

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):

Cyfluthrin: cyano(4-fluoro-3-phenoxyphenyl)
methoxy-3-(2,2-dichloroethyl)-2,2-
dimethyl-cyclopropanecarboxylate

% by wt.

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 doses.

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	I

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 skin ~~or inhaled~~. Avoid contact with skin, eyes or clothing. Wear goggles, face shield or safety glasses. ~~Avoid breathing~~ ~~and vapors 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
 MRID No.: 421 062 - 01 Report Date: 8-13-92
 Testing Facility: Makay Corp., Kansas Report No. 90-012-144
 Author(s): L.P. Sheets, R.G. Gilmore
 Species: Rat, Sprague Dawley
 Age: young adult 10-12 weeks Observation days (Post
 Weight: M 276-356, F 197-229g Exposure): (14); other ()
 Source: Sarco, 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
 Conclusion: 1% cyfluthrin [REDACTED]

INERT INGREDIENT INFORMATION IS NOT INCLUDED

- LD₅₀ (mg/kg): Males = 2534 (114-3711) mg/kg; Females = 2075 (det. by nonlin. interp.) Combined = 2075
- The estimated LD₅₀ is 2075 mg/kg (by nonlinear interpolation)
- Tox. Category: III. Classification: Guadalupe

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

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, clonus & 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
 MRID No.: 421062-02
 Testing Laboratory: Mobay Corp., Kansas
 Author(s): L.P. Sheets
 Species: Rats, Sprague Dawley

Reviewer: Woodrow M. Waller
 Report Date: 8-13-92
 Report No. 90-022-HR

Sex: 15M, 5F Wt.: 252-297(M), 204-233(F) grams
 Test Material: Cyflutalin 17% Pout-on; liquid J-07.A-I-
 Quality Assurance (40 CFR §160.12): both G.L.P. and O.A.

Summary: females should have been dosed at higher levels

- LD50 (mg/kg): Males = 5894(2575 - 0) mg/kg Females = > 2000 mg/kg; Combined = —;
- The estimated LD50 is 22000 mg/kg;
- 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). Doses applied evenly to 16 cm² clipped areas, which

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
800 mg/kg	0/5	—	
2000 mg/kg	1/5	0/5	1/5
5000 mg/kg	2/5	—	2/5

Symptomatology & Gross Necropsy Findings:

were covered with gauze & secured w/ plastic ant tape and Vattap. Wrappings removed after 24 hours, sites wiped, animals observed 2x daily, once daily week ends. All animals subjected to gross necropsy exams:

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

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

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. Sturdivant
 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. & Q.A.

Summary:

1. LC₅₀ (mg/kg): Males = _____; Females = _____
 ; Combined = _____
2. The estimated LC₅₀ 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 weekdays, 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. An infusion pump delivered test material to nebulizer at 14 ml/hr. Compressed, filtered & dried air supplied to nebulizer at 14 lpm.

Normal Conc. of test chamber determined:

wt. test mat. exposed ÷ l. air through chamber in whrs.
 Analyzed concentration measured by collecting samples near breathing zones (hourly samples) - onto 45 µ filter & analyzed by liquid chromatography
 Concentrations expressed as mg/m^3

Particle size distribution determined using a TSI

Aerodynamic Particle Sizer Model #3310 and Diluter Model 3302 interfaced to an IBM PS/2-50. MMAD & GSD calculated.

Results:

Chamber concentration: Average of 4 (hourly) samples = $6930 \text{ mg}/\text{m}^3 = 6.9 \text{ mg}/\text{liter}$

Particle size distribution: $\frac{\text{mg into exposure}}{\text{sampling time} \times \text{MMAD}} \times \text{GSD}$

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 antheftness.

One female showed puppo activity, one - lacerations, one petined stain, 4L salivation, 5 - antheftness.

All animals gained weight.

Macroscopy: 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: Woodward
 MRID No.: 421062-04 Report Date: 8-25-92
 Testing Laboratory: Mobay Corp. Tax. Dept. Report No. 90-335-HU
 Author(s): L.P. Sheets
 Species: Rabbit, N 2 white
 Sex: Male (12 weeks) Weight: _____
 Source: Small Stock Industries, Atkan.
 Dosage: 0.1 ml undiluted
 Test Material: Cyfluthrin 1% Packer-On liquid
 Quality Assurance (40 CFR §160.12): both G.C.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 any 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
 Results: examined and scored for irritation at 1, 24, 48 & 72 hrs post
Observations treatment.

	(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	2/6	0/6	0/6		0/6	0/2	
Conjunctivae								
Redness	0/6	6/6	6/6	6/6		4/6	0/2	
Chemosis	6/6	6/6	6/6	6/6		4/6	0/2	
Discharge	6/6	6/6	3/6	3/6		0/6	0/6	

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

Woodrow

Product Manager: (13) 6-29-91 Reviewer: M. Waller
 MRID No.: 421062-06 Report Date: 8-25-92
 Testing Laboratory: Mohan 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% Dust-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

Results: with tape. Tape was overlain with a plastic sheet. 6 rabbits tested in first study - test material applied to scraped region on dorsal midline. Ten rabbits used in follow-up study - dorsal (3) along dorsal mid-line of each animal. 3 dorsal: 1) untreated (patch & wrappings) 2) treated w/ Cyfluthrin 1% 3) formulating agent alone.

24-hour dermal contact. All test sites scored for erythema & edema at 30-60 min and at 24, 48 & 72 hrs after patch removal, 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) - Primary irritation index
= 2.42

2nd study (10 animals) - Primary irritation index
= 2.65

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

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

Product Manager: (13) 12-26-90 Woodrow
 MRID No.: 421062-03 Reviewer: M. Waller
 Testing Laboratory: Mobay Corp. Report Date: 18-13-92
 Author(s): L.P. Sheets & M.K. Report No: 90-3244
 Species: Guinea Pig, Hartley
 Sex: Male Weight: 268-309g
 Source: Sasco, Madison WI
 Test Material: Cyfluthrin 1%
 Positive Control Material: DNIB - dinitro chlorobenzene
 Quality Assurance (40 CFR §160.12): both G.L.P. and Q.A.
 Method: Buchler 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 ~~distilled~~ 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 Weibel pad on hypo-allergic tape backing. Adhesive tape border around patch served as occlusion barrier. Patches applied, and were wrapped with Vetrap & secured with Elastoplast to prevent removal. Two groups of animals:

1. 15 males, Cyfluthrin 1% Pow-on (test)
2. 5 males, challenge only

All induction and challenge performed using undiluted material.

Animals in test group received 3 topical applications (6 hour duration) on days 0, 7 & 14, followed by a challenge application on day 27. Animals in vehicle control group received only a single 24 hour challenge on day 27 - these were non-induced animals. Induced animals were treated on left shoulders, while challenge applications were applied to left hips for a re-exposure sites. 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 unwrapping. Body weights recorded.

DNCB (dinitrochlorobenzene), 5 animals each set as "periodically included in routine studies to serve as positive control evidence to show animals may be sensitive in Tarter's Lab. DNCB applied at 0.1% (W/V) in 50% (V/V) ethanol/deionized water, at a volume of 0.4 ml.

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.

266 E

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-HU 1-16-91	Cyfluthrin 1% Powder-on liquid	421062 -01	LD50 = 2075mg/kg (by nonlinear interpolation)	III	Guide- line
acute dermal LD50, Rat Mobay Corp., Kansas #90-022-HR 1-14-91	"	421062 -02	LD50 = females at >2000mg/kg higher (should have closed levels)	III	mini- mum
acute inhalation LC50, Rat Mobay Corp. Tox. Labs. 90-042-HU 1-2-91	"	421062 -05	LC50 > 6.9 mg/L	IV	Guide- line
eye irritation, Rabbit Mobay Corp. Tox. Lab 90-335-HU 12-5-90	"	421062 -04	Conjunctival redness & chemosis 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 <u>not</u> sensitize guinea pigs.	-	Guide- line