MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 11556-RNT
Bayocide Pour On Insecticide

FROM: William S. Woodrow WSW 8-25-92
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C)

TO: G. Latocca / John Hebert (PM 13)
Insecticide - Rodenticide Branch
Registration Division (H75-05C)

APPLICANT: Mobay Corp.
P.O. Box 390
Shawnee Mission, KS
66201

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Cyfluthrin: cyano(4-fluoro-3-phenoxyphenyl) methyl-3-(2,2-dichloroethyl)-2,2-dimethyl-cyclopropanecarboxylate	1.0
Inert Ingredient(s):	99.0
Total	100.0%

BACKGROUND

Mobay Corp. submitted acute oral, dermal, inhalation, primary eye and skin irritation, and dermal sensitization studies to support registration of Bayocide Pour ON Insecticide (EPA Reg. NO. 11556-RNT). The MRID NOS. used were: 421062-01 through 421062-06.

RECOMMENDATION

1) The acute toxicity studies submitted by Mobay are acceptable. The acute dermal study was graded Core Minimum data because female rats should have been dosed at higher dose.

2) No additional acute toxicity studies are required.

3) Current acute toxicity profile for 11556-RNT:

study	Classification	Tox. Cat.
acute oral LD_{50} = 2075 mg/kg	Guideline	III
acute dermal LD_{50} > 2000 mg/kg	Minimum	III
acute inhalation LC_{50} > 6.9 mg/L	Guideline	IV
eye irritation redness thru 7 days	Guidelines	II
skin irritation P.I. Index = 2.65	Guideline	III
dermal sensitization - negative -	Guideline	-

LABELING

1) The WARNING signal word is appropriate

2) Change the Precautionary Statements as follows:

"Causes substantial but temporary eye injury. Harmful if swallowed or absorbed through skine ~~or inhaled~~. Avoid contact with skin, eyes or clothing. Wear goggles, face shield or safety glasses. ~~Avoid breathing dust, vapor or spray mist~~. Wash thoroughly with soap and water after handling. ~~Remove contaminated clothing and wash before reuse~~"

3) Under Statements of Practical Treatment, "If on Skin:"

Change to "If on Skin: Wash with plenty of soap and water. Get medical attention."

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

Product Manager: (13) 1-16-91 Reviewer: Woodrow ~~M. Waller~~
MRID No.: 421062-01 Report Date: 8-13-92
Testing Facility: Makay Corp., Kansas Report No. 90-012-14Y
Author(s): L.P. Sheets, R.G. Gilmore
Species: Rat, Sprague Dawley
Age: young adult 10-12 weeks Observation Days (Post Exposure): (14); other ( )
Weight: M 276-356, F 197-229g
Source: Sasco, Inc., St. Louis, Mo.
Test Material: Cyfluthrin 1% Pour-on, liquid 1.05% A.I.
Quality Assurance (40 CFR §160.12): both G.L.P. + Quality Assurance
1% cyfluthrin [redacted] INERT INGREDIENT INFORMATION IS NOT INCLUDED
Conclusion:

1. LD_{50} (mg/kg): Males = 2534 (1141-3711) mg/kg ; Females = 2075 (det. by nonlin. interpol.) Combined = ____
2. The estimated LD_{50} is 2075 mg/kg (by nonlinear interpolation)
3. Tox. Category: III. Classification: Guideline

Procedure (~~Deviations From §81-1~~): 5 animals acclimated at least 6 days prior to study. All animals fasted overnight prior to dosing. 4 groups of 5M+5F each individually dosed & test material by gavage in 0.2% (v/v) Cremophor EL in deionized water ——→ (10 ml/kg).

Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
1020 mg/kg	0/5	0/5	0/10
2305 "	2/5	3/5	5/10
3375 "	4/5	5/5	9/10
5450 "	5/5	5/5	10/10

~~Symptomology & Gross Necropsy Findings:~~

Rats observed for mortality and toxic signs to 14 days post treatment; 2 x daily, 1 time weekend days.
Clinical: included ataxia, decreased activity, clear red salivation, writhing, convulsions, labored breathing.
Gross necropsy: Evidence for lacrimation, reddened lungs, reddened nasal & ventrum staining.

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

Product Manager: (13) 1-14-91 Reviewer: ~~M. Waller~~ Woodbow
MRID No.: 421062-02 Report Date: 8-13-92
Testing Laboratory: McKay Corp., Kansas Report No. 90-022-HR
Author(s): L.P. Sheets
Species: Rats, Sprague Dawley
Sex: 15M, 5F Wt.: 252-297(M), 204-233(F) grams
Test Material: Cyfluthrin 17% Power-On, liquid, 0.7 A.I.
Quality Assurance (40 CFR §160.12): both G.L.P. and G.A.

Summary: females should have been dosed at higher levels

1. LD_{50} (mg/kg): Males = 5894 (2575 - ∞) mg/kg Females = —; Combined = —; > 2000 mg/kg.
2. The estimated LD_{50} is > 2000 mg/kg.
3. Tox. Category: III. Classification: Minimum

Procedure (~~Deviations From §81-2~~): Animals acclimated to lab. conditions for at least 6 days prior to test. Dorsal & lateral hair on trunks clipped day before dosing. Females received one dose, males received 3 different doses (groups of 5 animals each).

Results: Doses applied evenly to 16 cm^2 clipped area, which were covered with gauze & secured w/ plastic and tape and Vetrap. Wrappings removed after 24 hours, sites wiped, animals observed 2x daily, once daily weekends. All animals subjected to gross necropsy exams:

Clinical signs: included red nasal, lacrimal stain, urine stain, head stain, perianal stain, decreased motor activity, ataxia.

Necropsy: evidence of lactimation and/or clear fluid in the abdomen present in all 3 dead males. Minimal alopecia on chin was only lesion found on necropsies.

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
800 mg/kg	0/5	—	
2,000 mg/kg	1/5	0/5	1/5
5000 mg/kg	2/5	—	2/5

~~Symptomology & Gross Necropsy Findings~~:

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

Product Manager: (13) 1-2-91 Reviewer: W. Woodrow
MRID No.: 421062-05 Report Date: 8-25-92
Testing Laboratory: Mobay Corp. Tox. Dept. Report No. 90-042-HW
Author(s): D.L. Warren + D.W. Sturdivent
Species: Rat, Sprague-Dawley (24 rats)
Sex: M & F Weight: M 201-231, F 174-203g
Source: Sasco, Inc., St. Louis, Mo.
Test Material: Cyfluthrin 1% Pour-On liquid
Quality Assurance (40 CFR §160.12): both G.L.P.'s + Q.A.

Summary:

1. LC_{50} (mg/kg): Males = _____; Females = _____; Combined = _____
2. The estimated LC_{50} is > 6.9 mg/L
3. Mean Concentration: _____
4. Tox. Category: IV. Classification: Guideline

Procedure ~~(Deviations From §81-2)~~: Animals acclimated for at least six days prior to test. 6 male and 6 female rats were exposed for 4 hours to 1% Cyfluthrin, while contained in a 27 liter, nose only exposure chamber.

Results:

Reported Mortality

Exposure Concentration (mg/L)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
6.9 mg/L	0/6	0/6	0/12
air alone (control)	0/6	0/6	0/12

~~Symptomology & Gross Necropsy Findings:~~

The exposure chambers (27 l each) were cylindrical (24 cm x 59 cm). Animals placed individually in restrainers + positioned at ports (nose only). Continuous air flow. Following exposure, animals observed for toxic signs + mortality. Observations

twice weekday, once/day weekends. Body weights recorded days 0, 3, 7 & 14 post exposure. A concurrent control group of animals were similarly exposed to lab. air for a 4 hour period.

Cyfluthrin 1% aerosol was generated by nebulization - Bar infusion pump delivered test material to nebulizer at 14 ml/hr. Compressed, filtered & dried air supplied to nebulizer at 14 l/m.

Nominal Conc. of test chamber determined:
wt. test mat. expended ÷ L air flow chamber in 4 hrs.

Analytical concentration measured by collecting samples near breathing zones (hourly samples) - onto .45 µ filters & analyzed by liquid chromatography

Concentrations expressed as mg/m^3

Particle size distribution determined using a TSI Aerodynamic Particle Sizer Model #3310 and Dilutor Model 3302 interfaced to an IBM PS/2-50. MMAD & GSD calculated

Results:

Chamber concentration: Average of 4 (hourly) samples = 6930 mg/m^3 = 6.9 mg/liter

Particle size distribution:

(hr into exposure) sampling time	MMAD	GSD
0.8 hrs.	1.13	1.44
2.1 hrs.	1.13	1.44
3.1 hrs.	1.44	1.45

Mortality - No mortality

Toxic signs: Male rats exhibited (4) nasal discharge, 2 rats- red nasal stain, 3 rats salivation + all 6 m showed unthriftiness:
One female showed hypoactivity, over lacrimation; one perinasal stain, 4 salivation, 5 - unthriftiness.
All animals gained weight.
Necropsy: No gross lesions, with one exception; one female had a reduced left eye.

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

Product Manager: (13) 12-5-90 Reviewer: Woodrow ~~M. Waller~~
MRID No.: 421062-04 Report Date: 8-25-92
Testing Laboratory: Mobay Corp. Tox. Dept. Report No. 90-335-HU
Author(s): L. P. Sheets
Species: Rabbit, N Z White
Sex: male (12 weeks) Weight:
Source: small stock, Industries, Atkon.
Dosage: 0.1 ml undiluted
Test Material: Cyfluthrin 1% Pour-On liquid.
Quality Assurance (40 CFR §160.12): both G.L.P. & Q.A.

Summary:

Tox. Category: II Classification: Guideline

Procedure (~~Deviation From §81-4~~): Animals acclimated at least 6 weeks prior to test. 6 animals examined 24 hours before test for eye injury and corneal defects. 0.1 ml test material placed into conjunctival sac of one eye - eyelids held closed 1 second following treatment. Treated and control eyes examined and scored for irritation at 1, 24, 48 & 72 hrs post treatment.

Results:

Observations (number "positive"/number tested)

	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea Opacity	0/6	0/6	2/6	1/6		0/6	0/2	
Iris	0/6	3/6 1	0/6	0/6		0/6	0/2	
Conjunctivae Redness	6/6 1	6/6 1	6/6 1	6/6 1		4/6 1	0/2	
Chemosis	6/6 3	6/6 2-3	6/6 1-2	6/6 1		4/6 1	0/2	
Discharge	6/6 3	6/6 2-3	3/6 1-2	3/6 1		0/6	0/6	

~~Comments~~: Eyes also examined 7 & 14 days post treatment. "Corneal opacity or irritation clearing in 8-21 days" ⇒ Cat. II

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

Product Manager: (13) 6-29-91 Reviewer: Woodrow
MRID No.: 421062-06 Report Date: 7-25-92
Testing Laboratory: Mobay Corp. Tox. Dept. Report No.: 91-925-JF
Author(s): L.P. Sheets
Species: Rabbit
Age: young adult (9-12 weeks)
Sex: not given
Weight: not stated
Dosage: 0.5ml
Test Material: Cyfluthrin 1% Pour-On, liquid
Quality Assurance (40 CFR §160.12): both G.L.P. & Q.A.

Summary:

The Primary Irritation Index = 2.65

Toxicity Category: III

Classification: Guideline

Procedure ~~(Deviations From §81-5)~~: Animals acclimated approx. 1 week prior to test. Approximately 24 hours pre-test, the back and sides of animals were shaved. 0.5ml of test material was applied to a 6-cm² area of each test animal, and was covered with a gauze patch & secured with tape. Tape was overlain with a plastic sheet. 6 rabbits tested in first study - test material applied to scarified region on dorsal midline. Ten rabbits used in follow-up study - doses (3) along dorsal mid-line of each animal:
3 doses: 1) untreated (patch + wrappings)
2) treated = Cyfluthrin 1%
3) formulating agent alone.
24-hour dermal contact. All test sites scored for

~~Results~~:

~~Special Comments~~:

erythema & edema at 30-60 min and at 24, 48 & 72 hrs after patch removed, and at 7 and 14 days. Animals also examined at 6, 8, 10 and 13 days. Apparently, the Draize scoring system was used.

Results:

1st study (6 animals) - Priming irritation index
= 2.42

2nd study (12 animals) - Priming irritation index
= 2.65

Conclusion - using results of the second study (12 animals), the Priming irritation index is 2.65

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

Product Manager: (13) 12-26-90 Reviewer: ~~M. Waller~~ Woodrow
MRID No.: 421062-03 Report Date: 8-13-92
Testing Laboratory: Mobay Corp. Report No. 90-3244
Author(s): L.P. Sheets & M.K.
Species: Guinea Pig, Hartley
Sex: Male Weight: 268-309 g
Source: Sasco, Madison WI
Test Material: Cyfluthrin 1%
Positive Control Material: DNCB - dinitro chlorobenzene
Quality Assurance (40 CFR §160.12): both G.L.P. and Q.A.

Method: Buehler closed patch.

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

Procedure (~~Deviation From §81-6~~): Pre screen conducted to determine "the highest non-irritating conc. of test material, using closed-patch technique - 24 hour exposure. Test material applied at 1, 10, 50% V/V in ~~Patients:~~ distilled water), and at 100% - 4 patches on each animal. None of these prepared materials produced any irritation. Undiluted material used to sensitize.

Induction: On day prior to start, hair clipped appropriately. Following day 0.4 ml undiluted test mat. applied to 2x2 cm Webril pad on hypo-allergenic tape backing. Adhesive tape loaded around patch served as occlusive barrier. Patches applied, and were wrapped with Vetrap & secured with Elastoplast to prevent removal. Three groups of animals: 1. 15 males, Cyfluthrin 1% Pour-on (test)
2. 5 males; challenge only
All induction and challenge performed using undiluted material.

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4 animals in test group received 3 topical applications (6 hour duration) on days 0, 7 & 14, followed by a challenge application on day 27. 4 animals in vehicle control group received only a single 24 hour challenge (on day 27 - there were non-induced animals). Induced animals were treated on left shoulders, while challenge applications were applied to left flanks for 24 hour intervals. Irritation scale used:

0 = no erythema

1 = slight, barely perceptible erythema

2 = Moderate, clearly perceptible

3 = Severe, marked erythema.

Dermal irritation scores determined 24 and 48 hours after removal of patches. Body weights recorded.

DNCB (dinitrochlorobenzene), 5 animals each sex are "periodically included in routine studies to serve as positive control evidence to show animals may be sensitized in testing lab. DNCB applied at 0.1% (W/V) in 50% (V/V) ethanol / deionized water, at a volume of 0.4ml.

Results:

a) Scores during induction = 0.0

Induced animal challenge = 0.0

b) Test control (not induced) = 0.0 (animals challenged only - using same material as that used for induced animals).

Conclusion: Not a guinea pig sensitizer

Tox Chem. No.
266E
128831 (SHA)

File Last Updated

Current date
8-13-92

Study/Species/Lab/Study# Date	Material	MRID No.	Results	Tox. Cat.	Core Grade
acute oral LD50, Rat Mobay Corp., Kansas #90-012-HY 1-16-91	Cyfluthrin 1% Pour-on liquid	421062 -01	LD50 = 2075 mg/kg (by nonlinear interpolation)	III	Guide-line
acute dermal LD50, Rat Mobay Corp, Kansas #90-022-HR 1-14-91	"	421062 -02	LD50 = >2000 mg/kg (should have dosed females at higher levels)	III	minimum
acute inhalation LC50, Rat Mobay Corp. Tox. Labs. 90-042-HW 1-2-91	"	421062 -05	LC50 > 6.9 mg/L	[redacted] IV	Guide-line
eye irritation, Rabbit Mobay Corp. Tox. Lab 90-335-HU 12-5-90	"	421062 -04	Conjunctival redness & cemosis thru day 7	II	Guide-line
skin irritation, Rabbit Mobay Corp. Tox. Lab. 91-925-JF 6-29-91	"	421062 -06	P.I. Index: 2.65	III	Guide-line
skin sensitization, guinea pig. Mobay Corp. Tox. 90-344 12-26-90	"	421062 -03	Test mat. did not sensitize guinea pigs.	—	Guide-line

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