6-21-89

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 8329-GL
8329-GV
Strike 4-12 ULV
Magnum 44 ULV

FROM: William S. Woodrow WSW 6-20-89
Precautionary Review Section E 6/21/89
Registration Support Branch
Registration Division (H75-05C)

TO: LaRocca/Heyward (PM 15)
Insecticide-Rodenticide Branch
Registration Division (TS-767C)

APPLICANT: Clarke Outdoor Spraying Co., Inc.
159 N. Garden Ave.
Roselle, IL 60172

FORMULATION FROM LABEL:

(Strike 4-12 ULV)

Active Ingredient(s):	% by wt.
Permethrin (3-Phenoxyphenyl) methyl (±) cis. trans-3-(2,2-dichloroethenyl)-2,2-dimethyl-cyclopropane carboxylate	4.00
Technical Piperonyl Butoxide	12.00
Inert Ingredient(s):	84.00
Total	100.0%

(Magnum 44 ULV)

Active Ingredients:	
Permethrin (3-Phenoxy phenyl) Methyl (±) cis + trans -3-(2,2-dichloroethenyl)-2,2-dimethyl-cyclopropane carboxylate	4.00 %
Technical Piperonyl Butoxide	4.00 %
INERT INGREDIENTS:	92.00 %

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BACKGROUND:

The Clarke Spraying Co. submitted acute oral, acute dermal, acute inhalation, primary eye and dermal irritation, and dermal sensitization studies to support two products: Strike 4-12 ULV (4% Permethrin + 12% Piperonyl Butoxide), and Magnum 44 ULV (4% Permethrin + 4% Piperonyl Butoxide). MRID NOS. used were 408805-02 through 408805-07

RECOMMENDATION:

1) The acute toxicity studies submitted by Clarke Outdoor Spraying are acceptable to RSB/PRS, to support Strike 4-12 ULV (Reg. No. 8329-GU), however these data do not support Magnum 44 ULV. The acute toxicity studies currently submitted were conducted using Strike 4-12 ULV (12.00% piperonyl butoxide)

~~LABELING:~~

2) Registration of the Magnum 44 ULV product will requires submission of acute oral, dermal, inhalation, primary eye and dermal irritation, and a dermal sensitization studies, conducted using the Magnum 44 ULV formulation.

LABELING: (Strike 4-12 ULV)

1) The CAUTION label signal word is appropriate

2) The Precautionary Statements are acceptable.
3) Add the following to the Statements of Practical Treatment:

"<u>If on skin</u>: Wash with plenty of soap and water. Get medical attention.
<u>If in eyes</u>: Flush with plenty of water. Call a physician."

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

Product Manager: (15)
MRID No.: 408805-02
Testing Facility: Cosmopolitan Safety Eval.
Author(s): G.R. Robbins
Species: Rat, Sprague Dawley
Age: young adult
Weight: M 240-340, F 200-300g
Source: not given
Test Material: Strike 412 (Permethrin 47%, PB 47%), liquid
Quality Assurance (40 CFR §160.12): none

Reviewer: Woodrow
Report Date: 6-20-89
Report No. A1864
Observation Days (Post Exposure): (14); other ( )

Conclusion:

1. LD_{50} (mg/kg): Males = —; Females = —; Combined = —
2. The estimated LD_{50} is > 5.0 g/kg
3. Tox. Category: IV. Classification: Guidelines

Procedure (~~Deviations From §81-1~~): 5.0 g/kg administered to each of 5M & 5F by gavage. Animals observed for mortality and signs after day of dosing, 2x daily to 14 days & necropsy; Body wts. on day 0, weekly.

Results:

Reported Mortality

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

Symptomology & Gross Necropsy Findings:

Clinical signs: 1 hr, all rats showed yellow perineal staining. Day 1, 2 females had circumlocus. Daily 2-4 rats normal, except 3/5 females showed vaginal staining; All rats appeared normal thereafter. All rats gained weight. All organs and tissues appeared normal at necropsy.

DATA REVIEW FOR A[illegible]E DERMAL TOXICITY TESTING §81-2)

Product Manager: (15)
Reviewer: Woodrow ~~M. Waller~~
MRID No.: 408805-03
Report Date: 6-20-89
Testing Laboratory: Cosmopolitan Safety Eval. Report No. B1864
Author(s): G. R. Robbins
Species: Rabbits, NZ type
Sex: 5M+5F Wt.: ~~not stated~~ 2.5-3.5 kg.
Test Material: Strike 4-12 (4% Permethrin).
Quality Assurance (40 CFR §160.12): none

Summary:

1. LD_{50} (mg/kg): Males = —; Females = —; Combined = —;
2. The estimated LD_{50} is > 2.0 g/kg
3. Tox. Category: III. Classification: Guidelines

Procedure ~~(Deviations From §81-2)~~: 2.0 g/kg applied to clipped, intact skin of 5M+5F rabbits. Doses protected by "wraps" - 24 hour contact. Rabbits observed 14 days for mortality and toxic signs. At 14 days, rabbits subjected to necropsies.

Results:

Reported Mortality

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

Symptomology & Gross Necropsy Findings:

No pharmacologic or toxic signs. Some slight irritation at application ~~sight~~ sites. Necropsies did not reveal any tissue or organ abnormalities.

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

Product Manager: (15) Reviewer: W. Woodrow
MRID No.: 408805-04 Report Date: 6-20-89
Testing Laboratory: Cosmopolitan Safety Eva Report No. C1864
Author(s): G. R. Robbins
Species: Rat, Sprague Dawley
Sex: 5M/5F Weight: M240-340, F200-300g
Source: not given
Test Material: Strike 4-12 (4% Permethrin), liquid
Quality Assurance (40 CFR §160.12): none

Summary:

1. LC_{50} (mg/kg): Males = —; Females = —; Combined = —
2. The estimated LC_{50} is > 5.1 mg/L
3. Mean Concentration: —
4. Tox. Category: IV. Classification: Guidelines

Procedure (~~Deviations From §81-2~~): 47.4 liter exposure chamber, aerosol generation by DeVilbiss glass nebulizer, using Gast air pump. 4 hr exposure. A control group of 5M/5F was exposed 4 hours, to air only. The actual concentration measured 3X using an aerosol

Results:

Reported Mortality

Exposure Concentration (mg/L)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined

~~Symptomology & Gross Necropsy Findings~~:

analysis monitor & test. super imposed filters. Areas between filters contained activated charcoal. Samples collected at 1 liter/min. Particle size & geometric std deviation (2) measured 2X, using a Cascade Impactor.
Animals were observed for mortality & toxic signs.

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

Product Manager: (15) Reviewer: Woodruff ~~M. Waller~~
MRID No.: 408805-05 Report Date: 6-20-89
Testing Laboratory: Cosmopolitan Safety Eval. Report No. D1864
Author(s): G. R. Robbins
Species: Rabbits
Sex: not given Weight: 2.0 - 3.5 kg
Source: not given
Dosage: 0.1ml
Test Material: Strike 4-12 (4% Permethrin), liquid
Quality Assurance (40 CFR §160.12): none

Summary:

Tox. Category: III Classification: Guideline

Procedure ~~(Deviation From §81-4):~~ 0.1ml test material to 1 eye of each of 6 rabbits (conjunctival sac). Eyelids held together 1 second; treated eyes not washed. All eyes opened + scored for irritation according to Draize @ 1, 24, 48, 72 hrs.

Results:

	Observations (number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea Opacity	0/6	0/6	0/6	0/6				
Iris	0/6	0/6	0/6	0/6				
Conjunctivae Redness	6/6	3/6	1/6	0/6				
Chemosis	3/6	0/6	0/6	0/6				
Discharge	-	-	-	-				

Comments: No iris or corneal involvement. 1/6 animals 1-0 score for redness irritation @ 48 hours; absent by 3 days.

DATA REVIEW F\ SKIN IRRITATION TESTING (-5)

Product Manager: (15)
MRID No.: 408805-06
Testing Laboratory: Cosmopolitan Safety Eva
Author(s): G. R. Robbins
Species: Rabbit, N.Z. type
Age: not given
Sex: not given
Weight: 2.0—3.5 kg
Dosage: 0.5ml
Test Material: Ataflec 4-12 (4% Permethrin), liquid
Quality Assurance (40 CFR §160.12): none

Reviewer: Woodrow ~~M. Waller~~
Report Date: 6-20-89
Report No.: E1864

Summary:

The Primary Irritation Index = 0.5

Toxicity Category: III

Classification: Guidelines

Procedure ~~(Deviations From §81-5):~~ 0.5ml test material instilled under 1 sq. gauze pad held by Tape, to each of 6 clipped rabbit backs. Entire trunks wrapped ε plastic sheeting. 4 hr contact. Wrapping removed, sites wiped, 30-60min after dosing & @24, 48, 72 hrs sites scored for irritation according to Draize - (Max. score
Results: possible = 8.0

At 45min, 6/6 animals showed 1.0 for erythema, 3/6 showed edema.
At 24hrs 3/6 showed 1.0 for erythema, no edema.
At 48hrs 2/6 showed 1.0 for erythema.
At 72 hrs, no visible irritation.
A minimally irritating substance.

Special Comments:

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During exposure, & at 1, 3, 5 hrs post exposure, & 1x daily to 14 days & necropsies. Body wts at 0, 2, 3, 4, 7 & 14 days.

Results - Nominal concentration = 15.63 mg/L

The actual aerosol concentration (determined gravimetrically was:

Time	filter wt. gain	mg/L	mean
30 min	50.3	5.03	5.1 mg/L
2hr-17min	51.8	5.18	
3hr-17min	50.5	5.05	

Particle size:

MMDian = approx. 0.8μ at both 1hr 15min & at 3hrs. Geometric std. deviation = ± 2.9 & ± 3.0μ

Thus, the particles were in a respirable range.

Control rats appeared normal. Treated rats (exposed to test material), showed reduced activity, 3/5 females showed perianal staining, all animals wet on backs. Beginning day 2, all rats appeared normal. Body weight gain was comparable for treated & control rats.

Necropsies did not reveal any tissue or organ abnormalities.

No mortality.

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

Product Manager: (15)
Reviewer: Woodrow ~~M. Waller~~
MRID No.: 408805-07
Report Date: 6-20-89
Testing Laboratory: Cosmopolitan Safety Eval. Report No. E1864
Author(s): G. R. Rabkins
Species: Guinea pig
Sex: Male Weight: 300-500g
Source: Camm Res. Lab. Animals
Test Material: Stryke 4-12 (4% Permethrin), liquid
Positive Control Material: Not named.
Quality Assurance (40 CFR §160.12): none

Method: Buehler

Summary:
1. This product [is] / is not a dermal sensitizer.
2. Classification: Guidelines

Procedure ~~(Deviation From §81-6):~~ +control," periodically a known sensitizer is tested under the same conditions".

Induction: 0.5ml test material applied to clipped right sides of 10 m.g.p., under 20x20mm Webril cloth patch/adhesive tape + Trunk of g.p. wrapped c plastic wrap - 6hr contact. Wrappings removed, treated sites wiped - Each site examined and scored according to Draize @ 24 & 48 hrs, after wrap removal. This induction repeated 2 more times at weekly intervals (3 inductions total). Animals then rested 2 weeks before Challenge.

~~Results:~~

Challenge: 2 weeks after last induction application, animals challenged c 0.5ml as before (on right sides), and also on clipped left sides (virgin sites). 6hr contacts.

Re-challenge: 14 days after 1st challenge, animals again challenged on left sides, using a 2nd virgin test site. All challenge/re-challenge applications scored 24 & 48 hrs after patch removal.

Results: Challenge scores compared to as induction scores; if as - challenge score "substantially" higher

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than induction (ex.) scores, considered a + sensitizer.
+ criteria: 1) erythema score > 1 grade
2) edema score > 1 grade.
3) sum of diameter of erythema increased by more than 1 cm.

		24 hrs			48 hrs		
		induction	challenge	re challenge	induction	challenge	re challenge
Test Material	Et	1.0	1.6	1.3	1.0	1.4	1.2
	Ed	0.6	1.3	1.3	0.5	1.2	0.9
	D	2.7	3.2	3.4	2.6	3.1	3.3
Positive Control	Et	0.9	2.3		0.7	2.2	
	Ed	0.4	1.7		0.2	1.1	
	D	1.6	3.9		1.6	3.9	

Et = erythema, Ed = edema, D = dia. of erythema wheal (cm)

It may be seen in the average erythema & edema scores at 24 & 48 hours, that challenge & re challenge scores were "substantially" greater than induction scores.

Atrisk 4-12 is a dermal sensitizer - in guinea pigs.

670 Piperonyl Butoxide

Tox Chem No. 652 BB Permethrin File Last Updated _____ Current Date 6-20-89

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 Cosmopolitan Safety Eval. # A 1864. 5-15-88	Strike 4-12 ULV 4.0% Permethrin 12.0% Piperonyl Butox.	408805-02	LD_{50} > 5.0 g/kg	IV	Guidelines
Acute dermal LD_{50}, Rabbit Cos. Safety Eval. # B 1864 5-29-88	"	408805-03	LD_{50} > 2.0 g/kg	III	Guidelines
Acute inhalation LC_{50}, Rat. Cos. Safety Eval. # C 1864 6-10-88	"	408805-04	LC_{50} > 5.1 mg/L	IV	Guidelines
Primary eye irrit, Rabbit Cos. Safety Eval. # D 1864 4-22-88	"	408805-05	1/6 animals 1.0 score for redness irritation at day 2, all clear by day 3	III	Guidelines
Primary dermal irrit. Rabbits Cos. Safety Eval. # E 1864 4-20-88	"	408805-06	A minimally irritatory substance; no visible irritation by 72 hrs	III	Guidelines
Dermal sensitization, guinea pigs. Cos. Safety Eval. # F 1864 6-17-88	"	408805-07	Strike 4-12 ULV did sensitize guinea pigs	-	Guidelines

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