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

005281

JUL 9 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA File Symbol 53871-E - Stirrup-M; Pheromone Used
as a Mite Attractant in Pesticide Formulations.
Accession No. 261309

Caswell No. 801E

FROM: William S. Woodrow, Ph.D. *WSW 7-1-86*
Section VII, Toxicology Branch
Hazard Evaluation Division (TS-769C)

TO: Willie Nelson, PM Team 17
Insecticide-Rodenticide Branch
Registration Division (TS-767C)

THRU: Albin B. Kocialski, Supervisory Pharmacologist
Section VII, Toxicology Branch
Hazard Evaluation Division (TS-769C)

ABK 7/9/86

Registrant: Fermone Chemicals
305 South Second Avenue, Suite 101
Phoenix, AZ 85003

*W. J. ...
7/9/86*

Action Requested

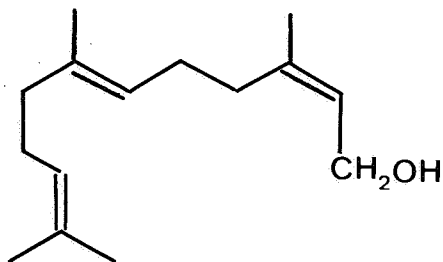
Fermone Chemicals requests registration of Stirrup-M pheromone intended for use as a mite attractant in pesticide formulations. Toxicity data were submitted for evaluation by the Agency to support Stirrup-M.

Background Information

The Stirrup M pheromone active ingredient (a.i.) is known as Farnesol. Farnesol is cleared under 21 CFR §172.515(b) as a synthetic flavoring substance that may be safely used in

food alone or in combination with flavoring substances and adjuvants generally recognized as safe in food, prior-sanctioned for such use. The chemical name, and structure of Farnesol follows:

3,7,11, Trimethyl-2,6,10-dodecatriene-1-ol.



The Stirrup-M formulation will be used in combination with miticides for control of Tetranychid species (of mites).

Stirrup-M Formulation:

Active Ingredient:

Multi-methyl alkenol 0.923%

Inert Ingredient: (Release agents) 99.077%

100.000%

Two to six ounces per acre of Stirrup-M are to be mixed with miticide pesticides to control the Tetranychid species of mites on:

Alfalfa	Melons
Clover	Pumpkins
Cotton	Squash
Peanuts	Eggplant
Sorghum	Peppers
Citrus	Tomatoes
Beans	Hops
Blackberries	Strawberries
Raspberries	Ornamentals
Corn	Grapes
Cucumbers	Tree, Fruit, and Nut Crops

Recommendations:

1. The use of Stirrup-M mixed with miticide pesticides to control mites on food crops is not supported toxicologically:

- a. * The following toxicity data are considered data gaps:

One 90-day subchronic feeding study
 One teratology study
 A battery of mutagenicity studies to detect:

- i. Gene mutation
- ii. Structural chromosomal aberrations
- iii. Other genotoxic effects, e.g., numerical chromosomal aberrations, direct DNA damage and repair.

- b. The following inert materials must be cleared by the Agency for food use:

i. 3,7,11-Trimethyl-1,6,10,dodecatriene-3-ol
 Nerolidol: Cas # 7212-44-4

ii. [REDACTED]

2. The toxicity data submitted with the application were reviewed by William Greear, and are summarized as follows:

- ✓ a. Acute Oral LD₅₀ - rat, using Stirrup-M (0.923% a.i.- Multi-methyl alkenol)

A O LD₅₀ > 5050 mg/kg.

Toxicity Category: IV

Classification: Core Guideline Data

- ✓ b. Acute Dermal LD₅₀ - rabbit, using Stirrup-M (0.923% Multi-methyl alkenol)

A D LD₅₀ > 2020 mg/kg

Toxicity Category: III

Classification: Core Guideline Data.

- c. Acute Inhalation LC₅₀ - rat, using Stirrup-M (0.923% Multi-methyl alkenol).

A I LC₅₀ > 3.37 mg/L for t = 4 hours

* See also 40 CFR §§ 158.165(c)

INERT INGREDIENT INFORMATION IS NOT PROVIDED

Toxicity Category: III

Classification: Core Minimum Data.

- d. Primary Ocular Irritation - rabbit, using Stirrup-M (0.923% Multi-methyl alkenol).

The test material produced mild ocular irritation in washed and unwashed rabbit eyes.

Toxicity Category: III

Classification: Core Guideline Data.

- e. Primary Dermal Irritation - rabbit, using Stirrup-M (0.923% Multi-methyl alkenol).

The test material caused slight irritation at 1 hour, which cleared within 24 hours.

Toxicity Category: IV

Classification: Core Guideline Data.

The label is adequate provided the phrase, avoid inhalation, is added to it.

DATA EVALUATION RECORD

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Subject: Acute Oral Toxicity (LD₅₀) - Rat

Test Material: Stirrup™-M (0.923% Multi-methyl alkenol) -
described as a very viscous opaque off-white liquid

EPA File Symbol: 53871-E

Accession Number: 261309

Testing Facility: Stillmeadow, Inc.
Biological Testing Laboratory
Houston, TX 77036

Project No.: 3812-85

Report Date: September 30, 1985

Project Director: J.. Maedgen

Classification: Guideline

Toxicity Category: Category IV

Material and Methods:

Five male and five female TAS:(SD) albino rats were obtained from Texas Animal Specialties, Humble, Texas. Males weighed 262 to 307 g and females weighed 178 to 210 g. The rats were allowed to acclimate to laboratory conditions for at least 1 week. The animals were housed 1 to 3 per cage in suspended wire bottom stainless steel cages with automatic watering systems. The rats were transferred to clean cages once weekly and the paper and aspen litter pan lining was changed three times weekly. Purina Formulab Chow #5008 and water were available ad libitum. The rats were fasted for 16 hours and then administered the undiluted test material by gavage at a dose level of 5,050 mg/kg. Observations for mortality and toxic signs were made at least three times on the day of dosing and once daily thereafter for 14 days. Individual body weights were determined initially and on days 7 and 14. Gross necropsies were conducted on all animals at termination.

Results:

No deaths occurred. The rats exhibited piloerection, exophthalmos, lacrimation, and ptosis. All animals gained weight during the study. No observable abnormalities were noted at necropsy.

Conclusions: LD₅₀ > 5,050 mg/kg.

Toxicity Category: Category IV.

Classification: Guideline.

DATA EVALUATION RECORD

Subject: Acute Dermal Toxicity (LD₅₀) - Rabbit

Test Material: Stirrup™-M (0.923% Multi-methyl alkenol) -
described as a very viscous opaque off-white
liquid.

EPA File Symbol: 53871-E

Accession Number: 261309

Testing Facility: Stillmeadow, Inc.
Biological Testing Laboratory
Houston, TX 77036

Project No: 3813-85

Report Date: September 27, 1985

Project Director: J.L. Maedgen

Classification: Guideline

Toxicity Category: Category III

Materials and Methods:

Five male and five females New Zealand White albino rabbits weighing 3.325 to 4.200 kg were obtained from Ray Nichols Rabbitry, Lumberton, Texas. The rabbits were allowed to acclimate to laboratory conditions for a period of at least 1 week. The rabbits were individually housed in suspended wire bottom galvanized steel cages. The rabbits were transferred to clean cages once weekly and the paper litter pan lining was changed daily. Purina Rabbit Chow and tap water were available ad libitum. Twenty-four hours prior to treatment, the dorsal surface of the trunk of each animal was clipped free of hair to expose at least 10 percent of the total body surface. The test material was applied undiluted at a dose level of 2,020 mg/kg to the trunk of each animal under surgical gauze which was held in place with nonirritating surgical tape. The entire trunk of each animal was then wrapped with a semipermeable material (Tomac Tubular Stockinette) to retard evaporation of volatile substances and prevent ingestion of the test material. The wrappings, tape and gauze were removed 24 hours after treatment and the exposure areas were washed with tap water to remove the remaining test material. Observations for mortality and toxic signs were made at 1/2, 3 and 6 hours after removal of the wrappings and once daily thereafter for 14 days. Individual body weights were determined initially, and on days 7 and 14. Gross necropsies were conducted on all the animals at termination.

Results:

No deaths occurred. The rabbits exhibited decreased urination and defecation and small feces. All rabbits gained weight during the 14-day observation period. The gross necropsy examination was unremarkable.

Conclusions: LD₅₀ > 2020 mg/kg.

Toxicity Category: Category III.

Classification: Guideline.

DATA EVALUATION RECORD

Subject: Acute Inhalation Toxicity (LC₅₀) - Rat

Test Material: Stirrup™-M (0.923% Multi-methyl alkenol) -
described as a very viscous opaque off-white liquid.

EPA File Symbol: 53871-E

Accession Number: 261309

Testing Facility: Stillmeadow, Inc.
Biological Testing Laboratory
Houston, TX 77036

Project No.: 3816-85

Report Date: November 22, 1985

Project Director: J.L. Maedgen

Classification: Category III

Toxicity Category: Supplementary

Materials and Methods:

Five male and five female TAs:(SD) albino rats were obtained from Texas Animal Specialties, Humble, Texas, and were allowed to acclimate to laboratory conditions for at least 1 week. Male rats weighed 280 to 341 g and female rats weighed 191 to 219 g. The rats were housed 1 to 3 per cage in suspended wire bottom stainless steel cages. The rats were transferred to clean cages once weekly and the paper and aspen bedding material was changed 3 times per week. Purina Formulab Chow #5008 and tap water were available ad libitum. The animals were exposed to an aerosol generated from the liquid test material for a period of 4 hours. The aerosol was generated by pumping the test material through a pressure-operated air nozzle. The aerosol was then diluted with dried, filtered air and drawn into the exposure chamber. Air flow into the chamber was regulated with a calibrated orifice. Air flow, temperature, and humidity were recorded at 30-minute intervals. The concentration of the test material in the exposure chamber was determined analytically and gravimetrically once per hour. The nominal concentration was calculated at the end of the exposure period. The analytical concentration was determined with a Tracor Model 560 gas chromatograph. The gravimetric concentration was determined by passing a known volume of chamber air through a pre-weighed filter and dividing the amount of test material deposited on the filter by the volume of air passing through the filter. Particle size determinations were made at 1 and 3 hours using an Anderson cascade impactor. Observations for mortality and toxic signs were made "frequently" on the day of exposure and at least once daily thereafter for 14 days. (Due to chamber design only 4 animals could be observed during the exposure period.) Individual body weights were determined initially and on days 7 and 14. Gross necropsies were conducted on all animals at termination.

Results:

The chamber relative humidity ranged from 91 to 100% and temperature ranged from 72 to 73 °F. The mean analytical and mean gravimetric chamber concentrations were determined to be 3.37 and 6.02 mg/l, respectively. The nominal concentration was 26.5 mg/l. The mass median aerodynamic diameter ranged from 3.573 to 4.597 micrometers. More than 84 percent of the particles were under 10 micrometers. No deaths occurred. All animals gained weight during the observation period. Rats exhibited the following toxic signs: piloerection, clear nasal discharge, polyuria, dilated pupils, salivation and constricted pupils. No observable abnormalities were noted at necropsy.

Conclusions: $LC_{50} > 3.37$ mg/l for $t = 4$ hours.

Toxicity Category: Category III.

Classification: Minimum.

Justification of Classification:

Three or more dose levels should have been used to determine the LC₅₀. However, the study need not be repeated as it serves to fulfill the intent of the guidelines for regulatory purposes. No deaths occurred at a sufficiently high concentration (3.37 mg/l) which closely approximates the level (5 mg/l) specified in the "Limit test" in the guidelines above which further testing is not required.

DATA EVALUATION RECORD

Subject: Primary Eye Irritation - Rabbit

Test Material: Stirrup™-M (0.923% Multi-methyl alkenol) -
described as a very viscous opaque off-white
liquid.

EPA File Symbol: 53871-E

Accession Number: 261309

Testing Facility: Stillmeadow, Inc.
Biological Testing Laboratory
Houston, TX 77036

Project No.: 3814-85

Report Date: September 19, 1985

Project Director: J.L. Maedgen

Classification: Guideline

Toxicity Category: Category III

Materials and Methods:

Three male and six female New Zealand White albino rabbits were obtained from Ray Nichols Rabbitry, Lumberton, Texas, and were allowed to acclimate to laboratory conditions for at least 1 week. The rabbits were individually housed in suspended wire bottom galvanized steel cages. The rabbits were transferred to clean cages once weekly and the paper litter pan lining was changed daily. Purina Rabbit Chow and tap water were available ad libitum. Both eyes of each animal were examined 24 hours prior to treatment with 0.2 percent sodium fluorescein. Both eyes of each animal were again examined just prior to treatment. One-tenth milliliter of the undiluted test material was placed into the conjunctival sac of the left eye of each animal. The lids were then held together for one second. The treated eyes of three females were washed with room temperature deionized water for 1 minute beginning 30 seconds after treatment. The treated eyes of the remaining six rabbits were unwashed. The treated eyes of all animals were examined for irritation at 1, 24, 48 and 72 hours and at 4 and 7 days. At the 24 hour examination, the corneas of all treated eyes were reexamined with the use of 0.2 percent sodium fluorescein.

Results:

No corneal opacity was present. All nine rabbits exhibited redness, chemosis, and discharge at 1 and 24 hours. The maximum average irritation score was 9.0/110 for unwashed eyes at 1 hour and 10.0/110 for washed eyes at 1 hour. All irritation subsided within 7 days.

Conclusions:

The test material produces mild ocular irritation in the washed and unwashed eyes of rabbits.

Toxicity Category: Category III.

Classification: Guideline.

DATA EVALUATION RECORD

Subject: Primary Dermal Irritation - Rabbit

Test Material: Stirrup™-M (0.923% Multi-methyl alkenol) -
described as a very viscous opaque off-white
liquid.

EPA File Symbol: 53871-E

Accession Number: 261309

Testing Facility: Stillmeadow, Inc.
Biological Testing Laboratory
Houston, TX 77036

Project No.: 3815-85

Report Date: September 19, 1985

Project Director: J.L. Maedgen

Classification: Guideline

Toxicity Category: Category IV

Materials and Methods:

Three male and three female New Zealand White albino rabbits were obtained from Ray Nichols Rabbitry, Lumberton, Texas, and were allowed at least 1 week to acclimate to laboratory conditions. The rabbits were individually housed in suspended wire bottom galvanized steel cages. The rabbits were transferred to clean cages once weekly and the paper litter pan lining was changed daily. Purina Rabbit Chow and tap water were available ad libitum. Twenty-four hours prior to treatment, the dorsal area of the trunk of each rabbit was clipped free of hair to expose an 8 cm x 8 cm area. The test material was applied at a dose level of 0.5 ml to one intact skin site on each animal under a 1-inch square gauze patch. Each patch was held in place with a strip of non-irritating adhesive tape and the entire trunk was wrapped with a semipermeable dressing (Tomaç Tubular Stockinette); then the edges of the dressing were wrapped with nonirritating adhesive tape. Four hours after treatment the wrappings were removed and the back of each animal was washed with tap water to remove the remaining test material. The test sites were scored at 1, 24, 48, and 72 hours after removal of the wrapping.

Results:

Very slight erythema was observed in 4 of 6 rabbits at 1 hour. No other irritation was observed.

Conclusions:

The test material causes slight irritation at 1 hour which clears within 24 hours. ✓

Toxicity Category: Category IV.

Classification: Guideline.