

(8-12-92)

MEMORANDUM:

Subject: EPA File Symbol/EPA Reg. No.:62637-A

From: Lucy D. Markarian, Biologist
Precautionary Review Section
Registration Support Branch
Registration Division (H7505C)

4 8/4/92

To: Phil Hutton, PM 18
Insecticide-Rodenticide Branch
Registration Division (H7505C)

Thru: Thomas C. Ellwanger, Section Head
Precautionary Review Section
Registration Support Branch
Registration Division (H7505C)

E 8/12/92

Applicant: Becker Microbial Products, Inc.
9464 N.W. 11 th Street
Plantation, Florida 33322

FORMULATION FROM LABEL:

<u>Active Ingredient(s)::</u>	<u>% by wt.</u>
Bacillus Thuringiensis, Subspecies Kurstaki	2.15 %
10,750 IU/mg	
<u>Inert Ingredient(s):</u>	
.....	97.85 %
Total:	100.00 %

1-Ingredients of the test material BMP concentrate, and their percentages present in the formulation.

2-The reasoning for the excessive moistening of the test material during the tests requiring dermal application.

3-Present a new eye study conducted with the formulation BMP 123 (49 LC). The new study by virtue of being more dilute may be in category IV toxicity, and the evaluations of the eyes in the presented study are equivocal. PRS recommends the use of the Draize scale with no modifications. Discharge must be included in the evaluations.

If the inerts of the tested product (BMP technical powder) are substantially similar to the inerts in the formulation BMP 123, and there is justification for moistening the test material to the extent that it has been moistened, then the dermal toxicity and dermal irritation tests may be acceptable as support. If this is not possible, new dermal toxicity and dermal irritation studies need to be submitted using BMP123 (48 LC).

The following is the rationale behind the rating of the tests conducted with BMP technical powder:

Oral Toxicity- Core minimum

1-The source of the animals is not specified.

2-Judged by the weights, the males were not truly young adults, at fasting weight all were over 300 grams.

Dermal Toxicity- Supplementary

1-An animal weighing 2.5 K would require 5.0 g of test material. This moistened with 9 ml of saline would be equivalent to a 1: 1.8 dilution. The guidelines call for using the test material moistened and not diluted. The form in which the product was tested does not reflect the actual toxicity of the formulation. The test may support a more dilute formulation.

2-The source of the animals is not specified.

3-60 % of the animals were above the specified weight range by the guidelines.

Inhalation Toxicity - Supplementary

1-The average particle size (5.07 um) is too large to be respirable to the test model. Percentage of particles under 2 um ranges from 11.0%-18.7 %. There is not enough uniformity in the particle size during exposure. Milling the test material prior to packing the dust generator canisters might have improved the particle size of the aerosol.

1.4) dilution and could not have given guidance. Also there is a difference in irritation between a six hour and a four hour exposure, even with species differences. The guidelines call for moistening of the test material when applied in solid form. The way it was applied in this test, it was diluted. It was not completely non irritating; therefore, it was possible to be tested at a higher concentration and perhaps cause irritation. In this sense it was not induced at the lowest irritating concentration.

2-Challenge was at the same concentration as elicitation, this was not the highest non irritating level either.

Buehler defines this concentration as that concentration that results in two grades of 0 and two of $\pm$ when tested in four guinea pigs. This was not demonstrated.

The principle on which sensitization assays work is that most assays induce at a slightly irritating concentration and elicit at a remote site at a lower non irritating concentration. If no reaction is observed with the lower challenge concentration, sensitization is not established, provided that the challenge concentration is not so low as to pass the threshold beyond which elicitation is not possible. This is the reason it is important to determine the highest nonirritating concentration for challenge. Induction and elicitation cannot be at the same concentration unless induction is at 100 %, and it was demonstrated to be completely nonirritating.

3-The guinea pigs were not restrained. Buehler states that restraining the animals is essential to the success of the test, because it improves contact between test material and skin and helps to hydrate it.

4-There were no naive controls. The base for comparison in deciding whether the formulation is a sensitizer are the reactions in the naive control animals and not the positive controls.

The only time when naive controls can be eliminated is when it is demonstrated that 100 % test material is unequivocally non irritating. This was not the case.

5-No information about the positive controls is included in the report. It is not known if the test was run within an acceptable time frame (within three months of the controls), nor were the actual results of the positive controls included. PRS prefers to reach conclusions independently, based on actual results.

6-PRS encourages the use of the Buehler grading system in a Buehler test. This avoids much confusion. It has a quantal approach and for general purposes is not graded like the Draize scale.

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

Product Manager:18

MRID No.:418266-02

Testing Facility:Cosmopolitan Safety Evaluation Inc.

Report No.A1824

Author(s):Geoffrey Robbins

Species:Rat, Sprague Dawley

Age:Young adult

Weight:229 - 309 g

Source:Unspecified

Test Material:BMP Technical (110,000 IU/mg) Lot 28 brown powder

Quality Assurance (40 CFR §160.12):Included

Reviewer: L. Markarian

Report Date:3/23/88

Conclusion:

1. The estimated LD₅₀ is > 5000 mg/kg

2. Tox. Category:IV

Classification:Core minimum ✓

Procedure (Deviations from §81-1):

Fasted animals from an unspecified source were intubated with the test material as a 50 % mixture in distilled water (20 g qs to 40 ml). Observations were at 1, 3, and 5 hours after treatment and daily thereafter. Body weights were recorded at initiation and on days 7 and 14. Necropsy was performed on all animals.

Results:

Dosage mg/kg	(Number Killed/Number Tested)		
	Males	Females	Combined
5000	0/5	0/5	0/10

Symptoms & Gross Necropsy Findings:

There was no mortality, symptom of toxicity or sin of gross pathology.

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

Product Manager:18

MRID No.: 418266-04

Testing Laboratory:Cosmopolitan Safety

Author(s):Geoffrey Robbins

Species:Rat, Sprague Dawley

Weight:M 240 - 340 g, F 200 - 300 g

Source:Unspecified

Test Material:Bmp Technical Powder 110,00 IU/mg, Lot 28, Powder
Quality Assurance (40 CFR §160.12):Included

Reviewer: L. Markarian

Report Date:4/24/88

Report No.:C1824

Summary:

1. The estimated LC_{50} is
2. Mean Concentration:
3. Tox. Category: Classification:supplementary

Procedure (Deviation From §81-3):

Two groups of ten animals were used for the test. A group exposed to the test atmosphere and a control group exposed to air only.

Exposure was in a semicylindrical, 47.4 L chamber. The test material was introduced from a portal at the top and exhausted from the bottom with a vacuum pump.

The test atmosphere was generated using a Wright dust generator and Gast Air pump supplied the air(3.0 psi). A discharge tube delivered the aerosol from the dust generator to the chamber. Exhaust was maintained at 10 lpm as measured by a flowmeter. In addition to the 240 minute exposure time was allowed for equilibration (15 Minutes).

Chamber concentrations were measured gravimetrically using an "aerosol analysis monitor" that consisted of two superimposed filters with activated charcoal between them. Sampling was from the breathing zone at ± 1 lpm for no more than 10 minutes.

Particle size determination was made four times during the exposure, using a cascade impactor (Casella).

The chamber temperature and humidity were monitored and recorded at 30 minute intervals. Mean air flow was constant at 10 lpm

Observations were hourly during the exposure. Animals were observed after being taken out of the chamber, at 1, 3, and 5 hour and daily thereafter. There were twice daily mortality checks on week days. Body weights were recorded at initiation and on days 2, 3, 4, 7, and 14.

Necropsy was performed on all animals.

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

Product Manager:18
MRID No.: 418266-05
Testing Laboratory:Cosmopolitan Safety
Author(s):Geoffrey Robbins
Species:Rabbit, NewZealand White
Sex: 4 M and 2 F
Weight:2.0 - 3.5 K
Source:Not specified

Reviewer: L. Markarian
Report Date:3/23/88
Report No.:D1824

Dosage:0.1 g

Test Material:BMP Technical Powder 110,000 IU/mg, Lot 28, Powder
Quality Assurance (40 CFR §160.12):Included

Summary:

1. Toxicity Category: **■**

2. Classification:supplementary

Procedure (Deviations From §81-4):

The test material was instilled in the conjunctival sacs of six pre examined eyes. Observations were at 1, 24, 48, and 72 hrs and on days 7 and 10 according to a scale similar to Draize. On this scale the laboratory states that grade 1 opacity is unremarkable. There is no evaluation of discharge. Although staining was positive in 5/6 eyes at 24 hrs the laboratory reports no opacity, and in the one eye where opacity is observed it seems to be in the area that did not stain. At 48 hrs no staining was done, and 4/5 eyes that had stained at 24 hrs were evaluated as negative for opacity. Yet at 72 hrs two of these still showed positive stain. They were still reported as negative for opacity. At 7 days no staining was observed in any eye, and the laboratory has claimed that the eyes had cleared. Grade 1 redness(4/6) and grade 1 chemosis (1/6) were present on day 7. All eyes are reported negative on day 10.

Results:

Observations	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	10	21
Cornea Opacity	0/6	5/6	1/6?	3/6	-	0/6	0/6	
Iris	4/6	3/6	2/6	2/6	-	0/6	0/6	
Conjunctivae								
Redness	6/6*	6/6*	6/6*	6/6*	-	4/6*	0/6	
Chemosis	5/6	4/6	4/6*	3/6*	-	1/6*	C/6	
Discharge	-	-	-	-	-	-	-	

* Grade 1 reaction, unremarkable ? Questionable observation

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

Product Manager:18

MRID No.: 418266-07

Testing Laboratory: Cosmopolitan Safety

Author(s):Geoffrey Robbins

Species:Guinea Pig, Hartley

Weight:300 - 500 g

Source:Camm Research Lab Animals, Wayne, NJ

Test Material:BMP technical Powder 110,00 IU/mg Lot 28 powder

Positive Control Material:p-phenylenediamine

Quality Assurance (40 CFR §160.12): Included

Reviewer: L. Markarian

Report Date:4/10/88

Report No.:F1824

Method:Modified Buehler

Summary:

1. This Product is / is not a dermal sensitizer.
2. Classification:Supplementary

Procedure (Deviation From §81-6):

There was no pre test screening for the definition of the induction and elicitation concentrations.

The application for induction and elicitation as a paste made of 500 mg of test material with 0.7 ml of saline (1:1.4 w/v), on the shaved right of the animals. The applications were under 20 X 20 mm Webril Cloth patch under plastic film. The trunks of the animals were wrapped in plastic wrap. Exposure was for 6 hrs. There were three inductions applied once a week for three weeks. Elicitation was two weeks after the last induction at the induction site and at a naive site. The animals were not restrained and there were no naive controls. Reference is given to a positive control test conducted with p-phenylenediamine; however, the results of the test and the time frame in which it was conducted is not included. Evaluations were at 24 and 48 hours after inductions and challenge according to Draize. The diameter of the reaction is also given.

Results:

All reactions were grade 1 erythema according to Draize as follows:

	I N D U C T I O N			C H A L L E N G E	
	I	II	III	INDUCTION SITE	NAIVE SITE
24 HRS	7/10	8/10	5/10	8/10	7/10
48 HRS	4/10	5/10	5/10	8/10	4/10

The laboratory has concluded that the test material is not a sensitizer.

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

Product Manager:18

MRID No.:419773-02

Testing Laboratory:Cosmopolitan Safety

Author(s):Geoffrey Robbins

Species:Rat, Sprague Dawley

Weight: M 241 - 268 g, F 201 - 215 g

Source:Laboratory colony

Test Material:BMP 123 (48 LC) Beige liquid

Quality Assurance (40 CFR §160.12):Included

Reviewer: L. Markarian

Report Date:7/1/91

Report No.:C3203

Summary:

1. The estimated LC_{50} is >3.59 ml/L ^{III}
2. Mean Concentration: 3.59 ml/L
3. Tox. Category:III Classification:Guideline

Procedure (Deviation From §81-3):

A test and a control group of ten animals each were use to determine the inhalation hazard potential of the test material. The test material was poured through a 20 mu sieve to separate large particles prior to exposure.

Exposure was in a 47.4 liter semicylindrical chamber with an entry port at the top for the aerosol. The exhaust portal was at the opposite side at the bottom. a vacuum pump exhausted the chamber.

The test atmosphere was generated using a DeVibliss model 841 nebulizer and a Gast air pump to supply air (pressure not given). The created aerosol was introduced into the chamber directly from the nebulizer.

Chamber concentrations were measured gravimetrically three times during the exposure. The sampling rate was 1 lpm and duration not more than 10 minutes. Two superimposed filters with activated charcoal inbetween were used for collection of the samples.

Particle size determination was made using a Casella cascade impactor twice during the test.

Chamber air flow, temperature and humidity were monitored and recorded at thirty minute intervals.

Observations were hourly during exposure, after removal from the chamber at 1, 3, and 5 hrs, and daily thereafter. There were twice daily mortality checks during week days.

Necropsy was performed on all animals.

Current Date 8/4/92

on, Inc., P.O.Box 71, Lafayette, NJ 07848

S	T	U	D	Y	M A T E R I A L	M R I D N O	R E S U L T	S	T O X C A T	C O R E G R A D E
Oral Toxicity	Limit test(Rats)	A1824	3/23/88		BMP Technical 110,000 IU/mg Lot 28 Powder	418266-02	LD ₅₀ > 5.0 g/kg	IV		Minimum
Dermal Toxicity	Limit Test(Rabbits)				" " " "	418266-03				Supplementary Upgradable
B1824	3/29/88									
Inhalation Toxicity	Limit Test (Rats)	C1824	4/24/88		" " " "	418266-04				Supplementary
Eye Irritation	in Rabbits	D1824	3/23/88		" " " "	418266-05	Clear on day 7			Supplementary
Dermal Irritation	in Rabbits	E1824	3/16/88		" " " "	418266-06				Supplementary Upgradable
Sensitization	in Guinea Pigs	F1824	4/10/88		" " " "	418266-07				Supplementary
Oral Toxicity	Limit Test(Rats)	A32C3	5/27/91		BMP 123 (48 LC) Lot 5123481	419773-01	LD ₅₀ > 5.0 g/kg	IV		Guideline
Inhalation Toxicity	Limit Test	C2203	7/1/91		" " " "	419773-02	LC ₅₀ > 3.59 mg/L	III		Guideline

Body weights were recorded at initiation and on days 2, 3, 4, 7 and 14.

Necropsy was performed on all animals.

Results:

	Test	Control
Chamber Concentration		
Gravimetric mg/L		
Average	3.19	-----
Range	3.08 - 3.32	
MMAD $\pm$ SGD μm		
Average	2.55	
I	2.3 $\pm$ 4.6	
II	2.8 $\pm$ 4.3	
% < 2 μ m		
I	35.4	
II	29.6	
Air Flow lpm	10 lpm	10 lpm
Temperature range $^{\circ}$ F	74 - 86	74 - 86
Humidity Range %	51 - 84	58 - 84
Mortality		
Males	0/5	0/5
Females	0/5	0/5
Combined	0/10	0/10
Signs of Toxicity		
During Exposure	Test material on fur Decreased response to tapping on wall	None
Post exposure	Chromorhinorrhea Decreased locomotion	
Days 1 - 14	Normal	
Necropsy Findings	None	None

BMP 123 (32 LC)
High Potency Biological Larvicide
Aqueous Suspension

ACTIVE INGREDIENT: Bacillus thuringiensis subspecies kurstaki,
Lepidopteran active toxins.....1.60%
INERT INGREDIENTS.....98.40%
POTENCY: 8,000 International Units (IU) per milligram (Equivalent
to 32 Billion IU/gallon; 8.45 Billion IU/liter)
Potency units should not be used to adjust use rates
beyond those specified in the Directions for Use Section.

TOTAL.....100.00%

KEEP OUT OF REACH OF CHILDREN

CAUTION: See additional precautionary statements and statements of practical treatment on side/back panel.

BMP 123 (32 LC) is a highly selective microbial larvicide effective against lepidoptera in a variety of habitats.

BENEFICIAL INSECTS: Honey bees which feed in areas treated with BMP 123 (32 LC) are not harmed by the product. BMP 123 (32 LC) does not affect the activities of parasitic and predaceous arthropods in integrated pest management programs.

DIRECTIONS FOR USE: It is a violation of federal law to apply this product in a manner inconsistent with its labeling.

BMP 123 (32 LC) is a highly selective, microbial larvicide for use against the listed lepidopterous insects. Close scouting and early attention to insect infestations are recommended. BMP 123 (32 LC) must be ingested to be effective. The following directions should always be followed:

1. Larvae must be actively feeding on exposed plant parts.
2. Applications should be made when larvae are in the early instars before extensive crop damage occurs. For control of mixed insect populations or overlapping generations, use BMP 123 (32 LC) in combination with another approved insecticide.
3. Thorough spray coverage with BMP 123 (32 LC) is required for consistent control. Spray nozzles and volume applied will vary depending on crop and pest. Under heavy pest pressure, higher rates, increased gallonage, and shorter spray intervals will improve crop coverage and pest control.

Crop	Pest	Ounces/Acre
Sunflowers	Loopers	32 to 64
Peanuts	Green Cloverworms	16 to 32
Safflower	Velvetbean	
Mint	Caterpillar	16 to 32
Canola	Podworm*	32 to 64
Rape	Armyworms	32 to 64
Cereal Grains	Diamondback	
Amaranth	Moth	32 to 64
Jojoba	Saltmarsh	
Okra	Caterpillar	32 to 64
Pawpaw	Hornworms	16 to 32
Lentils	Heliothis spp.***	32

* BMP 123 (32 LC) can be used to suppress podworm in an integrated pest management program.
 ** Suppression Only.

Crop	Pest	Ounces/Acre
Artichokes	Artichoke Plume	
	Moth	32 to 80
	Armyworms	32 to 96
	Loopers	16 to 80

Cotton	Tobacco Budworm*	32 to 64
	Cotton Bollworm*	32 to 64
	Loopers	32 to 64
	Cotton Leaf	
	Perforator	32 to 64
	Cotton Leafworm	32 to 64
	Saltmarsh	
	Caterpillar	32 to 64
	Armyworms	32 to 96

*Use in conjunction with regular scouting in an integrated pest management program when beneficial insects are present. Applications should be made against light to moderate populations of 1st and 2nd instar larvae. Repeat applications at 3 to 5 day intervals as required and as long as population suppression is satisfactory. For added control of budworms and bollworms, tankmixing of BMP 123 (32 LC) with an approved ovicide is recommended. Read and follow all precautions and restrictions on ovicide labels.

Crop	Pest	Ounces/Acre	
		Ground *	Air**
Forest	Gypsy Moth	32 to 128	32 to 128
Shade Trees	Eastern Tent		
Schrubs	Caterpillars	16 to 32	16 to 32
Ornamentals	Spruce Budworm	32 to 96	32 to 96
Sugar Maple Trees	Douglas Fir		
	Tussock Moth	16 to 64	16 to 64
	Western Tussock		
	Moth	16 to 32	16 to 32
	Browntail Moth	16 to 32	16 to 32
	Bagworm	8 to 16	8 to 16
	Spring and Fall		
	Cankerworms	16 to 32	16 to 32
	Elm Spanworm	16 to 32	16 to 32
	Fall Webworm	16 to 32	16 to 32
	California		
	Oakworm	16 to 32	16 to 32
	Redhumped		
	Caterpillar	16 to 32	16 to 32
	Pine Butterfly	32 to 48	32 to 48
	Blackheaded		
	Budworm	32 to 48	32 to 48
	Jack Pine Budworm	32 to 64	32 to 64
	Mimosa Webworm	16 to 32	-
	Saddle Prominent		
	Caterpillar	16 to 32	16 to 32
	Saddleback		
	Caterpillar	16 to 32	16 to 32
	Fruittree		
	Leafroller	16 to 32	-
	Forest Tent		
	Caterpillar	16 to 32	16 to 32

*Ground applications are made at the rate of 100 gallons per acre for hydraulic sprayers. For mist blowers mix the applicable amount in ten gallons of water.

**Use 1/2 to ten gallons of water depending on the type and density of tree.

Crop	Pest	Ounces/Acre	
		Ground	Air
Pome Fruits*	Gypsy Moth	32 to 96	32 to 96
	Cankerworms	16 to 32	16 to 32
	Tent		
	Caterpillars	32 to 64	32 to 64
	Tufted Apple		
	Budmoth	32 to 64	--
	Variegated		
	Leafroller	32 to 64	--
	Redbanded Leafroller	32 to 64	--
Citrus**	Fruittree		
	Leafroller	32 to 64	--
	Citrus Cutworm	32 to 64	32 to 64
	Orangedog	16 to 32	--
Avocado	Loopers	32 to 128	32 to 128
	Orange Tortrix	32 to 64	32 to 64
	Omnivorous		
	Leafroller	32 to 64	32 to 64
	Amorbia	64	--

Crop	Pest	Ounces/Acre	
		Ground	Air
Tropical Fruits***	Hornworm	32 to 128	--
Papayas	Leafrollers	32 to 128	--
Mangoes	Omnivorous Looper	32 to 128	--
Kiwi	Loopers	32 to 128	--
Persimmons			
Pomegranate			
Bananas****	Banana Skipper	24 to 64	--

*Apply BMP 123 (32 LC) in 450-450 gallons/acre for pest suppression in pest management programs.

**Apply in 100 to 400 gallons per care.

***Apply at least 200 gallons per acre.

****Hawaii Only, Ground Equipment Only, Apply to the Point of Runoff.