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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 21137-4
Funginex. Emulsifiable Concentrate

FROM: Sheila A. Moats, Ph.D.
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C)

11/16/90
E 11/26/90

TO: Lewis/Stone (PM 21)
Fungicide-Herbicide Branch
Registration Division (H75-05C)

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

FORMULATION FROM LABEL:

	Active Ingredient(s):	% by wt.
84-H17	Triforine	18.2
	Inert Ingredient(s):	81.8
	Total	100.0

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Background

EM Industries submitted acute oral, dermal, inhalation, primary eye, + skin irritation, + dermal sensitization studies to amend the formula of Triforine by omitting an inert chemical [redacted] from the fungicide formula.

The MRID Nos used for the re-registration of [redacted] formulation of Triforine - Funginex Emulsifiable Concentrate were: 41S-T10-03-05.

Recommendations.

1. The acute toxicity studies submitted by EM Industries are acceptable to RSB/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 shield. 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 ~~get~~ GIVE artificial respiration, preferably mouth to mouth. E

4. The product MUST BE considered for restricted use classification since corneal involvement persisted through Day-21 40 C.F.R. part 152.170. PM TEAM SHOULD DECIDE IF ALTERNATIVE LABELING LANGUAGE IS SUFFICIENT TO OFF SET 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): Ullman, L. et al
Species: Wistar - Rats
Age: 9 - 11 weeks. Observation Days (Post Exposure): (14); other ( )
Weight: 170 - 230 g.
Source: BRL - Biological Res. Labs Ltd Wolferstrasse 4
Test Material: Fungi nex - Emulsifiable concentrate
Quality Assurance (40 CFR §160.12): Adequate.

Conclusion:

1. LD_{50} (mg/kg): Males = 3868 mg/kg ; Females = 3017 mg/kg. ; Combined = 3487 mg/kg
2. The estimated LD_{50} is
3. 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 & Gross Necropsy Findings:

Clinical signs, at dose level 3500 mg/kg BW 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) Reviewer: S. Moats
MRID No.: 415 710-05 Report Date: 11/15/90
Testing Laboratory: R.C.C. Research + Consulting Ltd. Report No. 258300
Author(s): Duchosal, F. et al. Switzerland.
Species: Wistar Rats
Sex: 2♂ + 2♀ Weight: 180.4 — 199.6 gms.
Source: BRL - Biological Res. Labs Ltd. Switzerland
Test Material: Funginex - Emulsifiable Concentrate
Quality Assurance (40 CFR §160.12): Adequate.

Summary: * confidence limits

1. LC_{50} (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_{50} is
3. Mean Concentration:
4. Tox. Category: III. Classification: Guidelines

Procedure (Deviations From §81-2): 5♂s + 5♀s per dosage gp were 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 ensures 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 means of high pressure liquid chromatography (HPLC) Temp. & humidity were monitored regularly. Cascade Impactor was used for particle sizing.

Reported Mortality

Exposure Concentration (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 & Gross Necropsy Findings:

Clinical signs included hunched posture, labored respiration, ruffled fur + uncoordinated movements. Gross necropsy findings revealed discoloration + red staining of lungs in a few animals.

Concentration	Gram %	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: 3's + 9's. Weight: 2.5 - 3.0 kg.
Source: BRL Biological Research Labs Ltd. Wolferstrasse 4.
Dosage: 0.1 ml.
Test Material: Funginex - Emulsifiable concentrate
Quality Assurance (40 CFR §160.12): Adequate

Reviewer: S. Moats
Report Date: 11/15/90
Report No. 271596

Summary:

Tox. Category: I Classification: Guideline.

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 (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	/6	0/6	0/6	0/6	0/6	
Conjunctivae Redness	6/6	6/6	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.

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

Product Manager: (21)
MRID No.: 415710-07
Testing Laboratory: RCC Research + Consulting Lab.
Author(s): Ullman, L. et al
Species: New Zealand White - Rabbits
Age: 14-15 weeks
Sex: ♂s + ♀s
Weight: 2.4-2.9 kg
Dosage: 0.5 ml
Test Material: Fenginex - 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: III

Classification: Guidelines

Procedure (Deviations From §81-5): Prior to treatment fur was shaved from an area approx. 10 x 10 cm². 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 pd, the dressing was removed + the site cleansed of residues. Scoring 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)

Product Manager: (21)
Reviewer: S. Moats
MRID No.: 415710-08
Report Date: 5/28/90
Testing Laboratory: RCC-Research + Consulting Lab.
Report No. 258298
Author(s): Ullman, L. et al.
Species: SPF-quality Guinea Pigs - Himalayan Spotted
Sex: females
Weight: 373-489 g.
Source: Biological Research Labs. Ltd Wolferstrasse-4.
Test Material: Funginex - Emulsifiable Concentrate
Positive Control Material: Ethanol in saline.
Quality Assurance (40 CFR §160.12): Adequate

Method: Maximixation Test

Summary:

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

Procedure (Deviation From §81-6): 10 g's were used for the control Gp. 20 g's were used for the test Gp. Highest non-irritating dose for the 1st challange was: 20% concentration + 10% + 20% concentrations were used for the 2nd challenge applications.

Induction: - Intradermal injecns. 3 pairs of injecns were made in a previously clipped area of the scapular (6 x 8 cm²) - as follows:

Test Gp: - 1) Freund's complete adjuvant 50:50 in distilled H_2O. 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_2O 2. Vehicle used in test gp. (ethanol in saline) 3. Freund's adjuvant 50:50 with distilled water.

Epidermal applications: A week after the injecns a 6 x 8 cm² area of the scapular was clipped again + a 2 x 4 cm² filter paper saturated with test article in ethanol/saline was placed on the injecn 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 applicns. The wrappings were removed after a 24-hr exposure pd. 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 on the animals for both the contrs + 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 Lab. Switzerland.
Author(s): Ullman, L. 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: 11/12/90
Report No. 25 & 265

Summary:

1. LD_{50} (mg/kg): Males = ; Females = ; Combined = >2000 mg/kg;
2. The estimated LD_{50} is
3. 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 + semi-occluded with a dressing + held in place with elastic bandage. After 24 hrs. exposure the wraps were removed + the sites cleansed of residues. Observers for toxicity + mortality were made 4 times during Day-1, + once 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

Symptomology & Gross Necropsy Findings:

Clinical signs were unremarkable.

Necropsy findings showed no abnormalities.

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