, liquid

Summary:

1. LD50 (mg/kg): Males = ; Combined = 
2. The estimated LD50 is > 200.0 mg/kg
3. Tox. Category: IV. Classification: Guideline

Procedure (Deviations From §81-2): Animals acclimated 15-21 days 24 hrs prior to dosing, hair from animal back removed by clipping (dorsal + lateral surfaces). Two groups of 5 males quickly washed separately dosed with test material spread directly to exposed skin (60%)

Results: Body surface) groups wrapped around the animal 3 groups covered with 3M/5P tape. Blotter Blotter Blotter. Animals filled with colloidal

<table>
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<tr>
<th>DOSAGE (g/kg)</th>
<th>(NUMBER KILLED/NUMBER TESTED)</th>
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<tbody>
<tr>
<td></td>
<td>Males</td>
</tr>
<tr>
<td>2.1 g/kg</td>
<td>0/5</td>
</tr>
<tr>
<td>20.1 g/kg</td>
<td>0/5</td>
</tr>
</tbody>
</table>

Symptomology & Gross Necropsy Findings:

24 hours skin contact. Wrapping, delayed, sites wiped Animals examined for topic signs of mortality 2x daily for 14 days.

Body weight gained days 0, 7, 14. All animals subjected to necropsy.

Clinical: 2/5 males in high dose group exhibited necrosis of test eschar, which persisted. Day of dosing: irregular gait, tremors, hypopnea, maldag, hyperactivity.

Post mortem: Presence of dermal lesions.
DATA REVIEW FOR A.JTE EYE IRRITATION TESTING (81-4)

Product Manager: (18) 1-24-91  Reviewer: Woodrow  
MRID No.: 418349-02  Report Date: 7-8-91  
Testing Laboratory: Biodynamics, Inc.  Report No.: 5903-90  
Author(s): D.L. Bleszczak  
Species: Rabbit, N2 white  
Sex: 5M/4F  Weight: Not given  
Dosage: 0.1ml  
Test Material: RF-322 (Control without R-11 Liquid)  

Summary:  
Tox. Category: I  Classification: Guideline  
Procedure (Deviation from 81-4): 24 hrs prior to dosing, all animal eyes examined for defects, seeing fluorescein. 0.1ml introduced into lower conjunctival sac, right eye of 5 male female rabbits. Treated eyes held together with post-closure. 6 eyes examined weekly. 3 treated area washed untreated control.  
Results:  
Eyes observed for irritation + scored according to what appears  

| Observations | Number "positive"/Number tested | Days  
|--------------|----------------------------------|------  
| Unwashed eyes Only | Hour | Cornea | 1 | 1 | 2 | 3 | 4 | 7 | 10 | 21 |  
| Opacity | % | % | % | % | % | % | % | % | % |  
| Iris | % | % | % | % | % | % | % | % | % |  
| Conjunctivae | % | % | % | % | % | % | % | % | % |  
| Redness | % | % | % | % | % | % | % | % | % |  
| Chemosis | % | % | % | % | % | % | % | % | % |  
| Discharge | % | % | % | % | % | % | % | % | % |  

Comments:  
A modified Draize scale.  
Results: Cornea opacity (1/10) through 7 days; area 10 days. Conjunctival redness (3/10) through day 10.
DATA REVIEW FOR SKIN IRRITATION TESTING ($81-5$)

Product Manager: (18) 1-24-91  
MRID No.: 418348-04  
Reviewer:  
Report Date: 7-8-91  
Report No.: 5902-90  

Testing Laboratory: Bio/Dynamics, Inc.  
Author(s): O.L. Blaszkack  
Species: Rabbit, NZ White  
Age: At least 8 weeks  
Sex: MALE  
Weight: not stated  
Dosage: 0.5 ml  
Test Material: RF-372-Orvitsol Without R-111 Liquid Batch 6013  

Summary:

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

Toxicity Category: 1V

Classification: Guideline

Procedure (Deviations From $81-5$): Animals acclimated at least 36 days, 24 hrs prior to test, bedding 3mm-38 tablets closed  
free of hair. 0.5ml test material beneath its gauge on test  
site, secured in tape. Group then wrapped around animal  
followed by tape to provide semi-occluded dressing. Animal  
restrained with fitted collars. 4 hour exposure.  
Wrapping removed, site wiped, scored for irritation; scale similar  
to Dermal system @ 30-60 min. 24, 48, 72 hours  
Result: No irritation (in any animal) at any  
scoring interval.

Special Comments:
DATA REVIEW FOR SKIN SENSITIZATION TESTING ($81-6)

Product Manager: Woodrow 1.24.91
MRID No.: 418344-06
Testing Laboratory: Biodynamics, Inc.
Author(s): L. L. Bierly, C.A.
Species: Guinea Pig, Hartley
Sex: Female, Res. Animals, PA
Weight: 314-337, P360-3379
Source: Hartley Res. Animals, PA
Test Material: RF-322, Control without P-11
Positive Control Material: Dimethylchlorobenzene (DMCB)
Quality Assurance (40 CFR §160.12): yes (QA)
Method: Modified Buehler - closed patch

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

Procedure (Deviation from §81-6): Test Method:

Quoted:

Concentration

Group Material tested Animal Induction Challenge

A DMCB (+ control) 5/0.025F 0.30 0.37

Results:

DMCB (irritation control 5/0.025F) - 0.37

1A RF-322 25 (loco, 10E) 100% 100%

1B RF-322 5 w/1F - 100%

(irritation control)

Quoted:

Animals acclimated 9 days. A 4 week study was conducted "in order to select a slightly irritating concentration for typical induction." 100%, 50%, 25%, 10% evaluated. IV test material in test water using 0.3ml volume in Hilltop Chambers. Chambers included with plastic adhesive; extra tape then wrapped around plastic adhesives. Grew skin contact. Material removed after 48 hours. Determination for irritant marked 24h.

Undetected used in main test for both induction and challenge.
The positive control material:
- DMSO 0.05 g
- 80% ethanol 95 g to 10 ml
  → 0.005 g/ml (0.5% W/V) mixture
- 0.03 g DMSO + acetone 95 g to 10 ml volume
  → 0.003 g/ml (0.3% W/V) mixture

Test and control materials - 0.3 ml in Hilltop chamber directly on test site left side medial.
- Chamber covered with Xero haptic, impermeable plastic secured by elastic bandage. Show contact.
- Wrapping/ chamber removed, inspected.

Procedure repeated once/week, to 3 applications.

Challenge: Fourteen days after first induction.

For positive, challenges made: The same test, 0.3 ml test material placed on the same sites as:
- For induction. A hind (ringer) site also challenged.
- Mouse skin contact - irritating constituent also challenged.

Results: Dermal reactions made about 24-48 hours after 1 st induction. Challenge also scored.

Group 1A (DNCB) 0.3% conc. 24/48 h score 4.30,
4/0.20, 4/3.0 score 48/48, 4/2.0, 1/0.3. 3/2.0 and
2/0.2. 1/3.0. (Challenge score)
Group 1B (DNCCB irritation control) 0.37 cmx 3 cm cube 0.5% p.a. 0.05 hr x 3 times 70 minutes 20.5.

Challenging:
Group 1A RF-322 100% cmx 2.4 cm cube 0.5% 8 cm x 8 cm x 8 cm at 10 cm and lateral 0.7 cm same.
Group 1B RF-322 (irritation control) 3.2 cm

Irritation scoring.

Conclusions:
1) The DNCCB patch control material did not irritate equal size.
2) The RF-322 test material did irritate green test, and therefore could be considered a dermal sensitizer.
<table>
<thead>
<tr>
<th>Material</th>
<th>Accession No.</th>
<th>LD_{50}, LC_{50}, PIS, NOEL, LEL</th>
<th>TOX. CONC. Grade/ Cat, Doc. No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>cate oral LD_{50}, Rat</td>
<td>RF-322 control without R-11</td>
<td>LD_{50} &gt; 5100 mg/kg</td>
<td>1U Guideline</td>
</tr>
<tr>
<td>cate dermal LD_{50}, rabbit</td>
<td>418348-01</td>
<td>LD_{50} &gt; 20.1 g/kg</td>
<td>1U Guideline</td>
</tr>
<tr>
<td>eye irritation, rabbit</td>
<td>418348-02</td>
<td>Corneal opacity third day (10%) (1/6), conjunctival reddness third day 10(1/6)</td>
<td>1U Guideline</td>
</tr>
<tr>
<td>skin irritation, rabbit</td>
<td>418348-03</td>
<td>No irritation, Rat</td>
<td>1U Guideline</td>
</tr>
<tr>
<td>formal sensitization, guinea pigs</td>
<td>418348-04</td>
<td>Test material did not affect growth</td>
<td>1U Guideline</td>
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