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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 275-EUP-TG
Bacillus Thuriengiensis (Berliner) Aizawai ABG-6314

FROM: Lucy D. Markarian 5/2/91
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C)

E 5/8/91

TO: Phillip Hutton / Michael Mendelsohn (PM 17)
Insecticide - Rodenticide
Registration Division (H75-05C)

APPLICANT: Abbott Laboratories
Chemical and Agricultural Product s Division
1401 Sheridan Road
North Chicago, Illinois 60064-4000

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
NO CSF OR LABEL PROVIDED	
Inert Ingredient(s):	
Total	100.0%

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BACKGROUND: Abbot Laboratories Chemical and Agricultural Division has applied for experimental use Permit for ABG-6314 under EPA Symbol 275-EUP-TG. This is a microbial pesticide Bacillus Thuriengiensis (Berliner) var. Aizawai That is supposed to be used on cabbage, Lettuce, broccoli, cauliflower, Minor Cruciferous crops, Cotton and Alfealfa. At present four studies have been submitted for review: Dermal and Inhalation Limit Tests, and Eye and Dermal irritany assays. The inhalation Test has two issues - one is a revised form of the first. The revision is in expression of milling the test material prior to the Test. The first version erroneously states that the test material was unmilled.

RECOMMENDATION:

Acute Dermal and Inhalation studies and the Acute Dermal irritation test are accepted as guideline data. The eye irritation test is accepted as core minimum data. While the discussion of the results of the test in the report acknowledges the occurrence of mild iridical hyperemia, This information does not appear in the 1 hour observations. Hyperemia, however mild, as long as it is observed must appear as an iridial effect as Grade 1 initis. It is either present or it is not, it cannot be just somewhat present and discounted. If it is mild, as it was in this case, It will be resolved in a short interval and will not change the eventual rating of the Toxicity catagory.

Similarly if There is positive staining of the eye at any interval it must be reported as opacity. In this particular

incidence the opacity should have been recorded. The explanation would have been acceptable under those circumstances also, as it is unlikely for opacity to occur. 7 days after instillation and repeated washing as fluorescein was used.

Label and CSF were not submitted. The Registrant indicated that the submitted data were "supplemental data". If oral toxicity has not been submitted 40 CFR ch I §158.740 requires that it be submitted for an experimental use permit for a microbial pesticide.

Based on the presented data the signal word is "Caution"

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

Product Manager: (17) Reviewer: L. Markarian
MRID No.: 418 533-01 Report Date: 5/8/91
Testing Laboratory: Ricerca, Inc. Report No. 90-0471
Author(s): Steven K. Shultz
Species: Rabbit, New Zealand white (Mohican Valley Rabbitry, Loudonville Ohio)
Sex: 5♂ & 5♀ Wt.: 2200 - 2750 g
Test Material: ABG-6318 Lot No 46-095 BR 15691 IU/mg 2×10^10 spores/g
Quality Assurance (40 CFR §160.12): Included

Summary:

1. LD_{50} (mg/kg): Males = _____; Females = _____; Combined = _____;
2. The estimated LD_{50} is > 2000 mg/kg
3. Tox. Category: III. Classification: Guideline

Procedure (Deviations From §81-2): The test material was applied to the shaved skin of the rabbits at approximately 4×8 inch areas (approximately 10% of body surface) by moistening it with deionized water and spreading onto skin. The sites were covered by gauze backed by Dermicel tape. The trunks of the animals were wrapped with elastic Vetrap secured with tape. Plastic collars were placed at the necks. At 24hrs bandages & collars were removed and the sites Rinsed with water and wiped with wet paper towels. Observations were frequent after the treatment and daily to fourteen days. Application site were scored for dermal
Results: irritation. Body weights were taken on days 1, 3, 7, 10 & 14. Necropsy was performed on all animals. Euthanasia was with T-61.

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
2000	0/5	0/5	0/10

Symptomology & Gross Necropsy Findings:

There was no mortality. The adverse findings included soft feces and nasal discharge are reported not to be product related. All animals showed normal gains in body weight There was some dermal irritation expressed as well defined erythema (Grade 2) and one case of Grade 1 edema. All dermal irritation subsided by day 7.

Necropsy revealed no abnormalities

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

Product Manager: (17)
MRID No.: 418533-02 Revised to 418594-01
Testing Laboratory: Stillmeadow Inc.
Author(s): Mark S. Holbert
Species: Rat, Sprague Dawley
Sex: 50♂ & 5♀ Weight: ♂ 231-289 g ♀ 212-240 g
Source: Harlan Sprague Dawley Inc. Houston Texas
Test Material: ABG 6314 Lot No 46-095-BR/LB94-010-4 (Tan powder) 12323 Tu 2 x 10^10 spo
Quality Assurance (40 CFR §160.12): included

Reviewer: L. Markarian
Report Date: 5/8/91
Report No. 7789-91

Summary:

1. LC_{50} (mg/kg): Males = _____; Females = _____; Combined = _____
2. The estimated LC_{50} is > 3.05 mg/L
3. Mean Concentration: 3.05 mg/L
4. Tox. Category: III. Classification: Guideline

Procedure (Deviations From §81-2): Exposure was in a 500L New York Glass & design stainless steel dynamic flow chamber. The aerosol was generated using a Gem T-Trost Air Mill coupled to a motor driven recessed disc delivery system and spraying into a baffling chamber. The Aerosol was diluted with filtered air and drawn into the chamber. Air flow was monitored through calibrated critical orifice. Air flow, Temperature & humidity were recorded at 30 minute intervals. The chamber atmosphere concentrations were determined gravimetrically from the breathing zone. The number of bacterial spores was determined by blending the test material in the gravimetric filter with phophate buffer (pH 7.2) and aseptically on Tryptic Soy Agar by incubating at 25°C for 48 hrs & counting CFU's

Results:

Reported Mortality

Exposure Concentration (mg/L)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
3.05	0/5	0/5	0/10

Particle size determination were made twice during the 4hr exposure by (Andersen cascade impactor) sampling from the breathing zone at 23-31 Lpm for 1.5 minutes. Animals could not be observed during exposure due to the cloudiness of the atmosphere

Animals were observed at the end of exposure (4.5hr) and at 6.0 hrs. All animals were observed daily to 14 days. Body weights were taken on days 0, 7, & 14. Necropsy was performed on all animals

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Results

Average chamber concentration was 3.05 mg/L (range 2.84 to 3.28 mg/L)

Viable BT spore concentration (CFU/L) averaged $5.8 \times 10^7 \pm 3.1$ with a range of 4.0×10^7 to 11.0×10^7

	MMAD ± S.D. um	Distribution % 2.1 - 3.3 um	1.1 - 2.1 um	< 1.1 um
1st Determination	3.055 ± 3.131	13.50	11.60	12.02
2nd Determination	3.830 ± 2.418	12.92	10.88	4.53

Immediately after removal from the chamber all animals showed decreased activity (moderate) piloerection (slight to moderate) slight polyuria, nasal discharge and salivation, additionally one male showed slight lacrimation. These symptoms subsided by 24 hrs and the animals appeared normal to the end of the observation period. All showed some gain in body weight at Termination Average male gain was 24 grams and female gain 11 grams. At necropsy There were no gross signs of pathology.

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

Product Manager: (17) Reviewer: L. Markarian
MRID No.: 418533-04 Report Date: 5/8/91
Testing Laboratory: Ricerca, Inc. Report No. 90-0473
Author(s): Steven K. Shultz
Species: Rabbit, New Zealand White (Mohican Valley Rabbitry, Loudonville, Ohio)
Age: Young Adult
Sex: 3♂ & 3♀
Weight: 2250 - 2800g
Dosage: 0.5 g 15691 Iu/mg, 2×10^{10} spores/g
Test Material: ABG-6314 Lot No 46-095 BR (Light brown granular)
Quality Assurance (40 CFR §160.12): included

Summary:

The Primary Irritation Index = 1.04

Toxicity Category: IV

Classification: Guideline

Procedure (Deviations From §81-5): The Test material was applied wetted with 0.5ml of deionized water and covered with 1 in² of gauze patch backed with 2 in² of hypoallergenic tape (Denicol) The Trunks of the animals were wrapped with elastic bandage (Vetrap) secured with tape. A plastic collar was placed around the rabbit necks for the duration of the 4hr exposure. At 4hrs the wrappings & collars were removed and the skin gently wiped with wet disposable towels. Observations were within 30 to 60 minutes of removal of the patches and at 24, 48 & 72 hrs and on days 4, 5, 6, & 7. Mortality checks were made twice a day.

Results:

Grade 2 erythema was observed at 1 & 24 hrs in 2/6 rabbits. Grade 1 erythema persisted in 2/6 to 7 days. There was no edema at any site.

Special Comments:

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

Product Manager: (17) Reviewer: L. Markarian
MRID No.: 418533-03 Report Date: 5/8/91
Testing Laboratory: Ricerca, Inc. Report No. 90-0472
Author(s): Steven K. Shults
Species: Rabbit, New Zealand white
Sex: 5♂ & 4♀ Weight: 2160 - 2650 grams
Source: Mohican Valley Rabbitry, Loudonville, Ohio
Dosage: 0.1ml (equivalent to 0.09g)
Test Material: ABG-6314 Lot No 46-095-BR 15691 IU/mg 2x10^10 spores/g
Quality Assurance (40 CFR §160.12): Included

Summary:

Tox. Category: III Classification: Core Minimum

Procedure (Deviation From §81-4): The test material was instilled in the conjunctival sacs of the right eyes of nine rabbits. Six were observed unwashed and three observed after flushing the eyes with room water. Observations were at 1, 24, 48 & 72 hrs and on days 4, 7, 10 & 14. Fluorescein was used to confirm the corneal findings at 24 hr and subsequent observation intervals.

Results:

Observations (number "positive"/number tested)

	Hour	Days						
	1	1	2	3	4	7	10	14
Cornea Opacity	*0/6	0/6	0/6	0/6	0/6	0/6	**0/6	0/6
Iris	6/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6
Conjunctivae Redness	6/6	6/6	6/6	6/6	4/6	0/6	0/6	0/6
Chemosis	5/6	2/6	0/6	0/6	0/6	0/6	0/6	0/6
Discharge	5/6	1/6***	0/6***	0/6	0/6	0/6	0/6	0/6
Purulent Discharge	0/6	4/6	5/6	1/6	0/6	0/6	0/6	0/6
Conjunctival Blistering	0/6	3/6	3/6	3/6	0/6	0/6	0/6	0/6
Conjunctival Petechial Hemorrhage	0/6	0/6	1/6	1/6	0/6	0/6	0/6	0/6

* 1/6 showed dullness of the cornea
** 1/6 showed sporadic minimal corneal opacity effect - considered not product related
*** Yellow crusting around the edges of eyelid in 6/6

Comments: Washed eyes not required. Whenever there is iridial hyperemia, even of minimal intensity, it must be noted as iridial effect and not discounted. The inclusion of this effect in the findings would not have effected the Toxicity classification.

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Tox Chem No. _____ File Last Updated _____ Current Date 5/8/91

Bacillus Thuringiensis (Berliner)
Var. Aizawai

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX. Cat.	CORE Grade/ Doc. No.
Acute Dermal Toxicity Limit Test Ricerca, Inc. 7528 Auburn Rd. Painsville, OH 20850 10-0471 1/31/91	ABG-6314 Lot 46-095BR 15691 IU/mg 2×10^{10} spores/g	418533-01	$LD_{50} > 2000$ mg/kg	III	Guideline
Acute Inhalation Toxicity Limit Test Stillmeadow Inc. 12852 Park One Dr. Sugar Land, Texas 77478 788-91 1/31/91	ABG-6314 Lot 46-095BR/ LB4-010-4 Tan powder Ball-milled potency 12 323 Iu/mg 2×10^{10} spores/g	418533-02 Revised no 418599-01	$LC_{50} > 3.05$ mg/L	III	Guideline
Acute Eye Imitation Test Ricerca, Inc 7528 Auburn Rd. Painsville, OH 20850 -0472 1/31/91	ABG-6314 Lot 46-095 BR 15691 IU/mg 2×10^{10} spores/g	418533-03	All irritation subsided by day 7	III	core minimum
Acute Dermal Imitation Test Ricerca, Inc. 7528 Auburn Rd Painsville, OH 20850 -0473 1/31/91	ABG-6314 Lot 46-095BR 15691 IU/mg 2×10^{10} spores/g	418533-04	PII 1.09	IV	Guideline