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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: FPA Reg. No./File Symbol 21137-4

Funginex Emulsifiable Concentrate

FROM: Sheila A. Moats, Ph.D.  
Precautionary Review Section  
Registration Support Branch  
Registration Division (P75-05C)

AM 11/16/90  
E 11/26/90

TO: Lewis/Stone (PM 21)  
Fungicide-Herbicide Branch  
Registration Division (P75-05C)

APPLICANT: EM Industries  
Plant Protection Division  
5 Skyline Drive  
Hawthorne, New York 10532

FORMULATION FROM LABEL:

| Active Ingredient(s):          | % by wt.    |
|--------------------------------|-------------|
| 84.14 <u>Triforine</u>         | <u>18.2</u> |
| _____                          | _____       |
| _____                          | _____       |
| _____                          | _____       |
| Inert Ingredient(s): . . . . . | <u>81.8</u> |
| Total                          | 100.0%      |

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## Background

E M Industries submitted acute oral, dermal, inhalation, primary eye, + skin irritation, + dermal sensitization studies to amend <sup>the</sup> formula of Triforine by omitting an inert chemical [REDACTED] from the fungicide formula.

The MRLD Nos used for the re-registration of [REDACTED] formulation of Triforine - Euginex Emulsifiable Concentrate were: 415-710-Q3-C5.

## Recommendations.

1. The acute toxicity studies submitted by E M Industries are acceptable to ASB/PRS.

2. No further acute toxicity tests are required.

## Labeling.

1. The "DANGER" signal word is acceptable.

2. The Precautionary Statements must be stated as follows:

"Corrosive, causes irreversible eye damage. Do not get in eyes or on skin or clothing. Wear goggles or face shields. Harmful if swallowed, inhaled or absorbed through skin. Wash thoroughly with soap + water after handling."

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Remove contaminated clothing + wash before re use.

### 3. The Statement of Practical Treatment

"If in Eyes" and "If on Skin" are acceptable.

"If swallowed" add "or Call Poison Control Center" to the last sentence after "Get medical attention"

"If on Skin" add Get medical attention.

"If Inhaled" insert after the first sentence "If not breathing <sup>GIVE</sup> ~~artificial~~ artificial respiration, preferably mouth to mouth. E

4. The product <sup>MUST BE</sup> ~~is~~ considered for restricted use classification since corneal involvement persisted through Day-31  
40 C.F.R. part 152.70. PM TEAM SHOULD DECIDE IF ALTERNATIVE LABELING LANGUAGE IS SUFFICIENT TO OFFSET THE EYE HAZARD AND THE NEED FOR RESTRICTED USE CLASSIFICATION.

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

Product Manager: (21) Reviewer: S. Moats  
 MRID No.: 415710-03 Report Date: 11/15/90  
 Testing Facility: RCC Research + Consulting Co. Switzerland Report No. 271585  
 Author(s): Ulman, L. et al.  
 Species: Wistar - Rats  
 Age: 9 - 11 weeks Observation Days (Post  
 Weight: 170 - 230 g. Exposure): (14); other ( )  
 Source: BRL - Biological Res. Lab Ltd Wolfersstrasse 4  
 Test Material: Funginex - Emulsifiable Concentrate  
 Quality Assurance (43 CFR §160.12): Adequate

## Conclusion:

- LD<sub>50</sub> (mg/kg): Males = 3868 mg/kg; Females = 3017 mg/kg; Combined = 3487 mg/kg
- The estimated LD<sub>50</sub> is
- Tox. Category: III. Classification: Guidelines

Procedure (Deviations From §81-1): Rats of both sexes were dosed by oral gavage at varying dose levels. The animals were observed for toxicity & mortality 4 times during day - 1, & daily thereafter until Day - 15.

## Results:

## Reported Mortality

| DOSAGE (mg/kg) | (NUMBER KILLED/NUMBER TESTED) |         |          |
|----------------|-------------------------------|---------|----------|
|                | Males                         | Females | Combined |
| 2000           | 0/5                           | 0/5     | 0/10     |
| 3500           | 0/5                           | 4/5     | 4/5      |
| 5000           | 5/5                           | 5/5     | 10/10    |
|                |                               |         |          |
|                |                               |         |          |

## Symptomology &amp; Gross Necropsy Findings:

at dose level 3500 mg/kg BW  
Clinical signs included dyspnea, unco-ordinated movements etc.

Necropsy findings were unremarkable.

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## DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3)

Product Manager: (21)  
 MRID No.: 415 710-05  
 Testing Laboratory: RCC Research + Consult  
 Author(s): Duchosal, F et al  
 Species: Wistar Rats  
 Sex: 2♂ + 9♀  
 Source: BRL - Biological Res. Labs Ltd. - Switzerland  
 Test Material: Funginex - Emulsifiable Concentrate  
 Quality Assurance (40 CFR §160.12): Adequate  
 Reviewer: S. Moats  
 Report Date: 11/15/90  
 Report No.: 258300  
 Lab. Switzerland

## Summary:

1. LC<sub>50</sub> (mg/kg): Males = 3.22 mg/L \* (2.93-3.53) Females = 4.69 mg/L \* (4.42-4.98) Combined = 3.99 \* (3.66 - 4.34)  
 2. The estimated LC<sub>50</sub> is  
 3. Mean Concentration:  
 4. Tox. Category: III. Classification: Guidelines

5♂s + 5♀s per dose gp were

Procedure (Deviations From §81-2): subjected to nose-only inhalation exposure for a 4-hr. pd. The animals were placed individually in tubes located radially around the exposure chamber. The stream of test article reaches the animal's nose thru port-holes situated at diff. levels around the axis of the exposure chamber. Each level has 8 ports allowing close observation of the animals. System also insures uniform distribution of the test article & provides a constant stream of fresh air. Test article was generated by means of a syringe pump feeding into a nebulizer. Next it was diluted with air to attain the req'd. concentration for the study & drawn into the exposure chamber. Analytical determinations were made by chromatography (HPLC) Temp. & humidity were recorded regularly. Cascade impactor was used for particle sizing.

| Exposure Concentration<br>(mg/L) | (NUMBER KILLED/NUMBER TESTED) |         |          |
|----------------------------------|-------------------------------|---------|----------|
|                                  | Males                         | Females | Combined |
| 1.35                             | 0/5                           | 0/5     | 0/10     |
| 3.24                             | 2/5                           | 0/5     | 2/5      |
| 7.54                             | 4/5                           | 3/5     | 7/10     |
|                                  |                               |         |          |
|                                  |                               |         |          |

## Symptomology &amp; Gross Necropsy Findings:

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Clinical signs included hunched posture, labored respiration, muffled fur + unco-ordinated movements

Gross necropsy findings revealed discoloration, + red staining of lungs in a few animals

| Concentration | Survival % | particle size |
|---------------|------------|---------------|
| 1.35 mg/L     | 82.6       | 3 µm or less  |
| 3.24 mg/L     | 88.8       | " "           |
| 7.54 mg/L     | 83.7       | " "           |

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

Product Manager: (21)  
 MRID No.: 415710-06  
 Testing Laboratory: RCC Research & Consulting Lab.  
 Author(s): Ullman, L. et al.  
 Species: New Zealand White Rabbits  
 Sex: 2♂ + 9♀ Weight: 2.5 - 3.0 kg  
 Source: BRL Biological Research Labs Ltd. Wolfenstrasse 4  
 Dosage: 0.1 ml  
 Test Material: Funginex - Emulsifiable concentrate  
 Quality Assurance (40 CFR §160.12): Adequate

## Summary:

Tox. Category: I Classification: Guidelines

Procedure (Deviation From §81-4): 0.1 ml of the test material was instilled into the conjunctival sac of the left eye of each of six rabbits. The right eye served as the untreated control. The eyes were examined at 1, 24, 48 + 72 hrs + 7, 14 + 21 days after treatment.

## Results:

|                      | Observations<br>(number "positive"/number tested) |      |     |     |     |     |     |  |
|----------------------|---------------------------------------------------|------|-----|-----|-----|-----|-----|--|
|                      | Hour                                              | Days |     |     |     |     |     |  |
|                      | 1                                                 | 1    | 2   | 3   | 7   | 14  | 21  |  |
| Cornea Opacity       | 6/6                                               | 6/6  | 6/6 | 6/6 | 6/6 | 4/6 | 3/6 |  |
| Iris                 | 0/6                                               | 0/6  | 1/6 | 0/6 | 0/6 | 0/6 | 0/6 |  |
| Conjunctivae Redness | 6/6                                               | 4/6  | 6/6 | 6/6 | 3/6 | 0/6 | 0/6 |  |
| Chemosis             | 6/6                                               | 4/6  | 3/6 | 2/6 | 0/6 | 0/6 | 0/6 |  |
| Discharge            | 6/6                                               | 6/6  | 6/6 | 6/6 | 2/6 | 0/6 | 0/6 |  |
|                      |                                                   |      |     |     |     |     |     |  |
|                      |                                                   |      |     |     |     |     |     |  |
|                      |                                                   |      |     |     |     |     |     |  |

Comments: Corneal opacity present through Day 21.  
 Corrosive.

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

Product Manager: (21)  
 MRID No.: 415-710-07  
 Testing Laboratory: RCC Research &  
 Author(s): Ullman L. et al Consulting Lab.  
 Species: New Zealand White Rabbits  
 Age: 14-15 weeks  
 Sex: ♂s + ♀s  
 Weight: 2.4 - 2.9 kg  
 Dosage: 0.5 ml  
 Test Material: Funginex - Emulsifiable Concentrate  
 Quality Assurance (40 CFR §160.12): Adequate

Reviewer: S. Moats  
 Report Date: 11/15/90  
 Report No. 258276

## Summary:

The Primary Irritation Index = 3.25

Toxicity Category: II

Classification: Guidelines

Procedure (Deviations From §81-5): Prior to treatment the animal was shaved from an area approx. 10 x 10 cm<sup>2</sup>. A dose of 0.5 ml of the test material was applied to the intact skin of the shaved area. The site was next covered with gauze + semi-occlusive dressing + held in place with an elastic bandage. After a 4-hr exposure period the dressing was removed + the site cleansed of residues. Fixing was done at 1, 24, 48 + 72 hrs + 7 + 14 days.

## Results:

The test material is a moderate irritant.

## Special Comments:

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

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Product Manager: (21)  
 MRID No.: 415710-08  
 Testing Laboratory: RCC-Research + Consulting Lab.  
 Author(s): Ullman, L. et al.  
 Species: SPF-quality Guinea Pigs - Himalayan Spotted  
 Sex: females Weight: 373-489g  
 Source: Biological Research Labs. Ltd. Wolfershoose - 4  
 Test Material: Funginex - Emulsifiable Concentrate  
 Positive Control Material: Ethanol in saline  
 Quality Assurance (40 CFR §160.12): Adequate  
 Method: Maximisation Test

Reviewer: S. Moats  
 Report Date: 5/28/90  
 Report No. 258298

Summary:

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

Procedure (Deviation From §81-6): 10 Gs were used for the control Gp. Highest non-irritating dose for the 1st challenge was 20% concentration + 10% + 20% concentrations were used for the 2nd challenge applications.  
 Induction: - Intradermal injections. 3 pairs of injections were made in a previously clipped area of the scapular (E & B) - as follows:

Test Gp: 1) Freund's complete adjuvant, 50:50 in distilled H<sub>2</sub>O.  
 2) The test article diluted with ethanol + saline 3) The test article emulsified in Freund's adjuvant + the vehicle.

Control Gp: 1, Freund's complete adjuvant in distilled H<sub>2</sub>O  
 2. Vehicle used in test gp. (ethanol in saline) 3. Freund's adjuvant 50:50 with distilled water.

Epidermal applications: A week after the injections a 6 x 8 cm<sup>2</sup> area of the scapular was clipped again + a 2 x 4 cm<sup>2</sup> filter paper saturated with test article in ethanol-saline was placed on the injection sites. The patch was covered with al. foil + secured by elastic plaster wrapped around the animals trunk + held in place with tape for 48 hrs. The same procedure was used for the control Gp. The animals were scored for irritation at 24 + 48 hrs after removal of the patches + wraps.

Challenge: 2 weeks after the epidermal induction the animals were challenged at clipped sites on the left + right flanks of each animal using epidermal applications. The wrappings were removed after a 24-hr exposure period. The sites were examined at 24 + 48 hrs after patch removal. The same procedure was used for the controls.  
 Rechallenge: Two weeks after the challenge a 2nd challenge was performed. The control gp. was re-challenged with the vehicle only.

Results: - The test article is not a sensitizer.

No toxic symptoms were seen in the animals for both the control + test gps.

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

Product Manager: (21)  
 MRID No.: 415710-04  
 Testing Laboratory: R.C.C. Research & Consulting  
 Author(s): Ullmann, I. et al.  
 Species: Wistar - Rat  
 Sex: ♂s + ♀s  
 Wt.: 194 - 282 g.  
 Test Material: Funginex - Emulsifiable Concentrate  
 Quality Assurance (40 CFR §160.12):  
 Reviewer: S. Moats  
 Report Date: 11/15/90  
 Report No. 258-265  
 Lab. Switzerland.

Summary:

- LD50 (mg/kg): Males = ; Females = ; Combined = 22000 mg/kg.
- The estimated LD50 is
- Tox. Category: III. Classification: Guidelines

Procedure (Deviations From §81-2): 5♂s + 5♀s were treated with the test material, 10% of the total body surface was clipped of fur prior to dosing. The test article was applied with a syringe + semioccluded with a dressing + held in place with elastic bandage. After 24 hrs. exposure, the wraps were removed + the sites cleansed of residue. Observers for toxicity + mortality were made 4 times during Day-1, + once daily thereafter until Day-15.

| DOSAGE (mg/kg) | Reported Mortality            |         |          |
|----------------|-------------------------------|---------|----------|
|                | (NUMBER KILLED/NUMBER TESTED) |         |          |
|                | Males                         | Females | Combined |
| 2000           | 0/5                           | 0/5     | 0/10     |
|                |                               |         |          |
|                |                               |         |          |
|                |                               |         |          |
|                |                               |         |          |

Symptomology & Gross Necropsy Findings:

Clinical signs were unremarkable.  
 Necropsy findings showed no abnormalities.

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