

***Beauveria bassiana* Strain GHA (128924)**

Technical Document

Reason for Issuance: Unconditional Registration Amendment of a Biological Insecticide

Date Issued: Sept. 6 2000

Summary

Summary text

I. Description of the Biochemicals

Generic Name(s) of the Active Ingredient(s): *Beauveria bassiana* Strain GHA

OPP Chemical Codes: 128924

Year of Initial Registration: 1995 (Conditional)

Year of Unconditional Registration: 1999

Pesticide Type: Microbial Insecticide

U.S. and Foreign Producers:

Mycotech Corp.

2500 Continental Drive

Butte, MT 59701

II. Use Sites, Application Timing & Target Pests

- **Target pests:** Several varieties of the following: scarab beetles, leaf-feeding beetles (including Colorado potato beetle), whitefly, aphids, thrips, psyllids, mealy bugs, leafhoppers and plant hoppers, weevils, plant bugs (including chinch, lygus and flea hoppers), borers, leaf-feeding insects, grasshoppers, locusts and Mormon crickets, stem-boring lepidoptera (including European and Southwestern corn borer).
- **Registered Uses:** For use in rangeland, improved pastures, all food/feed commodities (including herbs, spices and edible flowers), forestry, greenhouse, indoor, outdoor nursery, shade house, commercial landscape, interiorscape, turf, ornamentals, organic farming.

III. Food Clearances /Tolerances

An exemption from tolerance for all raw agricultural commodities was granted in 1995 prior to the Food Quality Protection Act. This exemption from tolerance for all food commodities

was reassessed on January 21, 1999, and found to comply with the Food Quality Protection Act of 1996. There is a reasonable certainty that no harm will result from cumulative and aggregate exposure to *Beauveria bassiana* strain GHA. This includes all anticipated dietary exposures, as well as potential exposure via drinking water.

IV. Science Findings

A. Product Chemistry

Products containing *Beauveria bassiana* strain GHA were conditionally registered in 1995. One condition of registration was the standard requirement for the registrant to provide analyses of production batches to demonstrate adequate quality control measures of nominal limits, potential contaminants and metabolites. This condition of registration was satisfied provided the manufacturing method did not change. On modifying the manufacturing method, the company provided new data regarding potential metabolite production during production. These modifications were considered in the reassessment of the exemption from tolerance in 1999, and the database supports both the exemption from tolerance and the unconditional registration. Potential metabolites are within regulatory levels. Batches containing human pathogens and other contaminants and metabolites not within regulatory levels are to be destroyed.

B. Toxicology:

The reviews of the following toxicity studies were found acceptable and in compliance with the Food Quality Protection Act (FQPA) of 1996.

a. Acute Toxicology

1. **Acute Oral Toxicity/Pathogenicity in Rats, Guideline No. 81-1/152-30 (Technical):** *B. bassiana* Strain GHA was not pathogenic, infective or toxic in CD® train rats when dosed orally with 1×10^8 colony forming units (cfu)/animal. Clearance was complete within three (3) days of dosing. The Technical Grade Active Ingredient (TGAi) was placed in acute oral toxicity category IV.
2. **Acute Dermal Toxicity in Rabbits, Guideline No. 81-2/152-31 (Technical):** *B. bassiana* Strain GHA was not pathogenic, infective or toxic in rabbits dosed dermally at 2 gm per animal which was equivalent to 1.6×10^{11} cfu/animal. There was slight to moderate dermal irritation which persisted to day 14. Toxicity Category III for dermal irritation and Toxicity Category III for dermal irritation are supported.
3. **Acute Pulmonary Toxicity/Pathogenicity in Rats, Guideline No. 81-3/152-32 (Technical):** *B. bassiana* Strain GHA was not

pathogenic, infective or toxic in CD® strain rats when dosed intratracheally with 1×10^8 cfu/animal. Clearance was complete within seven (7) days of dosing. The TGAI was considered an acute pulmonary toxicity category IV pesticide.

4. **Acute Intraperitoneal Toxicity/Pathogenicity Testing in Rats, Guideline No. 81-4/152-33 (Technical):** *B. bassiana* Strain GHA was not pathogenic, infective or toxic in CD® strain rats when dosed intraperitoneally with 1×10^7 cfu/animal. Clearance was complete within three (3) days of dosing. The Technical was placed in Toxicity Category IV for intraperitoneal toxicity/pathogenicity effects.
5. **a. Primary Eye Irritation in Rabbits, Guideline No. 81-5/152-35 (Technical):** At the time of registration studies submitted demonstrated that rabbits displayed corneal and iridial effects when given a single 0.1 gm dose of the technical. Ocular lesions persisted in one rabbit to day 21. The TGAI is considered in Toxicity Category I for primary eye irritation. Later studies submitted in 2000 after the manufacturing process was modified, showed that each of the six adult albino rabbits tested with the technical displayed positive effects as a result of dosing. However, these positive effects were reversible and all positive effects cleared by the 72 hour observation. All other minor effects of the conjunctivae (non-positive according to Draize scoring) were resolved by the Day 7 observation point. Therefore, it appears that the test material is a mild irritant that does not produce irreversible effects and is considered as a Toxicity Category III microbial pesticide for primary eye irritation effects.
 - b. **Primary Eye Irritation in Rabbits, Guideline No. 81-5/152-35 [End-Use Product (EP), Mycotrol GH-Oil Flowable (OF)]:** Rabbits displayed minimal ocular irritation when given a single 0.1 ml dose. The irritation dissipated by day 7. This oil flowable EP is considered as Toxicity Category III for primary eye irritation effects.
 - c. **Primary Eye Irritation in Rabbits, Guideline No. 81-5/152-35 [EP, Mycotrol GH-Emulsifiable Suspension (ES)]:** Rabbits displayed minimal ocular irritation when given a single 0.1 ml dose. The irritation dissipated by day 7, placing this emulsifiable suspension EP in Toxicity Category III.
 - d. **Primary Eye Irritation in Rabbits, Guideline No. 81-5/152-35.** Other EPs are tested on registration for primary eye irritation and appropriate Toxicity Categories assigned upon evaluation of data submissions. One wettable powder formulation was placed in Toxicity Category I based on studies conducted before the manufacturing process was modified. Reclassification of this product is possible on submission and review of appropriate data.
2. **Acute Dermal Toxicity and Primary Dermal Irritation, Guideline Nos. 81-2/152-31 and 81-6/152-35 (End-use Mycotrol GH-OF and Mycotrol GH-ES):** Material Safety Data (MSD) sheets were submitted for the inert ingredients in the OF and ES end-use product formulations. Information provided in the MSD sheets for the inert

ingredients support Toxicity Category III for the Mycotrol-OF and Mycotrol-EC products. Other EPs are tested on registration for acute dermal and primary dermal irritation effects and appropriate Toxicity Categories assigned upon evaluation of data submissions.

3. **Hypersensitivity Incidents:** No incidents of hypersensitivity have been reported for this microbial pesticide active ingredient, *Beauveria bassiana* strain GHA.

b. **Subchronic, Chronic Toxicity and Oncogenicity**

Tier II tests and Tier III toxicology tests involving *Beauveria bassiana* strain GHA were not required since Tier I tests satisfied guideline requirements.

A. Food Quality Protection Act Requirements

No unreasonable adverse effects to human health are expected from the use of *Beauveria bassiana* strain GHA when used as labeled. An exemption from the requirement of a tolerance has been established under Section 408(c)(2)(A)(I) of the Federal Food, Drug, and Cosmetics Act. The Agency has assessed the toxicology data base for products containing the active ingredient *Beauveria bassiana* strain GHA in light of the safety factors listed in the Food Quality Protection Act and has concluded with reasonable certainty that the proposed uses of this microbial insecticide do not pose aggregate and/or cumulative risks to the general population, including infants and children as summarized below under Human Health Risk Assessment.

B. Human Health Risk Assessment and FQPA Considerations

1. Acute and Chronic Dietary Risks for Sensitive Subpopulations, Particularly Infants and Children

a. **Food**

This microbial pesticide is intended for use on food crops. Thus, dietary exposure to the microbial pesticide is likely to occur. The Agency did not require subchronic and chronic dietary exposure studies, since the Tier 1 acute oral studies demonstrated a low toxicity (Category IV) and no pathogenicity potential via oral infectivity/pathogenicity exposure. The microbial pesticide can be easily removed from foods by washing, peeling, cooking and processing, thus further minimizing the acute dietary exposure and

risk. Similarly, chronic risks posed by dietary exposure to the pesticide are likely to be minimal to non-existent for sensitive subpopulations, such as infants and children.

b. Drinking Water Exposure and Risk Characterization

The microorganism *Beauveria bassiana* is common in the soil. It is not known as an aquatic microorganism, and therefore is not expected to proliferate in aquatic habitats. Drinking water is not being screened for *Beauveria bassiana* Strain GHA as a potential indicator of microbial contamination. Both percolation through soil and municipal treatment of drinking water would reduce the possibility of exposure to *Beauveria bassiana* Strain GHA through drinking water. Therefore, the potential of significant transfer to drinking water is minimal to nonexistent. However, even if negligible oral exposure should occur through drinking water, the Agency concludes that such exposure would present no risk due to the lack of toxicity and the ubiquitous nature of the microbe.

2. Common Mode of Action

There is one other strain of *Beauveria bassiana* registered at this time. EPA does not believe that there is any concern regarding the potential for cumulative effects of *Beauveria bassiana* strain GHA and the other currently registered *Beauveria bassiana* ATCC 74040 due to a common mechanism of toxicity. The toxicology studies performed on both strains of *B. bassiana* demonstrate a low toxicity potential for each fungal strain.

3. Risks Posed by Potential Residential, School or Daycare Exposure

Exposure and risk to adults, infants and children via treated lawns or recreational areas are likely if the pesticide is used as labeled. However, the pesticide is a naturally occurring microbe and is ubiquitous in the environment. Based on the low toxicity potential as evidenced by the data submitted, the microbial pesticide active ingredient is likely to pose minimal to non-existent risks if used as labeled.

4. Aggregate Exposure and Risk from Multiple Routes Including Dermal, Oral, and Inhalation

The Agency has considered the various routes of exposure (dietary, drinking water, and dermal and inhalation exposure from non-occupational sources). Workers are expected to be most exposed to the pesticide via dermal and

inhalation exposure as discussed below (see Occupational and Residential Exposure). Based on the labeled use patterns, the general US population, including infants and children, are likely to be exposed to the active ingredient. *Beauveria bassiana* strain GHA is not known to be a human pathogen nor is it known to produce metabolites which are dermally absorbed. The acute oral and inhalation toxicology studies also demonstrated a low toxicity/pathogenicity potential. In addition, dietary exposure and risk have been assessed and determined minimal to non-existent for all segments of the population, including infants and children.

To summarize, the Agency anticipates that the potential risks to the general population from aggregate exposure to the active ingredient are not likely to be significant. This decision is based on the low toxicity/pathogenicity potential as demonstrated by the studies submitted in support of the registration of both the TGAI and the EP. Aggregate non-occupational exposure and risk to registered strains of *Beauveria bassiana* is an ongoing assessment as products seek registration.

5. **Safety Factors**

FFDCA section 408 provides that EPA shall apply an additional tenfold margin of exposure (safety) for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the database. Alternatively, EPA can determine that a different margin of exposure (safety) will be safe for infants and children. In this instance, EPA believes there are reliable data to support the conclusion that there are no threshold effects of concern to infants, children and adults when *Beauveria bassiana* strain GHA is used as labeled. As a result, the provision requiring an additional margin of exposure does not apply.

6. **Cumulative Effects**

There is a reasonable certainty that no harm will result from aggregate exposure to the U.S. population, including infants and children, to *Beauveria bassiana* Strain GHA from the use pattern of this microbial pesticide. This includes all anticipated dietary exposures and all other exposures for which there is reliable information.

7. **Other Considerations**

Endocrine Disruptors

The Agency is not requiring additional information specifically on the endocrine effects of this microbial pesticide at this time. However, the Agency has considered, among other relevant factors, available information concerning whether this microorganism may have an effect in humans similar to an effect produced by a naturally occurring estrogen or other endocrine effects. At this time, there is no information indicating that *Beauveria bassiana* strain GHA produces a metabolite that may be an endocrine disruptor. As expected from a non-pathogenic microorganism, the submitted toxicity/pathogenicity studies in the rodent (required for microbial pesticides) indicate that following several routes of exposure, the immune system is still intact and able to process and clear the active ingredient. Therefore, no adverse effects to the endocrine or immune systems are known or expected.

A. Occupational and Residential Exposure and Risk

There is likely to be occupational and residential exposure and risk to the microbial pesticide from the proposed uses on agricultural crops, ornamentals, turf and greenhouses. Because of the lack of significant mammalian toxicity, worker exposure data (i.e. occupational exposure data) to the active ingredient are not required at this time. It is the Agency's opinion that these occupational exposures and subsequent risks are negligible because this strain of the organism has been determined not to be toxic or pathogenic to humans. The risks are expected to be minimal based on evaluations of submitted Tier 1 acute toxicity tests described above (see Toxicology). Summaries of dermal and inhalation exposure and risk follow.

1. Dermal exposure and risk.

Workers are most likely to be dermally exposed during treatment of all registered sites which include food commodities, turf, landscape, ornamentals, greenhouses, indoor and outdoor nurseries. Dermal exposure via the skin would be the primary route of exposure for mixer/loaders, applicators and early-entry workers. Since unbroken skin is a natural barrier to microbial invasion of the human body, dermal absorption could occur only if (a) the skin were cut, (b) the microbe were a pathogen equipped for mechanisms for entry through or infection of the skin, or (c) metabolites were produced that could be dermally absorbed. *Beauveria bassiana* strain GHA is not known to be a human pathogen, nor is it known to produce metabolites which are dermally absorbed. Based on the demonstrated lack of adverse effects in the intravenous study, it is the Agency's opinion that even

cut skin should not pose a risk to health via entry of absorbed *Beauveria bassiana* strain GHA into the body. Because the pesticide is placed in acute toxicity category III for dermal effects, the exposure and risk to workers is likely to be minimal, if appropriate Personal Protective Equipment is used as labeled. Also, during the Restricted Entry Intervals (REI), early entry workers may enter treated fields if wearing appropriate Personal Protective Equipment as labeled.

2. **Inhalation exposure and risk.**

Inhalation would be another route of exposure for mixer/loaders, applicators and early-entry workers engaged in post application activities. The pesticide is considered an acute Toxicity Category IV microbial pesticide on the basis of intratracheal pulmonary toxicity/pathogenicity studies. Because of its low toxicity potential, the risk posed via inhalation exposure to workers is likely to be minimal to nonexistent. However, because of the microbial nature of the pesticide, the Agency requires that workers mixing, loading and applying the pesticide to agricultural sites wear appropriate respirators with NIOSH approval prefix N-95, P-95 or R-95. Early-entry workers engaged in post application activities are also required to wear these respirators during the Restricted Entry Intervals (REIs). These respirators are required to mitigate against potential inhalation exposure and risk.

B. Environmental Exposure and Risk

The microbial active ingredient is a naturally occurring ubiquitous fungus, which is found in soils. It is not known to proliferate in aquatic habitats. Based on its low toxicity potential, it is not likely to have undue adverse effects on the environment.

C. Ecological Exposure and Risk

a. **Ecological Effects**

1. **Avian Oral Toxicity/Pathogenicity in American Kestrel, Guideline Nos. 154-6 and 154-7 (Mycotrol OF):** This study did not meet guideline specifications; however, it did demonstrate that *B. bassiana* Strain GHA was not pathogenic or toxic to young American Kestrels singly dosed at 1 µl/g of body mass per animal. Data waivers have been granted for these requirement due to lack of toxicity and pathogenicity to young American kestrels treated with

Beauveria bassiana oil flowable formulation and review of public literature which indicates that birds are not adversely affected by this fungal entomopathogen.

2. **21 Day Toxicity to Daphnids (*Daphnia magna*) Under Static Renewal Conditions, Guideline No. 154-9 (Technical):** At a dosage rate of 9.3×10^8 cfu/l, *Beauveria bassiana* Strain GHA had minor growth effects on *Daphnia*. The 21-day EC50 was greater than 9.3×10^8 colony forming units (cfu)/l. The NOEC was 4.7×10^8 cfu/l and the lowest observed effect concentration (LOEC) was 9.3×10^8 cfu/l. This study was rated core
3. **3. Evaluation of Potential Embryo-Larval Toxicity/Pathogenicity to Fathead Minnow (*Pimephales promelas*) Under Static Renewal Conditions, Guideline No. 154-28 (Technical):** There were no indications of infectivity or pathogenicity among treated fish dosed with 7.5×10^8 cfu/l of water. There were no adverse effects on the percent hatch of fathead minnow embryos or their survival for 27 days after hatching. This Tier 3 study was required due to adverse effects reported from tests conducted by EPA/Office of Research and Development. This study was rated core.
4. **Acute Toxicity/Pathogenicity to the Beneficial Insect Herbivore: *Apthona flava* Guill. (Coleoptera: Chrysomelidae), Guideline No. 154-23 (Technical):** There was 37% mortality of field collected and laboratory treated beetles dosed at the recommended label use rate of 1×10^{13} conidia/acre. The LD₅₀ was 2.11×10^{13} and LD₉₀ was 9.4×10^{13} conidia/acre. This study was rated core.
5. **Acute Toxicity/Pathogenicity to *Tenebrio molitor* (Coleoptera: Tenebrionidae), Guideline No. 154-23 (Technical):** This study was deficient and rated supplemental; however, it does indicate that this strain of *B. bassiana* does not readily infect *Tenebrio molitor* under the conditions of the test.
6. **Acute Toxicity/Pathogenicity to Predators/Parasites: *Xylocoris flavipes* (Hemiptera: Anthcoridae), Guideline No. 154-23 (Technical):** Following ten days exposure of nymphs of *Xylocoris flavipes* to live conidia of *Beauveria bassiana*, there were mortalities of 16% at 10X (1×10^{14} conidia/acre) the intended field use rate of 1×10^{13} conidia per acre. At 100X (1×10^{15} conidia/acre), the mortality was 41%. The LD₅₀ at ten days was determined to be 1.55×10^{15} conidia/acre and the LD₉₀ was 3.3×10^{16} conidia/acre. This study was rated core.
7. **Effects of *Beauveria bassiana* Strain GHA on Non-Target Insects, Guideline 154-23:** This submission consists of a review of the nontarget insect studies submitted by Mycotech Corporation plus public literature citations that support the applicants claims that *B. bassiana* Strain GHA is not persistent in the environment and has negligible effects on nontarget insects. Although the information provided supports the claims, it does not preclude effects on nontarget insects directly after application and within a few days of application, particularly to plants with dense canopies and soil surfaces under these canopies where there are shade and high humidity. This information was rated supplemental. Additional data

were found sufficient to remove the condition of registration provided the Environmental Hazard statement remained on the label.

8. **Honeybee Acute Toxicity/Pathogenicity, Guideline No. 154-24 (Technical):** Because of the uncertain relevance of the results of the honeybee toxicity/pathogenicity test other than determining infectivity, this study was rated supplemental. The Agency recommended that a hive test be conducted as a condition of registration and submitted within a year of the registration date. The registrant provided data which were sufficient to remove the condition of registration, provided that the product label stated under Environmental Hazards: "This product is potentially pathogenic to honeybees. Avoid application to areas where honeybees are actively foraging or around bee hives."
9. **Physical Stability under Temperature Extremes, Guideline No. 155-18 (Technical):** *Beauveria bassiana* strain GHA conidia maintained original viability for 56 days at 5°C and 25°C. At 50°C, the conidia steadily lost viability with germination of 6.8% at 14 days and 0.2% at 28 days. The germination half-life at 50°C was 4.6 days and the quarter-life was 10.0 days at that temperature. Since exposure at 5°C and 25°C resulted in virtually no loss of viability from 56 days exposure and these temperatures are more representative of field conditions than 50°C, the study indicates that conidia of *B. bassiana* will likely be unaffected by ambient field temperatures for at least 56 days and remain infectious to susceptible insects. The study was rated core.
10. **Physical Stability: Sunlight Effects, Guideline 155-18, (Technical):** The viability of *B. bassiana* strain GHA conidia decreased very rapidly after two hours of direct exposure to direct natural sunlight. The estimated half-life of *B. bassiana* GHA conidia was 2.58 hours and the quarter-life was 3.11 hours based on the results of this study. These data predict that conidia of *B. bassiana* strain GHA are rapidly inactivated by natural sunlight under the conditions of the study. However, the exposure scenario (directly exposed glass cover slips) is not analogous to typical field, foliage and soil surface habitats of the insect pests for which the product is intended to infect and control. The natural habitat can provide ample niches of shade and humidity which would favor *B. bassiana* conidia survival and infectivity for target pest species as well as susceptible nontarget insects. The study was rated core.
11. **Persistence of the Entomopathogenic Fungus, *Beauveria bassiana*, on Phylloplanes of Crested Wheatgrass and Alfalfa, Guideline 155-18:** This publication demonstrates short persistence of *B. bassiana* conidia in certain crop canopies, four days in the upper canopy and about 16 days in the middle canopy of the test crops. Persistence was greater in the middle canopy of the broadleaf crop, alfalfa, than the grass crop, crested wheatgrass. The major environmental factor reducing persistence of conidia was thought to be ultraviolet light which is consistent with the published findings of others and the previous study. These data do not preclude effects on nontarget insects directly after application and within a few days of application, particularly to plants with foliage that provides shade. The study was rated core.

b. **Ecological Risk**

This microbial active ingredient occurs ubiquitously in the environment and it demonstrates a low toxicity profile. Based on these factors and the data submitted, the potential ecological risk due to exposure to this microorganism, is likely to be minimal.

D. Summary of Data Gaps

There are no outstanding data gaps for the full unconditional registration provided the label bears the required Environmental Hazards statements regarding potential pathogenicity to honey bees. Should the registrant wish to remove this statement from the label, data must be submitted to demonstrate higher doses of the pesticide are not pathogenic to honey bees.

II. Regulatory Actions

The Agency does not expect undue adverse human health and environmental effects from the use of *Beauveria bassiana* Strain GHA if the pesticide is used as labeled. The health effects database supported an exemption from the requirement of tolerance for residues of *Beauveria bassiana* Strain GHA in/on all food/feed commodities which was granted in April , 1995. The exemption from tolerance for residues of *Beauveria bassiana* Strain GHA in/on all food commodities was reassessed in January 1999, and found to comply with the Food Quality Protection Act of 1996.

Products containing this microbial active ingredient were conditionally registered in April/May 1995 through 1998 while the registrant modified the manufacturing method and provided additional manufacturing and ecological effects data to proceed to full unconditional registration. The registrant provided data to remove the conditions of registration for all its products, but voluntarily withdrew certain products in order to consolidate its manufacturing and market strategies. Existing stocks of the voluntarily withdrawn products must not be sold after December, 2000. Full unconditional registrations were granted to the remaining products. Registration of products containing *Beauveria bassiana* Strain GHA is an ongoing process as the registrant formulates new products or reformulates old products to decrease any potential adverse effects.

III. Label Requirements

a. **Agricultural Use Directions**

To protect workers and all classes of pesticide handlers, the label must include appropriate Personal Protective Equipment (PPE). At a minimum, the Agency recommends that mixer/loaders, applicators and Restricted-entry workers wear long sleeve shirt, long pants, shoes, socks and a dust-mist filtering respirator meeting NIOSH standards with prefix N-95, R-95 or P-95. A Restricted-Entry Interval and appropriate PPE must also be on the labels as required during registration of EPs.

b. **Environmental Hazard Statements**

. **Technical Product Labels**

i. "Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or public waters unless this product is specifically addressed in an NPDES permit. Do not discharge effluent containing this product to sewer systems without previously notifying the sewage treatment plant authority. For guidance, contact your State Water Board or Regional Office of the EPA."

ii. Where appropriate, technical active ingredients to be formulated into products must bear the appropriate manufacturing use label language.

a. **End-use Product Labels**

. The label for EPs must state under an Environmental Hazards heading: "Avoid application to areas where honeybees are actively foraging or around bee hives because this product is potentially pathogenic to honeybees."

i. The following additional precautionary statements must be placed on the label under Environmental Hazards as required: "Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water by cleaning of equipment or disposal of equipment wash waters. Do not discharge into lakes, streams, ponds or public waterways."

IV. Additional Contact Information

[Ombudsman, Biopesticides and Pollution Prevention Division](#) (7511P)
Office of Pesticide Programs
Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460