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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 121-UA Evergreen Cutter Insect Repellent Formula MMM II

FROM: William S. Woodrow WSW 2-6-91
Precautionary Review Section E 2/26/91
Registration Support Branch
Registration Division (H7505C)

TO: Phillip Hutton / Joseph Tavano (PM 17)
Insecticide - Rodenticide Branch
Registration Division (H7505C)

APPLICANT: Miles Inc.
Consumer Household Products Div.
7123 West 65 Street
Chicago, IL 60638

FORMULATION FROM LABEL:

	% by wt.
Active Ingredient(s):	
Deet (N,N-diethyl-m-toluamide	28-50
other isomers	1-50
Inert Ingredient(s):	70-00
Total	100.0%

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BACKGROUND

Miles, Inc. submitted primary eye and skin and dermal sensitization studies to support registration of Evergreen Cutter Insect Repellent Formula N.N. II (EPA Reg. No. 121-UA) MRID NOS. used were 416933-01, 415757-02, and 415757-03. This product is to be sprayed from pressurized cans from 6-to-8 inches away from skin or clothing, keeping nozzle pointed away from the face.

RECOMMENDATION

1) The primary eye and skin irritation and the dermal sensitization studies submitted by Miles are acceptable to RSB/PRS.

2) A requirement for acute oral, acute dermal, and acute inhalation studies to support # 121-UA registration remains. However, the Deet Pesticide Registration Standard published by the Agency in December, 1980 does address acute toxicity data requirements for Deet Ready-to-use and Pressurized Liquid products.

a. From page 42 of the Deet Standard :
Quote — Acute oral toxicity)

"

(2) Pressurized Liquid (PrL)

Because technical Deet and the 15% and 30% PrL formulations are in Toxicity Category III, and because the inert ingredients in the PrL formulations are not expected to increase the acute oral toxicity potential, existing PrL products between 12% and 75% concentrations, except those that contain freon propellants, are classified in Toxicity Category III. Toxicity Category III corresponds to a low acute oral toxicity potential. "

b. From page 43 — Deet Standard
Quote " (2) Pressurized Liquid (PrL) — (Acute dermal tox).

Because technical Deet is placed in Toxicity Category III, and because the inert ingredients in PrL products are not expected to increase the acute dermal toxicity potential, all existing PrL products between 12% and 75% concentrations, except those that incorporate from propellants, are classified in Toxicity Category III. Toxicity Category III corresponds to a low acute dermal toxicity potential. "

c. From page 45 - Deet Standard - Acute Inhalation Toxicity.
Quote

(2) Pressurized Liquids (PrL)

Because technical Deet is placed in Toxicity Category IV, and because the inert ingredients in PrL products are not expected to increase the acute inhalation toxicity potential, all existing PrL products between 12% and 75% concentrations, except those that incorporate freon propellants, are placed in Toxicity Category IV. Toxicity Category IV, corresponding to a very low acute inhalation Toxicity potential.

Thus, according to the Deet Standard it

will not be necessary to submit additional acute oral, acute dermal, or acute inhalation studies Evergreen Cutter Insect Repellent Formula MM II (pressurized), EPA Reg. NO. 121-UA.

3) Current acute toxicity profile for Evergreen Cutter Insect Repellent (EPA Reg. NO. 121-UA):

study	MRID/Acc.#	Tox. Cat.	Grade
Eye irritation	415757-02	III	Guideline
Skin irritation	415757-03	IV	Guideline
Skin sensitization	416953-01	Meta sensitizer	Guideline
Acute oral	(Deet std.)	II	—
Acute dermal	(Deet std.)	III	—
Acute inhalation	(Deet std.)	IV	—

No additional acute toxicity studies for EPA Reg. NO. 121-UA are required.

LABELING

1) Change the product signal word from WARNING, to read "CAUTION".

2) The Precautionary Statements and Statement of Practical Treatment are acceptable.

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

Product Manager: (17)
MRID No.: 415755-01
Testing Laboratory: Tox. Dept., Miles, Inc.
Author(s): R.W. Kowalski, R.E. Hartnagle
Species: Rabbit, NZ White
Sex: 9 females, 12 mo. old Weight: 3.5 – 4.7 kgs
Source: Miles Corporate animal facility
Dosage: 1 - Sec spray
Test Material: Electrotech Cutter insect Repellent Formula mmbb
Quality Assurance (40 CFR §160.12): adequate

Reviewer: Woodrow ~~M. Waller~~
Report Date: 1-2-91
Report No. MTD0164

Summary:

Tox. Category: III Classification: Guidelines

Procedure ~~(Omission From [illegible])~~ Eyes tested for defects using fluorescein prior to study. Test eyes anesthesized prior to treating; aliquots (by spraying) of approx. 0.023g, 23mg, or 0.2 ml were administered as a single burst of 1 second from a

Results: NOTE: washed & unwashed eye results are similar so scoring have recorded as 3+6 = 9 animals

Observations (number "positive"/number tested)

	Hour	Days					
	1	1	2	3	7	14	21	
Cornea Opacity	9/9	9/9	9/9	8/9	0/9			1.0 scores
Iris	0/9	0/9	0/9	0/9	0/9			
Conjunctivae Redness	9/9	9/9	9/9	6/9	0/9			1.0 scores
Chemosis	9/9	9/9	9/9	8/9	0/9			½/3.0 scores
Discharge	9/9	9/9	3/9	4/9	0/9			3/2/1.0 scoring

~~Comments~~: Distance of 10cm, directly in front of treated eye. Dose estimated by weighing can before and after application. Eyelids held together 1 second - Treated eyes of three animals washed by irrigation = water for 1 minute, beginning 20-30 sec

Corneal involvement or irritation clearing in 7 days or less

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post exposure. Each animal observed daily for up to 7 days, and were graded for irritation according to ~~[illegible]~~ Draize at 1 hour, 1, 2, 3 and 7 days post exposure, using the scale devised by Draize.

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

Product Manager: (17)
MRID No.: 415755-03
Testing Laboratory: Tox. Dept. Miles, Inc.
Author(s): R.L. Kowalski; R.E. Hartnagle
Species: Rabbit; NZ White
Age: 10.5 months
Sex: not given
Weight: 3.5-4.2 kg
Dosage: 0.5ml
Test Material: Evergreen Cutter Insect Repellent Formula MMRI
Quality Assurance (40 CFR §160.12): adequate

Reviewer: Woodrow Waller
Report Date: 1-2-91
Report No.: MTD 0146

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Summary:

The Primary Irritation Index = 1.37

Toxicity Category: IV

Classification: Guidelines

Procedure ~~(Deviations From §81-5):~~ 0.5ml test material applied to clipped, depilated dorsal area of skin of 6 rabbits each, under a Webril pad, held in place by Blenderm tape. Entire trunks covered w occlusive dressing secured w tape. 4 hour skin contact; dressings removed, no test material evident.

~~Results~~: Each animal observed 13 days; test sites observed & scored according to Draize for erythema/edema.

Results: - All test rabbits showed total lesions (initiation by Day 10 for erythema); 2 of the treated animals showed 2.0 scores on Days 2 and 3, all other erythema scores (to and through Day 6) were 1.0 - 4/6 animals showed slight (1.0) scoring for edema initially, absent by Day 2.

Primary irritation index: (mean)

time	mean P.I. scores - erythema	edema
1 hr.	0.83	0.67
24 hrs	1.0	0.33
48 hrs	1.33	0.0
72 hrs	1.33	0.0

~~Special Comments~~:

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

Product Manager: (17)
MRID No.: 416953-01
Testing Laboratory: Tex. Dept. Miles, Inc
Author(s): R.C. Kowalski R.E Hartnagle
Species: Guinea Pig, Hartley
Sex: male
Source: Charles River
Test Material: Evergreen Critter Insect Repellent Formula MM 31
Positive Control Material: 1-chloro-2,4-dinitrobenzene (DNCB)
Quality Assurance (40 CFR §160.12): adequate

Reviewer: ~~M. Walker~~ Woodrow
Report Date: 1-2-91
Report No. MTD 0136

Method: Modified Draize intradermal injection.

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

~~Procedure (Deviation From §81-6):~~ A preliminary screening to determine the maximum non-irritating product concentration for use in the main study was conducted (ID test). 5%, 10% (W/V in corn oil), minimal irritation @ 1% W/V in corn oil, 0.05, 0.10, 0.25; ~~Results:~~ 0.5, and 1.0% W/V in corn oil.; 0.5% W/V in Corn oil used for main study. The results indicated 0.5% mix. gave same results as corn oil alone. Positive control study employed 1-Chloro-2,4-Dinitrobenzene (DNCB). DNCB formulated as 0.05% W/V sd in 5.0% V/V ethanol in normal saline. 10 males induced & test mat., 5 naive control. DNCB induced & naive control, 5 animals each. (25 animals total).

Induction: 10 test mat. & 5 DNCB animals clipped & depilated 2 days before test. 10 animals injected intradermally, ~ 0.05 ml test (0.5% V/V in Corn oil) near left pelvic girdle, on days 0, 2, 4, 7, 9, 11, 14, 16, 18, 21 over 21 day period. After 1st injection, 0.1 ml injected in staggered pattern. 5 DNCB animals induced using 0.05% W/V DNCB in 5.0% V/V ETOH in normal saline.; these (DNCB) injected using same repeat pattern for 10 injections. Induced animals rested 2 weeks

prior to challenge injection.

Challenge - Depilatory not used. Test material injected as 0.1 ml in right (naive site) scapula and also injected at a naive site with 0.1 ml corn oil. DNCB animals similarly challenged (induced and naive animals) with 10 injection of 0.1 ml DNCB near right scapula (naive sites), and also challenged at naive sites with 0.1 ml of ethanol/saline vehicle (Test material also administered to 5 naive animals) Each injection and challenge site scored for erythema & edema @ 24 and 48 hours post injection. Body wts. days 0 & 3 (Termination).

Note: Tests conducted with product formulation minus the propellant.

Draize scale 0—3.

Results: All test animals gained weight, all test naive animals gained weight. All induced and non-induced DNCB animals gained weights.

induced
- Test (induced): 24 hrs - severity index 0.7-1.0; 48 hrs - severity index 0.8-0.8
- DNCB (induced): 24 hrs - severity index 0.4-1.0, 48 hrs - 0.3-0.6
- Test (naive): 24 hrs test → 0.7, vehicle → 0.8, 48 hrs test 0.3, vehicle 0.7.

DNCB (naive): 24 hr challenge severity score 0.4, 48 hr 0.5. vehicle 0.0 @ 24 & 48 hrs

DNCB challenged - 24 hrs severity index = 2.6, vehicle = 0.0
48 hrs = 2.6, vehicle = 0.0

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Conclusions:

1. Test material did not sensitize guinea pigs

2. DNCB control (positive control) showed did sensitize guinea pigs.