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SUBMISSION #

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TYPE OF PRODUCT(S) : I,D,H,F,N,R,S Biological Insecticide

DATA ACCESSION NO(S). \_\_\_\_\_

PRODUCT MANAGER (NO:.) Mike Mendelsohn/Phil Hutton (PM18)

PRODUCT NAME(S) Centari - Bacillus thuringiensis Berliner  
subsp. aizawai (ABG-6305). Strain ABTS-1857

COMPANY NAME Abbott Laboratories

SUBMISSION PURPOSE Section 3 registration

SHAUGHNESSY NO.	CHEMICAL & FORMULATION(S)	% A.I.
_____	<u>Bacillus thuringiensis subsp. aizawai</u>	<u>10.3</u>
_____	_____	_____

## EEB REVIEW

Pesticide Name Centari - *Bacillus thuringiensis* Berliner subsp. aizawai (ABG-6305). Strain ABTS-1857.

### 100.0.0 SUBMISSION PURPOSE AND LABEL INFORMATION

#### 100.1.0 Submission Purpose and Pesticide Use

Abbott Laboratories has requested a Section 3 Registration for Centari, which has *B. thuringiensis* subsp. *aizawai* as the active ingredient. The product is active against lepidopterous larval pests of trees, field crops, and stored agricultural commodities.

#### 100.2.0 Formulation Information

Water Dispersible Granule Biological Insecticide

Active Ingredient: <i>B. thuringiensis</i> subsp. <i>aizawai</i> .....	10.3% w/w.
Inert Ingredients: .....	89.7% w/w.
Total:.....	100.0%

Potency: 35,000 diamondback moth units/mg

#### 100.3.0 Application Methods, Directions, and Rates

Centari can be applied by conventional or aerial application equipment in enough water to adequately cover target plant parts (3 to 100 gallons/acre). Approved sticker-spreaders can be used to improve deposition and/or weather-fastness of spray deposits. Agitate tank mix continuously during mixing and application. Repeat applications when necessary, usually 3 to 14 days depending upon rainfall, plant growth rate, age of pest larvae, and degree of pest infestation. Centari can be applied up until the time of harvest. Centari can be tank mixed with other compatible labeled insecticides to enhance control. Use all mixed Centari within three days.

Application rates on field crops and trees range from 1/4 to 2 3/4 lbs/acre. See attached label for recommended rates for individual pest species on specific crops. For control of lepidopterous pests of stored agricultural commodities the application rate is 3/8 lb/100 bu. As a stored grain surface treatment mix into the top four inches 1/2 lb Centari in 5-10 gal of water/500 ft<sup>2</sup> of grain surface area. For stored peanuts mix 1/4 lb/ton into the top four to eight feet of nuts.

#### 100.4.0 Target Organisms

Lepidopterous insect pests of trees, field crops, and stored agricultural commodities. See attached label for complete listing of species.

### 100.5.0 Precautionary Labeling

The label contains the following precautions:

KEEP OUT OF REACH OF CHILDREN

CAUTION

HAZARDS TO HUMANS AND DOMESTIC ANIMALS (adequate)

STORAGE AND DISPOSAL (adequate)

No mention of hazards to beneficial insects or freshwater aquatic invertebrates. Precautionary labeling is necessary in these cases due to toxicity of ABG-6305 to honey bees, predatory mites, and *Daphnia*.

### 101.0.0 HAZARD ASSESSMENT

#### 101.1.0 Discussion

The *B. thuringiensis* subsp. *aizawai* isolate used as the a.i. in this product is an indigenous naturally occurring bacterium isolated from a Wisconsin soil in 1987. Its flagellar antigens react only with anti-H7 antibody, thus it is classified as serotype H-7. The isolate is somewhat unique in that it produces two crystals per cell under normal fermentation conditions. There was no detectible  $\beta$ -exotoxin in the ABG-6305 technical powder when examined by both HPLC and *Musca domestica* L. larval bioassay. However, the fly larval bioassay indicates that ABG-6305 technical powder contains an unidentified heat-labile toxin, which is possibly  $\alpha$ -exotoxin.

Review of the submitted studies indicate that there is some intrinsic toxicity to aquatic invertebrates (*Daphnia magna*), nontarget arthropods (predatory mite, *Metaseiulus occidentalis*; and green lacewing, *Chrysoperla carnea*), and honey bees (*Apis mellifera*). Since sterile culture filtrate and purified, well washed spore-crystal complex were not tested it is not possible to determine what is responsible for the unexpected nontarget activity.

Since its requested label uses (terrestrial food and nonfood, greenhouse food, forestry, and indoor) includes application to aquatic environments (forestry use), an acute risk to aquatic invertebrates may be expected. As ABG-6305 is slightly to somewhat toxic to predaceous arthropods at field dosages, it is expected that when CenTari is used in situations where such natural enemies are exerting a significant degree of natural control that said control will be reduced. Because ABG-6305 is highly toxic to adult honey bees, EEB recommends that a precautionary statement regarding honey bee toxicity be added to the label.

## 101.2 LIKELIHOOD OF ADVERSE EFFECTS TO NONTARGET ORGANISMS

### Avian Studies

When administered by oral gavage at 1.71 g/kg body weight daily for 5 days, ABG-6305 had no apparent adverse effects upon mallard ducks or bobwhite quail over a period of 30 days. In both cases the estimated LC<sub>50</sub> exceeded 8.57 g/kg. Based on these results, no avian hazard is expected from the proposed uses of the *B. thuringiensis* product Centuri.

### Fish Studies

A 96 hr static renewal toxicity test using rainbow trout was conducted using 100 mg/l of ABG-6305. No mortality or sublethal effects were observed in the 96 hr test period. As ABG-6305 contains living spores, a valid 30 day toxicity and pathogenicity test is required for registration [Section (b)(6) 154A-19 Subdivision M].

### Mammalian Wildlife

These studies are required only when toxicology data are inadequate for assessment of hazard to wild mammals. The anticipated low exposure of mammalian wildlife during use of this microbial pest control agent indicates that risk to wild mammals from the proposed uses of Centari is minimal.

### Aquatic Invertebrate Studies

A 21 day static renewal toxicity and pathogenicity study of ABG-6305 was conducted using *Daphnia magna*. The estimated EC<sub>50s</sub> were 0.8 ppm when the daphnids were held individually, and 2.7 ppm when they were held multiply, indicating that ABG-6305 may be moderately to highly toxic to *D. magna*. The NOEL and LOEL were 0.07 and 0.97 ppm, respectively, for first generation survival, number of young produced, and dry weight of survivors. The NOEL and LOEL for time to first brood were 0.97 and >0.97 ppm, respectively. EEB recommends that an accurate LE<sub>50</sub> be determined by repeating the toxicity tests using a graded series of dilutions (minimum of five, preferably seven) where about 0-5%, and 90-100% mortality is expected at the lowest and highest dosages, respectively. In addition, a sterile fermentation culture filtrate should be used as one of the controls in order to determine if the unexpected activity against *D. magna* is due to an exotoxin which is contaminating the ABG-6305 spore-crystal preparation.

### Estuarine and Marine Animal Studies

None submitted. These studies would need to be submitted prior to the use of this product on or near estuarine or marine environments.

### Honey Bee Studies

Nine to twelve day feeding studies indicate that ABG-6305 is highly toxic *per os* to adult worker honey bees. The calculated  $LE_{50}$  is 15 ppm with 95% confidence limits of 10-21 ppm. The  $LT_{50}$  of the highest dose tested (1000 ppm) was 6.7 days. The Centari label should contain the statement that its use could be hazardous to honey bees depending upon the degree of contamination of plant pollen and nectar by Centari, and to the degree that honey bees are utilizing that pollen and nectar.

### Nontarget Beneficial Insect Studies

1. Parasitic Hymenoptera (*Trichogramma pretiosum*, egg parasite): Invalid study due to excessive untreated control mortality (50%).
2. Predatory mite (*Metaseiulus occidentalis*): ABG-6305 is somewhat toxic to *M. occidentalis*. The recommended field dosage (2.4 g/l) killed about 24% of the treated gravid females. The estimated  $LC_{50}$  was approximately 300 g/l. The use of the product Centari on crops where *M. occidentalis* is exerting a significant degree of natural control of pest mites would probably reduce the level of that control.
3. Green lacewing larvae (*Chrysoperla carnea*): ABG-6305 is toxic (61% mortality) to *C. carnea* at the 10X field rate (24 g/l). ABG-6305 is slightly toxic (17% mortality) to *C. carnea* larvae at the recommended field rate of 2.4 g/l (1 lb/acre), although the mortality at this rate is not significantly different from the 5% control mortality. The use of Centari on crops where *C. carnea* is responsible for some amount of natural control of a pest insect would probably slightly lessen the degree of that control.

### 101.3 ENDANGERED SPECIES CONSIDERATIONS

This product may be expected to be used throughout the United States with possible exposure to all endangered/ threatened species that are susceptible to the *Bacillus thuringiensis* subsp. *aizawai* delta endotoxin. Based on the toxicity and exposure data, EEB feels that there will not be a "may effect" situation for endangered mammals, birds, plants and noninsect aquatic species.

The use of Centari insecticide in California, Colorado, Florida, Indiana, Michigan, Minnesota, New Hampshire, Oregon, Washington, and Wisconsin, however, may affect endangered lepidopteran insect species. Based on information available to EEB, the following are counties in which the use of anti-lepidopteran *Bacillus thuringiensis* delta endotoxin may result in hazard to endangered/threatened lepidopteran species:

<u>County, State</u>	<u>Species of Concern</u>
Alameda, CA	Bay checkerspot butterfly
Contra Costa, CA	Lange's metalmark butterfly
Kern, CA	Kern primrose sphinx moth
Los Angeles, CA	El Segundo blue butterfly
	Palos Verdes blue butterfly
Marin, CA	Misson blue butterfly
	Myrtle's silverspot butterfly
Mendocino, CA	Lotis blue butterfly
Monterey, CA	Smith's blue butterfly
San Francisco, CA	Mission blue butterfly
San Mateo, CA	Mission blue butterfly
	San Bruno elfin butterfly
Santa Clara, CA	Bay checkerspot butterfly
Sonoma, CA	Myrtle's silverspot butterfly
Chaffee, CO	Uncompahgre fritillary butterfly
Douglas, CO	Pawnee montane skipper
Gunnison, CO	Uncompahgre fritillary butterfly
Hinsdale, CO	Uncompahgre fritillary butterfly
Jefferson, CO	Pawnee montane skipper
Park, CO	Pawnee montane skipper
Teller, CO	Pawnee montane skipper
Dade, FL	Schaus swallowtail butterfly
Monroe, FL	Schaus swallowtail butterfly
Lagrange, IN	Karner blue butterfly
Lake, IN	Karner blue butterfly
Porter, IN	Karner blue butterfly
Allegan, MI	Karner blue butterfly
Lake, MI	Karner blue butterfly
Montcalm, MI	Karner blue butterfly
Muskegon, MI	Karner blue butterfly
Newaygo, MI	Karner blue butterfly
Oceana, MI	Karner blue butterfly
Winona, MN	Karner blue butterfly
Merrimack, NH	Karner blue butterfly
Clatsop, OR	Oregon silverspot butterfly
Lane, OR	Oregon silverspot butterfly
Tillamook, OR	Oregon silverspot butterfly
Pacific, WA	Oregon silverspot butterfly

#### Reasonable and prudent alternatives

The 1978 Amendments to the Endangered Species Act include a mandate that "reasonable and prudent alternatives" be provided when a US Fish

and Wildlife Service Biological Opinion indicates a jeopardy to a listed species. The US Fish and Wildlife Service Biological Opinion, dated January 12, 1987, provides the following reasonable and prudent alternative for the use of *Bacillus thuringiensis* anti-lepidopteran delta endotoxin):

Anti-lepidopteran delta endotoxin, or any formulations thereof, should not be aerially applied within 1/4 mile of any habitats of endangered or threatened Lepidoptera. No manual application should be made within 300 feet of any threatened or endangered Lepidoptera.

1. In California these measures are to be applied to the following species and the area of concern:

Lotis blue butterfly - Mendocino County - 3 miles south of Mendocino City to Fort Bragg along a 2 mile corridor along Highway 1.

Lange's metalmark butterfly - Contra Costa County - Antioch Sand Dunes Wildlife Refuge.

Mission blue butterfly and San Bruno elfin butterfly - San Mateo County - San Bruno Mountain, Milgara Ridge, Skyline College (Guadalupe Canyon Parkway), Sweeney Ridge, and Montana Mountain.

Smith's blue butterfly - Monterey County - Seaside Marina coastal dune complex from the City of Monterey to Point Gorda, Fort Ord Military Reservation, Seaside Dunes, California Department of Fish and Game preserve near the mouth of the Salinas River, Monterey Sand Hills, Lobos State Preserve, Partington Canyon between Highway 1 and Partington Cove, Burns Creek, several west-facing canyons to Highway 1 between Malpaso and Garrapatacreeks, north-facing slopes adjacent to Carmel River between Boronda and Paso Hondo roads near Carmel Valley, Vasquez Knob, and Paraiso Springs.

El Segundo blue butterfly - Los Angeles County - International Airport and Chevron Refinery.

Kern primrose sphinx moth - Kern County - Walker Basin.

2. In Florida, the anti-lepidopteran delta endotoxin, or any formulations thereof, should not be used in the Dade County Keys in Key Biscayne national Park, thence southward to Lower Metacumbe Key in Monroe County

3. Anti-lepidopteran delta endotoxin, or any formulations thereof, should not be used within one mile of the Pacific Ocean in Tillamook County, Oregon and Pacific County, Washington, where the Oregon silverspot butterfly is known to occur.

#### 101.4 ADEQUACY OF TOXICITY DATA

The registrant has successfully addressed the data requirements outlined in the Pesticide Assessment Guidelines, Subdivision M, for 154A-16 Avian oral pathogenicity/toxicity test - mallard duck; 154A-16

Avian oral pathogenicity/toxicity test - bobwhite quail; 154A-23 Nontarget arthropod testing for toxicity/pathogenicity to arthropod predators/parasites - green lacewing; 154A-23 Nontarget arthropod testing for toxicity/pathogenicity to arthropod predators/parasites - predatory mite; and 154A-24 Honey bee toxicity/pathogenicity test

The registrant has not successfully addressed the data requirements outlined in the Pesticide Assessment Guidelines, Subdivision M, for 154A-19 Freshwater fish toxicity and pathogenicity testing - rainbow trout (supplemental); 154A-20 Freshwater aquatic invertebrate toxicity and pathogenicity testing - *Daphnia* (supplemental); and 154A-23 Nontarget arthropod testing for toxicity/pathogenicity to arthropod predators/parasite - *Trichogramma* (invalid). Please see the individual Data Evaluation Reports for the bases of the above determinations.

#### 101.5 ADEQUACY OF LABELING

The precautionary labeling is not adequate as there is no mention of hazards to beneficial insects or freshwater aquatic invertebrates. Precautionary labeling is necessary in these cases due to toxicity of ABG-6305 to honey bees, predatory mites, and *Daphnia*.

Endangered Species Labeling: Endangered species labeling is deferred until the Technical Bulletin information is made available by OPP.

The following statements should be added to the label:

**ENVIRONMENTAL HAZARD STATEMENT:** This pesticide is toxic to aquatic invertebrates. Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high-water mark. Drift and runoff may be hazardous to aquatic organisms in neighboring areas. Do not contaminate water when disposing of equipment washwater or rinsate.

In light of the toxicity of maximum hazard doses of CenTari to predatory mites, the label should not claim that the product does not harm beneficial insects. There is no precautionary labeling requirement at this time.

This product is highly toxic to bees exposed to direct treatment. Do not apply this product while bees are actively visiting the treatment area.

#### 102.0 CLASSIFICATION NA

#### 103.0 CONCLUSIONS

EEB has reviewed the proposed Section 3 Registration of CenTari by Abbott Laboratories for control of larval lepidopterous pests of trees, field crops, and stored agricultural commodities. EEB concludes that acute toxicity risks to nontarget avian and mammalian wildlife will be minimal to nonexistent at the proposed label use rates. It is apparent that CenTari is somewhat to highly toxic to

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nontarget terrestrial arthropods and to freshwater aquatic invertebrates. EEB requests that Abbott Laboratories add the above precautionary statements on the CenTari label to reflect the hazards that the use of CenTari pose to the above invertebrates.

In addition, the registrant will need to address the lack of pathogenicity data for freshwater fish as a consequence of doing the acute study for chemicals (96-hr) instead of the one for microbials (30-day). This is particularly important because of the unusual toxicity demonstrated by this Bt strain, which will make it difficult to use data from previously registered strains to fulfill these requirements. This also complicates the issue concerning the *Trichogramma pretiosum* study. Previous testing with other Bt products containing this strain could possibly have been used to fulfill this requirement, however this will not be possible because of the unusual toxicity.

EEB also requests that Abbott Laboratories determine the source of the unexpected activity against nontarget invertebrates, i.e. is the activity due to the spore-crystal complex or is it due to heat-labile ( $\alpha$ ) or heat-tolerant ( $\beta$ ) exotoxins contaminating the ABG-6305 material. Alternatively, if this toxicity is a characteristic of this particular Bt and not an artifact or contaminant, EEB requests that Abbott Laboratories develop chronic toxicity/pathogenicity data on honey bees, green lacewings, predatory mites, and *Daphnia magna* in order to determine the long term effects on the above organisms from prolonged use of this product. Need for additional testing of *Trichogramma pretiosum* and rainbow trout will depend upon the results of completed valid studies with these species.

#### Endangered species considerations

The use of CenTari insecticide in California, Colorado, Florida, Indiana, Michigan, Minnesota, New Hampshire, Oregon, Washington, and Wisconsin may affect endangered lepidopteran insect species. The location of the endangered species and restrictions for use of *Bacillus thuringiensis* delta endotoxin in these areas are listed in section 101.3.0.

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