US EPA ARCHIVE DOCUMENT

10-2290

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

432-1132

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 4816-688
Permanone Multi-Purpose 10% EC.

FROM: Sheila A. Moats, Ph.D. 10/16/90
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C)

10/22/90

TO: George La Rocca (PM 15)
Insecticide-Rodenticide Branch
Registration Division (H75-05C)

APPLICANT: Fairfield American Corporation
809 Harrison Street
Frenchtown N.J. 08825

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Permethrin	10.00
Inert Ingredient(s):	90.00
Contains Petroleum distillates [redacted] Total (Aromatic petroleum hydrocarbons).	100.0%

INERT INGREDIENT INFORMATION IS NOT INCLUDED

1-92

Background

Fairfield American Corporation submitted acute oral, dermal, inhalation, skin irritation, + dermal sensitization studies to support registration of Permanone - Multi Purpose 10% E.C. Reg. No 4816-688. MRID Nos used were 41628-01-05.

An eye irritation study was previously submitted + accepted by the Agency. The MRID No used was 412178-0

Recommendations

1. The acute oral, dermal, inhalation, + skin irritation studies are acceptable to PRS/RSB.

2. The dermal sensitization study was rated "Supplementary" since the reviewer was unable to reach an objective decision. The data in the report showed that the test material was a weak sensitizer, however, this may or may not be the case, since the report did not include data to for determining the highest non-irritating concentration. In the absence of data it is hard to decide whether the product is a sensitizer or that the highest non-irritating concentration was not chosen for testing. The study used Buehler's method + the following excerpt may be helpful to the registrant. It is a direct quote from an article by

Ritz, Harry L. + Buehler, Edwin V., 1980, Planning Conduct + Interpretation of Guinea Pig Sensitization

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Patch Tests... Current Concepts in Cutaneous Toxicity. Academic Press.

"It is often necessary to determine the primary irritancy of the test substance so that a non-irritating concentration may be chosen for response elicitation. For this purpose as many as four different concentrations of the test material in the appropriate solvent are applied as described for the induction procedure to four naive guinea pigs."

The registrant must therefore submit all pertinent data for the selection of the highest non-irritating dose.

Labeling.

1. The "CAUTION" signal word is acceptable.

2. The Precautionary Statements must be stated as follows:

"Harmful if inhaled, causes moderate eye injury. Avoid breathing vapor or spray mist, & contact with eyes, skin or clothing. Remove contaminated clothing, & wash contaminated clothing ~~with~~ before re use. Wash thoroughly with soap & water after handling.

3. To the Statement of Practical Treatment. "If Inhaled" _, add "Get medical attention" at the end of the statement.

"If on Skin" _ state as follows:

"If on Skin", wash with plenty of soap & water. Get medical attention if irritation persists.

The statement for "If in Eyes" is acceptable.

Upon receipt of acceptable RANGE-FINDING data in support of the Sensitization Study, labeling may need revision. E

Reg. No 4816-688

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

Product Manager: (15)
MRID No.: 416280-01
Testing Facility: Product Safety Labs
Author(s): Shapiro, Ralph.
Species: Wistar derived albinos — rats.
Age: Young adults
Weight: 186 - 228 g.
Source: Hilltop Lab Animals Scottdale, PA.
Test Material: Permanone Multi-Purpose 10% EC.
Quality Assurance (40 CFR §160.12): Adequate

Reviewer: S. Moats
Report Date: 10/11/90
Report No. T-020
Observation Days (Post Exposure): (14); other ( )

Conclusion:

1. LD_{50} (mg/kg): Males = _____; Females = _____; Combined = >5 g/kg.
2. The estimated LD_{50} is _____
3. Tox. Category: IV. Classification: Guidelines.

Procedure (Deviations From §81-1): 5♂ & 5♀ rats were administered 5 g/kg body wt. of the test material by gavage. The animals were observed for toxicity & mortality at 1, 2, 4 & 24 hrs & once daily thereafter.

Results:

Reported Mortality

DOSAGE (g /kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
5	2/5	0/5	2/10

Symptomology & Gross Necropsy Findings:

There were 2 mortalities.
Clinical signs included ano-genital staining, facial staining, tremors, hunched posture etc.
Necropsy findings included discoloration of the spleen, kidneys & small intestine.

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

Product Manager: (15)
MRID No.: 416280-02
Testing Laboratory: Stillmeadow Inc.
Author(s): Kuhn, Janice, O.
Species: New Zealand white rabbits
Sex: 5♂ + 5♀. Wt.:
Test Material: Permanone Multipurpose 10% EC.
Quality Assurance (40 CFR §160.12): Adequate

Reviewer: S. Moats
Report Date: 10/11/90
Report No. 7110-90

Summary:

1. LD_{50} (mg/kg): Males = ; Females = ; Combined = > 5050 mg/kg;
2. The estimated LD_{50} is
3. Tox. Category: IV. Classification: Guidelines

Procedure (Deviations From §81-2): 5♂s + 5♀s were used for the study. Prior to dosing the animals were clipped on their back sides to expose 10% body surface. 5050 mg/kg of the test material was applied to the clipped area of each animal. 10 x 10 cm^2 gauze covered the sites & kept in place with adhesive tape. The entire trunk was next wrapped with semi-permeable stockinette dressing. The wrappings were removed after 24 hrs & the sites gently wiped clean. Observations for toxicity & mortality were made at ½, 1, 3 & 6 hrs. & once daily thereafter for 14 days.
Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
5050			

Symptomology & Gross Necropsy Findings:

All animals survived the test.
Clinical observations showed no abnormalities.
Gross necropsy findings were unremarkable.

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

Product Manager: (15)
MRID No.: 416280-03
Testing Laboratory: Stillmeadow
Author(s): Holbert, Mark S.
Species: Harlan Sprague Dawley - Rat
Sex: ♂s + ♀s. Weight: 197-253 g.
Source: Harlan Sprague Dawley Inc. Houston Texas
Test Material: Permanone Multi-Purpose 10% EC
Quality Assurance (40 CFR §160.12): Adequate

Reviewer: S. Moats
Report Date: 10-15-90
Report No. 7112-90

Summary:

1. LC_{50} (mg/kg): Males = ____; Females = ____; Combined = >1.56 mg/L.
2. The estimated LC_{50} is ____
3. Mean Concentration: 3.96 mg/L.
4. Tox. Category: III. Classification: Guidelines

Procedure (Deviations From §81-2): The test animals (5♂ + 5♀) were housed individually within a 200 L. stainless steel dynamic flow inhalation chamber during the 4-hr exposure period. The animals were exposed to aerosol generated undiluted test material. Observations were made on the day of exposure + once daily for 14 days thereafter. A pressure operated atomizer with a nebulizer ball attached to it was used to generate the aerosol. The conc. aerosol was diluted with dried + filtered air + drawn into the exposure chamber. Air flow was regulated by use of a calibrated orifice. Air flow, temp. + humidity were recorded at 30 mts interval. Conc. of test material was determined by means of a spectrophotometer. Cascade impactor was used for particle sizing.

Results:

Reported Mortality

Exposure Concentration (mg/L)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
1.56	0/5	0/5	0/10

Symptomology & Gross Necropsy Findings:

All animals survived the study. Clinical signs included lacrimation, piloerection, activity decrease, polyuria + ptosis.

Gross necropsy findings were unremarkable.

Test Material	Hour	Stage	Size Range μm	Cum: %	MMAD	GSD
Dosage 1.56 mg/L	2 1/4	Reading a	1.1 → 2.1	30.21	1.185	2.649
		b	0.7 - 1.1	28.77		
"	3 3/4	Reading a	1.1 - 2.1	29.071	1.354	2.553
		b	0.7 - 1.1	24.00		

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

Product Manager: (15)
MRID No.: 416280-04
Testing Laboratory: Product Safety Labs
Author(s): Shapiro, Ralph
Species: New Zealand albino Rabbits.
Age: ____
Sex: 3♂s + 9♀s.
Weight: ____
Dosage: 0.5 mL.
Test Material: Permanone Multi-Purpose 10% E.C.
Quality Assurance (40 CFR §160.12): Adequate

Reviewer: S. Moats
Report Date: 10-11-90
Report No. T-029

Summary:

The Primary Irritation Index = 4.03.

Toxicity Category: III

Classification: Guidelines

Procedure (Deviations From §81-5): Prior to dosing 3♂+ 3♀ rabbits were clipped of fur over 10% of the body surface. 6 cm^2 site was delineated per animal as test area. 0.5 mL of the undiluted test material was applied on each site + covered with gauze patch. The patch + trunk on each animal was next wrapped with elastic cloth + neck collars were placed. After a 4-hr exposure period the wraps + patches were removed + the sites cleansed of residues. The sites were graded at 30-60 mts, 24, 48 + 72 hrs + 7, 10 + 14 days after patch removal.

Results:

The calculated PII is 4.03.
The test article is a moderate irritant.
Other than skin irritation, there were no signs of gross toxicity.
Epidermal sloughing + dried cracked tissue + flakiness were observed at many sites between Day-7 + Day 14.

Special Comments:

Sloughing is defined as a shedding or casting of dead tissues. The fact that this phenomenon was observed between Day-7 + Day 14 means that healing process occurred during that time.

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

Product Manager: (15) Reviewer: S. Moats
MRID No.: 416280-05 Report Date: 10-15-90
Testing Laboratory: Stillmeadow. Report No. 7111-90
Author(s): Kuhn, Janice O.
Species: Hartley strain - Albino guinea pigs
Sex: male Weight: 350-410 g.
Source: Harlan Sprague Dawley Inc. Houston, Texas
Test Material: Permanone Multi-Purpose 10% EC.
Positive Control Material: Dinitrochlorobenzene - DNCB.
Quality Assurance (40 CFR §160.12): Adequate

Method: Buehler

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

Procedure (Deviation From §81-6): 10 male guinea pigs were selected for each of two treatment gps. Gp I. (Positive Controls) were treated with 0.5 ml of DNCB. Gp II (Test Gp) were treated with 0.5 ml of a 10% w/v soln of the test material in ethanol (selected as highest non-irritating dose) Prior to treatment the back trunk of each animal was clipped to expose an 8 x 10 cm^2 area. The appropriate material was introduced beneath a gauze pad + secured with clear plastic wrapped around the entire trunk. The animals were restrained for 6 hrs. At the end of the exposure pd. The wrappings + patches were removed + the animals returned to their cages. Same test site location was used on each animal on all treatment days for Gp I animals. Gp II animals were dosed at a new site on Day-15 due to excessive irritation in the previous site. On Day-26 all animals were treated in an identical manner as the previous 10 treatments in addn a 2nd test site was chosen on the right rear quadrant of the exposed area.

Observations for skin reactions were made 24 hours after each treatment for each test site + 48 hrs after treatments 1 + 10 + after the challenge treatment on Day-3

* Results: This study is designated "Supplementary" because a weak sensitizing reaction was produced by the test material, this may or may not be the case, since data to determine the highest non-irritating concentration is lacking in the report. It is hard to determine without data, whether or not a non-irritating concentration was chosen for testing.

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4816-688

Permanone Multi-Purpose 10 EC

Tox Chem No. 652BB File Last Updated _____ Current Date 10/16/90

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX. Cat.	CORE Grade Doc. No.
Acute Oral LD-50, Rat Product Safety Labs #T-020 7-31-90	Permanone Multi-Purpose 10% EC	416280 -01	LD50 > 5000 mg/kg	IV	Guidelines
Acute Dermal LD-50, Rabbit Stillmeadow #7110-90 7-23-90	" "	416280 -02	LD50 > 5050 mg/kg	IV	Guidelines
Acute Inhalation LC-50 Rat Stillmeadow #7112-90 8/21/90	" "	416280 -03	LC50 > 1.56 mg/L	III	Guidelines
Skin Irritation LD-50 Rabbits #T-021 7/16/90	" "	416280 -04	It is a moderate irritant	III	Guidelines
Skin Sensitization Guinea Pig #7111-90 8/6/90	" "	416280 -05			Supplemental
Eye Irritation	" "	412178 -02	Previous Submission	III	