

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

002371

DATE: September 27, 1979

SUBJECT: Ortho Multipurpose Rose and Flower Spray. CASWELL#2A (Orthene), 890AA
(Triforine), 93 (Kelthane)

FROM: Krystyna K. Locke
Toxicology Branch (TS-769)

Krystyna K. Locke

TO: William H. Miller
Product Manager#16

9-27-79

EPA File No. 239-EUA1

Accession No. 238698, 238697, 238729

Applicant: Chevron Chemical Company
Ortho Division
940 Hensley Street
Richmond, California 94804

Action Requested: Registration of Ortho Multipurpose Rose and Flower Spray.

Recommendations:

Toxicology Branch has no objections to the registration of Ortho Multipurpose Rose and Flower Spray, to be used outdoors for control of diseases, insects and mites on roses, flowers and ornamentals (as listed on the label). The new formulation contains three already registered active ingredients: acephate systemic insecticide (4.0%), triforine fungicide (3.25%) and kelthane miticide (3.0%). This formulation should not pose any special health hazard, provided the label is followed. The proper use of this product should not result in residues in human food or animal feed. The overall toxicity category of this product, I, because of eye effects. Adequate toxicity data are available to support the registration of this formulation for the use specified.

Label to indicate: for outside use only.

SUMMARY

Chevron has applied for the registration of a new formulation, Ortho Multipurpose Rose and Flower Spray. According to Marilyn Mautz (Acting PM 16), this formulation has the following composition (CONFIDENTIAL):

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<u>Active Ingredient</u>	<u>Percent by Weight</u>
Orthene Technical*	1.55
Triforine Technical**	1.19
Kelthane Technical***	7.86

Inert Ingredients

*Acephate; O,S-dimethyl acetylphosphoramidothioate.

**N,N'-[1,4-piperazinediylbis(2,2,2-trichloroethylidene)]bisformamide.

***1,1-bis(p-chlorophenyl)-2,2,2-trichloroethanol.

Kelthane is a registered product of Rohm and Haas Co. Tolerances are established for residues of this insecticide (miticide) in or on many raw agricultural commodities (CFR, 40, 180.163).

Triforine (trademark, Funginex) is a product of Celamerck GmbH and Co. KG, Fed. Rep. of Germany. This material is registered, but no tolerance has yet been established for it in the U.S. There is apparently no undue hazard associated with technical triforine. However, this formulation contains [REDACTED] an inert ingredient which has not yet been cleared for use on raw agricultural commodities. (Memo from Charles Frick, T.B., to H. Jacoby, Product Manager, dated 7-17-79).

The label (copy attached) carries the signal word DANGER, in accordance with the overall toxicity category I (because of eye effects) of the formulation. The label contains adequate precautionary statements with regard to hazards to humans and domestic animals, as well as other hazards. The label is acceptable to the Toxicology Branch.

Chevron's application for the registration of Ortho Multipurpose Rose and Flower Spray is supported by 5 acute studies, submitted with this application, and by references to other studies which were used in support of the existing registrations of orthene products and of kelthane. The five acute studies are summarized below.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

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No.	Study	Animals used	LD50 g/kg	Toxicity Category	Valid. Categ.: Core-Minimum Data
1	Oral	M and F rats	M - 3.2 F - 2.6	III	yes
2	Dermal	Male rabbits	3.5	III	yes
3	Skin Irritation	Male rabbits	-	IV	yes
4	Eye Irritation	Male rabbits	-	I	yes
5	Inhalation	M and F rats	^{LC₅₀} > 60.7 mg/L	IV	yes

All of these studies were conducted by Chevron Standard Oil Company, Environmental Health and Toxicology Laboratory, San Francisco, California. Studies No. 3 and 4 are dated 7-14-76; studies No. 1, 2 and 5 are dated 2-12-78.

Two formulations were used in the acute studies. Formulation CC6219 was used in the skin and eye irritation studies, whereas formulation CC8170 was used in the oral, dermal and inhalation studies. As is shown below, these formulations are very similar in composition (CONFIDENTIAL).

Ingredient	Formul. CC8170	Formul. CC5219
	% by wgt.	% by wgt.
Orthene (98.3%)	4.55	4.15
Tri-orine (97%)	4.19	3.28*
Kelthane 42 MF	7.14	7.14

These formulations are also very similar in composition to Ortho Multipurpose Rose and Flower Spray.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

As far as the referenced studies with Orthene are concerned, nearly all of the subacute, chronic and special studies were conducted by IBT. Sixteen of these studies were validated in 1978. Three of these studies, teratology (rats), 2-year feeding study (dogs) and 90-day cholinesterase study (rats) were considered valid.

This submission also contains referenced studies on Kelthane, obtained from Rohm and Haas Company. The following studies are listed:

- 3 Acute Oral (rats)
- 1 Subacute Oral (rats)
- 2 Chronic Feeding (rats and dogs)
- 2 Metabolism (rats, dogs)
- 8 Reproduction (rats, mice)

This submission contains no toxicology data on Triforine. However, Triforine is a registered formulation and such data are available (PP#7F1921, PP#9F2184, and Registrations#21137-4 and 6).

EVALUATION OF ACUTE TOXICITY STUDIES

1. Acute Oral Toxicity (Rats)

S-1197; SOCAL 1196/31:126, dated 2-15-78.

Test Material: CC 8170; code SX-964

Experimental

Animals: Sprague-Dawley rats, 5 males (213-255g) and 5 females (201-222g) per dose level.

Dose levels: 0, 1.5, 2.2, 3.3 and 5.0 g/Kg of body wt.

Observation: 14 days

Necropsy: yes

Results

Mortality: No animals died at 0 and 1.5 g/kg levels. All of the male rats died at 5.0 g/kg level. All of the female rats died at 3.3 and 5.0 g/kg levels.

Signs of toxicity: depression, reduced food intake, salivation, ataxia and collapse.

Necropsy: No gross pathological changes could be attributed to the test material.

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LD50 (95% Limits)

Male - 3.2 (1.5 - 6.9) g/kg

Female - 2.6 (1.4 - 5.0) g/kg

Slope (95% Limits)

1.6 (0.69 - 3.9)

1.5 (0.83 - 2.7)

Validation Category: Core-Minimum DataToxicity Category: III2. Acute Dermal Toxicity (Male Rabbits)

S-1198; SOCAL 1197/29:80, dated 2-15-78.

Test Material: CC 8170; code SX-964ExperimentalAnimals: Male New Zealand White rabbits, 6 animals per dose level (3 abraded); wgt: 2.91 kg.Dose levels (g/kg): 0, 2.2, 3.3, 5.0 and 7.5.Exposure: 24 hoursObservation: 14 daysNecropsy: yesResultsMortality: 2/6, 3/6, 3/6 and 6/6 at dosages of 2.2, 3.3, 5.0 and 7.5 g/kg of body wgt., respectively. Most of the dead rabbits were those with abraded skin.Signs of toxicity: depression, diarrhea, reduced food intake, ataxia, bloody urine and collapse.Necropsy: Enlarged, heavily congested kidneys and no body fat were observed in one of the survivors of the 3.3 g/kg dose. Only trace amounts of body fat and about 10 ml of clear, red fluid in the abdominal cavity were found in one of the survivors of the 2.2 g/kg dose. No other gross pathological changes, except for dry, flaky skin in the treated areas, were observed.LD50 (95% Limits)

3.4 (1.2 - 10.1) g/kg

Slope (95% Limits)

2.4 (0.27 - 21.9)

Validation Category: Core-Minimum Data. Reasons for not using the Core-Supplementary Data category, since only male rabbits were used:

1. Considering the oral toxicity study (above), there is only about 19% difference between the LD50 values for male and female rats. If this difference also applied to rabbits in this dermal toxicity study, the LD50 for female rabbits would be about 2.8 g/kg and the formulation would still be in the toxicity category III.
2. Four dose levels, or more than is generally being used, were tested in this dermal toxicity study.

Toxicity Category: III, based on the LD50 value for male rabbits.

3. Skin Irritation Potential (Male Rabbits)

S-994, SOCAL 914/27:45, dated 7-14-76.

Test Material: CC 6219; code SX-807

Experimental

Animals: 6 male rabbits

Dose level: 0.5 ml, applied to an intact and abraded area on the back of each rabbit.

Exposure: 24 hours

Scoring: Done at 1, 2, 3 and 7 days, following treatment.

Results

There was no edema. Very slight erythema was observed in all of the rabbits for 48 hours, and in 3 rabbits for 72 hours, on both intact and abraded skin. The irritation score was 0.8/8.0 (slightly irritating).

Validation Category: Core-Minimum Data

Toxicity Category: IV

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4. Eye Irritation Potential (Male rabbits)

S-993; SOCAL 913/27:45, dated 7-14-76

Test Material: CC 6219; code SX-807ExperimentalAnimals: 12 male rabbits, 6 per group.Dose: 0.1 ml, placed in the conjunctival sac of one eye of each rabbit, in two separate groups.Grading: At 1 hour, and at 1, 2, 3, 7, 10 and 14 days, following treatment.Results

Group 1. Slight corneal opacity, mild iritis, moderate to severe conjunctival redness and slight to moderate chemosis were observed in the eyes of some rabbits during the first 72 hours after treatment. At seven days, slight corneal opacity and severe pannus were observed in one eye. All eyes appeared normal by 14 days.

Group 2. Slight to moderate corneal opacity, mild iritis, moderate to severe conjunctival redness, and slight to moderate chemosis were observed in the eyes of some rabbits during the first 72 hours after treatment. At 7 days, slight to dense corneal opacity, mild iritis and pannus were observed in some eyes. At 14 days, moderate or complete corneal opacity was present in 3 eyes. Mild iritis and pannus were also observed at this time.

Validation Category: Core-Minimum DataToxicity Category: 15. Acute Inhalation Toxicity (Rats).

S-1201; SOCAL 1200/28:146, dated 2-16-78

Test Material: CC 8170; code SX-964ExperimentalAnimals: Sprague-Dawley rats, 5 males (235-260g) and 5 females (224-236g) per exposure.

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Dose levels: Vapor exposure: 18.2 g/300 L = 60.7 mg/L of air
(indirect determination).

Aerosol exposure: 0.93 mg/L of air (see calculations
below).

Exposure: 1 hour

Observation: 14 days

Necropsy: yes

Results

Mortality: None

Toxicity Symptoms: rales and gasping in 2 male rats and rales in 2 female rats. All animals appeared normal the day following exposure, and for the duration of the study.

Body Weights: Loss of weight (insignificant) in the aerosol exposure group. Significant loss of weight in the vapor exposure group: males ($p = 0.01$) and females ($p = < 0.05$).

Necropsy: No gross pathological changes attributable to the test material were observed.

Calculations: Aerosol exposure level.

According to Chevron's report, 25g of the diluted test material were aerosolized in 420 liters of air. Dilution rate: 2 oz of the test material (undiluted) per gallon of distilled water.

Dilution factor = 64.15

2 oz: 1 gallon

1 oz = 29.5 ml

1 gallon = 3785 ml

2 X 29.5 = 59 ml

3785/59 = 64.15

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25g of the diluted material is equivalent to 390 mg of the undiluted test material.

$$\begin{aligned} 25\text{g}/64.15 &= 0.39\text{g} = 390 \text{ mg} \\ 390 \text{ mg}/420 \text{ liters of air} &= 0.93 \text{ mg/L} \end{aligned}$$

LC50: > 60.7 mg/L (vapor exposure).

Validation Category: Core-Minimum Data

Toxicity Category: IV

W. Butcher

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