MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 275 - EUP - TG
    Bakillus Thuringienis (Btlineri) Aizawai  AB36-6319

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

TO: Philip Hutcheson / Michael Mendelson (PM17)
    Insecticide - Rodenticide
    Registration Division (H75-05C)

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

FORMULATION FROM LABEL:

Active Ingredient(s): NO CSF OR LABEL PROVIDED

Inert Ingredient(s): ...................................

Total 100.0%
BACKGROUND: Abbott Laboratories' Chemical and Agricultural Division has applied for experimental use permit for AB6-6314 under EPA symbol 275Z-EUP-TG. This is a microbe in a particle Bacillus Thuringiensis (Berliner) var. Aizawa. That is supposed to be used on cabbage, lettuce, broccoli, cauliflower, sweet Cruciferae crops, cotton and alfalfa. At present, four studies have been submitted for review: dermal and inhalation Limit Tests and Eye and Dermal irritation 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 iridal hyperemia, this information does not appear in the 1 hour observation. Hyperemia, however mild, as long as it is observed must appear as an initial effect as grade 1 iritis. 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 recorded in a short interval and will not change the eventual rating of the Toxicity category.

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 explantion
would have been acceptable under those circumstances also, as
it is unlikely for opacity to occur 7 days after initiation
and repeated washing as fluorescein was used.

The Registrant indicated that Labed and CSF were not submitted. It indicated that
the submitted data was "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: ( ) Reviewer: L. Markarian
MRID No.: 412 S33-01 Report Date: 5/2/81
Testing Laboratory: Riceco, Inc. Report No. 96-0471
Author(s): Steven K. Shultz
Species: Rabbit, New Zealand White (Mohave Valley Rabbitry, Lambdale, CA)
Sex: 50% M & 5% Wt.: 2200 - 2750 g
Test Material: ABG-63d Lot No. 46-095 Bc 15691 IU/mg 2×10³ pm/4
Quality Assurance (40 CFR §160.12): Included

Summary:

1. LD₅₀ (mg/kg): Males = ______; Females = ______
   Combined = ______
2. The estimated LD₅₀ is > 2000 mg/kg
3. Tox. Category: ______ Classification: Guideline

Procedure (Deviations From §81-2): The test material was applied to the
shaved skin of the rabbits at approximately 4-8% body area (approx. 4% body
surface) by maintaining it with desangled water and spread over skin. The sites
were covered with gauze bandaged by Dermagrap tape. The heads of the animals were
wrapped with plastic. Jockstrap were placed
at the heads. At 5-6 hours after the excision the bandages were removed and the sites
quickly washed with soap and water and wiped with wet paper towels. Observations were frequent after the
Treatment and daily for fourteen days. Application sites were scored for dermatol
Results: Irritation. Body weights were taken on days 1, 3, 7, 10, and 14. Necropsy
was performed in all animals. Euthanasia was with T-61.

Reported Mortality

<table>
<thead>
<tr>
<th>DOSAGE (mg/kg)</th>
<th>(NUMBER KILLED/NUMBER TESTED)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3000</td>
<td>Males Females Combined</td>
</tr>
<tr>
<td></td>
<td>0/0 0/0 0/0</td>
</tr>
</tbody>
</table>

Symptomology & Gross Necropsy Findings:

There was no mortality. The adverse findings included

- soft faces and nasal discharge were reported not to be
- present related. All animals showed normal gain in body weight.
- There was some normal irritation expressed as well defined erythema
(Grade 2) and one case of Grade 1 ehrlich. All dermal irritation
- ensued by day 7.

Necropsy revealed no abnormalities.
DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3)

Product Manager: (17) Reviewer: L. Markarian
MPID No.: 418533-02 Revised 418594-01 Report Date: 5/2/84
Testing Laboratory: Stillwater Inc.
Author(s): Mark S. Holbert
Species: Rat, Sprague-Dawley
Sex: 50/50 50/50
Weight: 372/31.89 72/12.12 254/5.3
Source: Hadac Sprague-Dawley Inc., Houston, Texas
Test Material: AB 631, Lot No. 65-045-025, LB 6-040-014 (tan powder)
Quality Assurance (40 CFR §160.12): Included

Summary:
1. LC50 (mg/kg): Males = __________; Combined = __________; Females = __________
2. The estimated LC50 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 Soc'l New York Union's design stainless steel dynamic flow chamber. The aerosol was generated using a GenTec Air Mill coupled with a motor-driven recirculation delivery system and sprayer into a baffling chamber. The aerosol was diluted with filtered and heated air into the chamber. Air flow was maintained through a calibrated critical orifice. Air flow parameters were recorded at 60-minute intervals. The average atmosphere concentrations were determined geometrically over one hour from the beginning of the exposure. The number of rats exposed was determined by mixing the test material in the geometric filter with propylene glycol (1:3). Results: and continued on Tricolor Day After by incubating at 25°C for 48 hours before 

<table>
<thead>
<tr>
<th>Exposure Concentration (mg/L)</th>
<th>(NUMBER KILLED/NUMBER TESTED) Males</th>
<th>Females</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.05</td>
<td>0/5</td>
<td>0/1</td>
<td>0/10</td>
</tr>
</tbody>
</table>

Particle size determination was made twice during the air exposure. By (Andrew sampling) from the breathing zone at 2:00-3:00 pm for 1.5 minutes. Animals disposed of during exposure due to the chronic nature of the atmosphere.

Animals were observed at the end of exposure (9:00) and at 6:00 next day. All animals were observed daily for 14 days. Daily weight were taken in day 1

Day 7, ± 14. Necropsy was performed on all animals.
Results

Average chamber concentration was 3.05 mg/L (range 2.34 to 3.28 mg/L).

Usable BT spray concentration (CFU/L) averaged 5.3 x 10^7 ± 3.1 with a range of 4.0 x 10^7 to 11.0 x 10^7.

<table>
<thead>
<tr>
<th>MMAD ± SD</th>
<th>Distribution ± %</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1-3.3 µm</td>
<td>13.50 ± 11.60</td>
</tr>
<tr>
<td>1.1-2.1 µm</td>
<td>12.02 ± 4.63</td>
</tr>
<tr>
<td>≤ 1.1 µm</td>
<td></td>
</tr>
</tbody>
</table>

Immediately after removal from the chamber, all animals showed decreased activity (malaise), piloerection (shivering), slight palpebral, nasal discharge, and salivation. Additionally, one male showed slight lacrimation. These symptoms subsided by 24 hrs and the animals appeared normal by 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)  
MRID No.: 418535-04  
Testing Laboratory: Research, Inc.  
Author(s): Steven K. Shell  
Species: Rabbit, New Zealand White (Mohawk Valley Rabbitry, Loudonville, Ohio)  
Age: Young Adult  
Sex: 2♂ & 3♀  
Weight: 2200 - 2700g  
Dosage: 0.5ml 1569/15mg, 2 x 106 spores/l  
Test Material: ABE-6314 Lot No. 46 - 045 B2 (light brown granule)  
Quality Assurance (40 CFR §160.12): Included

Summary:

The Primary Irritation Index = 1.04

Toxicity Category: I

Classification: Guideline

Procedure (Deviations From §81-5): The test material was applied wetted with 0.5% of deionized water and covered with 1.5m² of gauge patch backed with 2m² of hypoallergenic tape (Tensoplast). The trunks of the animals were wrapped with elastic bandage (Vetrap) secured with tape. A plastic collar was placed around the neck and the site of application. At the end of the course, the wrapping and bandages were removed and the skin gently wiped with wet disposable towels. Observations were made within 30 to 60 minutes of removal of the patches and at 24, 48, and 72 hrs and 14 days. Mortality checks were made twice a day.

Results:

Grade 2 erythema was observed at 24 hrs in 3/4 rabbits.

Grade 1 erythema persisted in 3/4 to 7 days. There was no edema at any site.

Special Comments:
DATA REVIEW FOR ACUTE EYE IRRIGATION TESTING (§81-4)

Product Manager: (17)  
Reviewer: L. Markarian  
MRID No.: 418533-03  
Report Date: 5/17/41  
Testing Laboratory: Rivera Lab.  
Report No. 90-0472  
Author(s): Steven K. Shultz  
Species: Rabbit, New Zealand white  
Sex: 50% male  
Weight: 2100 - 2600 grams  
Source: Mexican Valley Rabbitry, Louisville, Ohio  
Dosage: 0.1 ml (equivalent to 0.02%)  
Test Material: ABG-6314 Lot No. 46-095-B 1594.14 u/l  
Quality Assurance (40 CFR §160.12): Included  

Summary:

Tox. Category:  
Classification: Corneal Minimum  

Procedure (Deviation From §81-4): The test material was instilled in the conjunctival sac of the right eye of nine rabbits. Six were observed immediately, three observed after lid closure the eyes with weak lighter. Observations were at 1, 24, 93, 12, and 24 days. Fluorescein was used to confirm the corneal findings at 24 hr and subsequent observation intervals.

Results:

<table>
<thead>
<tr>
<th></th>
<th>(number &quot;positive&quot;/number tested)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hour 1</td>
</tr>
<tr>
<td>Cornea Opacity</td>
<td>4%</td>
</tr>
<tr>
<td>Iris</td>
<td>6%</td>
</tr>
<tr>
<td>Conjunctivae Redness</td>
<td>6%</td>
</tr>
<tr>
<td>Chemosis</td>
<td>6%</td>
</tr>
<tr>
<td>Discharge</td>
<td>6%</td>
</tr>
<tr>
<td>Purulent Discharge</td>
<td>0%</td>
</tr>
<tr>
<td>Conjunctival Petechiae</td>
<td>6%</td>
</tr>
<tr>
<td>Conjunctival Petechiae</td>
<td>0%</td>
</tr>
</tbody>
</table>

Comments: Washed eyes were required. When 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 affected the toxicity classification.
<table>
<thead>
<tr>
<th>Study/Lab/Study &amp; Date</th>
<th>Material</th>
<th>EPA Accession No.</th>
<th>LD₅₀, LC₅₀, PIS, NOEL, LEI</th>
<th>TOX, CORE Grade/ Doc. No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Dermal Toxicity Limit Test</td>
<td>A BG-6314 Lot 46-095 BR 15691 IU/mg 2 x 10⁹ spores/g</td>
<td>418533-02</td>
<td>LD₅₀ &gt; 2000 mg/kg</td>
<td>III Guideline</td>
</tr>
<tr>
<td>Acute Inhalation Toxicity Limit Test</td>
<td>A BG-6314 Lot 46-095 BR/LB9-010-4 Tan powder Ball-milled potency 12,828 IU/mg 2 x 10⁹ spores/g</td>
<td>418533-04</td>
<td>LC₅₀ &gt; 3.05 mg/L</td>
<td>III Guideline</td>
</tr>
<tr>
<td>Acute Eye Irritation Test</td>
<td>A BG-6314 Lot 46-095 BR 15691 IU/mg 2 x 10⁹ spores/g</td>
<td>418533-04</td>
<td>No irritation observed by day 7</td>
<td>III Guideline</td>
</tr>
<tr>
<td>Acute Dermal Irritation Test</td>
<td>A BG-6314 Lot 46-095 BR 15691 IU/mg 2 x 10⁹ spores/g</td>
<td>418533-04</td>
<td>PI 1.0</td>
<td>IV Guideline</td>
</tr>
</tbody>
</table>