

***Beauveria bassiana* strain ATCC 74040 (128818)**

Technical Document

Reason for Issuance: Update of Fact Sheet with New Information Including Exemption from Tolerance for the Conditionally Registered New Biological Insecticide

Issued: 9/00

I. Description of the Biological Pesticide

Generic Name(s) of the Active Ingredient: *Beauveria bassiana* strain ATCC 74040

OPP Chemical Code: 128818

Year of Initial Registration: 1995 (conditional)

Pesticide Type: Microbial Insecticide

U.S. and Foreign Producers:

Troy BioSciences Inc.

113 S. 47th Avenue

Phoenix, AZ 85043

II. Use Sites, Application Timing & Target Pests

- **Target Pests:** Ants, Aphids, Armyworms, Bermuda Grass Mites, Billbugs, Budworm and Bollworm, Cutworms, Chinch Bugs, Citrus blackfly, Colorado Potato Beetle, Corn Borers, Leafhoppers, Beetles- Flea Cucumber, Elm Leaf, Fungus Gnats, Grasshoppers, Japanese Beetles, Elm Leaf Leafhoppers, Leaf-feeding caterpillars, Leafrollers, Loopers, Lygus bug, Mealybugs, Millipedes, Mole Crickets, Tetranychid Mites, Pear Psylla, Root Weevils, Psyllids, Sowbugs, Spittlebugs, Sod Webworms, Shore flies, Tarnished Plant Bug, Thrips, Tomato Fruitworm, Weevils and Whiteflies, Eggs of Lepidopteran Pests, Larvae of the following pests: White bugs, Annual White Grub, Black Turfgrass Ataenius, European Chafer, Green June Beetle, Japanese Beetle, Northern Masked Chafer, European Crane fly Larvae.
- **Registered Uses:** For use outdoors and in greenhouses on ornamental plants and on turf grass; agricultural use includes all terrestrial food/feed commodities; not for use on crops in aquatic habitats; homeowner uses include: home ornamental gardens (foliage and flowering plants, woody and herbaceous ornamentals, conifers, ornamental shrubs and trees) and all species and cultivars of both cool and warm season lawn grasses for home lawns.

III. Food Clearances/Tolerances

The Final Rule establishing an exemption from the requirement of a tolerance for residues of *Beauveria bassiana* ATCC 74040 (40 CFR 180.1205) in or on all food/feed commodities was published in the Federal Register on April 28, 1999 (Volume 64, Number 81, pp. 22793-22796). The exemption applies when *Beauveria bassiana* ATCC 74040 is applied as an insecticide at registered label rates and sites.

IV. Science Findings

A. Product Chemistry

All Product Identity requirements have been met for this conditional registration, and analytical methods are available and sufficient for quality control.

B. Toxicology

The reviews of the following toxicity studies were found acceptable and meet the safety standards of the Food Quality Protection Act (FQPA) of 1996.

a. Acute Toxicology

- 1. Acute Oral Toxicity/Pathogenicity in Rats, Guideline No. 885.3050 (Technical):** No animal mortality or overt toxic effects were noted in rats dosed orally with 1.9×10^8 colony forming units (cfu)/animal of *B. bassiana* Strain ATCC 74040. Red foci were noted on the lungs of three of the treated animals indicating possible pulmonary toxicity. However, the acute pulmonary toxicity/pathogenicity tests showed clearance within 15 days of dosing as discussed below. Based on these studies, and the nature of the inert ingredients in the end use product (EP) containing this active ingredient, the EP can be considered a Toxicity Category IV pesticide for acute oral effects.
- 2. Acute Dermal Toxicity in Rabbits, Guideline No. 870.1200 (Naturalis-L 225):** *B. bassiana* Strain ATCC 74040 was not pathogenic, infective or toxic in rabbits dosed dermally at 2 gm per animal containing 4.2×10^7 cfu/ml. It was therefore considered Toxicity Category IV for dermal toxicity.
- 3. Acute Pulmonary Toxicity/Pathogenicity in Rats, Guideline No. 885.3150 (Technical):** No mortality or toxic or pathogenic effects were found in the test animals dosed intratracheally with 2.5×10^9 cfu *B. bassiana* Strain ATCC 74040/animal. Clearance was complete from the lungs within 15 days of dosing. No significant clinical signs were observed. Brown or tan lesions were noted in the lungs of all treated animals starting on day 4 and an inflammatory response was evident in microscopic examination. The presence of an inflammatory response is expected as a component of the normal recognition and clearance of microbes by the immune system. Clearance was observed within 15 days of dosing. No inflammation was evident on tissues examined at the end of the study. The pesticide was categorized as Toxicity Category III on the basis of these acute pulmonary effects.
- 4. Acute Intraperitoneal Toxicity/Pathogenicity Testing in Rats, Guideline No. 885.3200 (Technical):** *B. bassiana* Strain ATCC 74040 was not pathogenic, infective or toxic in rats when dosed intraperitoneally with 2×10^7 cfu/animal. No animals had the test microbe recovered from their blood or had detectable visible lesions on their internal organs at gross necropsy.

5. **Primary Eye Irritation in Rabbits, Guideline No. 870.2400 (Naturalis-L 225):** Rabbits displayed minimal ocular irritation when given a single 0.1 ml ocular dose containing 2×10^6 cfu and is considered in Toxicity Category III.
6. **Primary Dermal Irritation in Rabbits, Guideline Nos. 870.2500 (Naturalis-L 225):** There was no mortality or significant toxic effects in animals singly dosed and exposed for four hours with 5 ml *B. bassiana* Strain 74040 containing 5.5×10^7 cfu which places it in Toxicity Category IV.
7. **Dermal sensitization.** Data provided to the Agency show that Naturalis-L is a dermal sensitizer. In several animals, the severity of irritation required relocation of test site for inductions 8 and 9. In addition, two animals died during the study - one prior to the challenge phase and one prior to the 48-hour challenge scoring interval. No cause for death was determined. This test was conducted with a test material at 100% concentration rather than at the 50% concentration recommended by the harmonized guidelines. The label for this product must state that it is a dermal sensitizer and proper protective equipment should be worn.
8. **Hypersensitivity Incidents:** No incidents of hypersensitivity have been reported for this organism.

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

Tier II tests and Tier III toxicology tests involving *Beauveria bassiana* ATCC 74040 were not required since Tier I tests satisfied guideline requirements.

C. Food Quality Protection Act Requirements

No unreasonable adverse effects to human health are expected from the use of *Beauveria bassiana* ATCC 74040 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 *Beauveria bassiana* ATCC 74040 and the sole registered End-use Product (EP) 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**.

D. Human Health Risk Assessment and FQPA Considerations

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

Dietary exposure to the microbial pesticide is likely to occur. The lack of acute oral toxicity/pathogenicity, and the ubiquitous nature of the microbial, support the exemption from the requirement of a tolerance for this active ingredient.

a. Food

The microbial pesticide can be easily removed from foods by washing, peeling, cooking and processing. Even if ingested, the low acute oral toxicity Category IV potential indicates minimal risk. Consequently, dietary exposure to the microbial and the risk posed by ingestion of foods treated with the microbial pesticide, are likely to be minimal for adults, infants and children by the oral route.

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* ATCC 74040 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* ATCC 74040 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* ATCC 74040 and the other currently registered *Beauveria bassiana* strain GHA 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 a minimal to non-existent hazard if used as labeled.

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

The Agency has considered the various routes of exposure (dietary, drinking water, and exposure from non-occupational sources) and potential risks of the subject microbial pesticide. The proposed use of the active ingredient does not pose significant risk over a lifetime to populations including infants and children. 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 exposure and risk to registered strains of *Beauveria bassiana* is an ongoing assessment as products seek registration.

5. Safety Factors and Determination of Safety for U.S. Population, Infants and Children

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* ATCC 74040 is used as labeled. As a result, the provision requiring an additional margin of exposure does not apply.

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* ATCC 74040 from the use pattern of this microbial pesticide. This includes all anticipated dietary exposures and all other exposures for which there is reliable information.

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* ATCC 74040 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.

E. **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.

0. **Dermal exposure and risk.**

Workers are most likely to be dermally exposed during treatment of all registered sites which include food commodities. Because the pesticide is placed in acute toxicity category IV for dermal effects, the exposure and risk to workers is likely to be minimal if appropriate recommended Personal Protective Equipment is used as labeled. During the Restricted Entry Interval (REI), early entry workers may enter treated fields if wearing appropriate Personal Protective Equipment as labeled.

1. **Inhalation exposure and risk.'**

The pesticide is considered an acute Toxicity Category III microbial pesticide on the basis of a rat acute pulmonary study which showed clearance within 15 days of dosing (see **Acute Toxicology** above). Taking the inert ingredients into consideration, the Agency considered the pesticide as acute

Toxicology Category III for pulmonary and inhalation effects. In the Agency's experience, inhalation exposure is not usually as great as dermal exposure to workers. Adequate Restricted Entry Intervals and the use of Personal Protective Equipment, including a respirator with NIOSH approval prefix N-95, P-95 or R-95, are required to mitigate against potential exposure and risk posed to pesticide handlers and all categories of workers.

F. Environmental Assessment 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 pose an undue hazard to the environment.

G. Ecological Exposure and Risk

Ecological Effects

0. **Avian Oral Toxicity/Pathogenicity Studies in the Northern Bobwhite Guideline No. 885.4050 (TGAI):** *Beauveria bassiana* Strain ATCC 74040 was practically nontoxic to bobwhite quail dosed with 2,667 mg/kg per day for five days. Ranging from 5.0×10^8 to 1.02×10^{12} cfu/ml. The treated group consumed slightly less food and their body weights were slightly lower than the untreated control group. It is improbable that *Beauveria bassiana* Strain ATCC 74040 is an infectious organism in birds because it does not grow at avian body temperatures. The no effect dosage was 2,667 mg/kg per day for five days. Application of this microbial pesticide at normal use rates is not expected to cause significant adverse effects on nontarget aquatic invertebrates in the environment. This study was rated core. This study fulfills all avian data requirements and no further testing is required.
1. **21 Day Toxicity to Daphnids (*Daphnia magna*) Under Static Renewal Conditions, Guideline No. 885.4240 (Technical):** *Beauveria bassiana* Strain ATCC 74040 was toxic to *Daphnia magna* dosed with 7.8×10^7 , 1.7×10^8 , 3.1×10^8 , 6.2×10^8 , and 1.2×10^9 spores/L. However, the significance of this toxicity could not be determined because of the use of invalid statistical assumptions. The study demonstrated an $EC_{50} = 9.9 \times 10^7$ spores/L. This study was rated supplemental. The study was upgraded to acceptable based on a submission which recalculated the statistics for *Daphnia*. Both an ANOVA test and a Bonferroni t-Test showed significant differences between the weights of the daphnids⁸ spores/L. This condition of registration was satisfied.
2. **Evaluation of Potential Embryo-Larval Toxicity/Pathogenicity to Fathead Minnow (*Pimephales promelas*) Under Static Renewal Conditions, Guideline No. 885.4280 (Technical):** There were no indications of infectivity or pathogenicity among fish dosed with 1.0×10^9 cfu/l *Beauveria bassiana* Strain ATCC 74040. Minimal adverse effects on percent survival, length and weight were

attributed to slight toxicity. Adverse toxic effects to fish are not expected under field use conditions. This Tier 3 study was required due to adverse effects reported from tests conducted by EPA/ORD. This study was rated core.

3. **Honeybee Acute Toxicity/Pathogenicity, (Guideline No. 885.4380 Technical):**)): Honeybees received a daily dietary dose of 1.65×10^6 cfu/l for 30 days and a single contact exposure of 1.7×10^8 cfu/l of *Beauveria bassiana* Strain ATCC 74040. The report generally indicates that risk to healthy bees would be minimal. Additional data, provided to compare the statistics from controls and treated, were considered acceptable. Results of an Analysis of Variance test and a T-test established that there were no significant differences between the treated and control bees. However, the emergence data indicates that there is some toxicity/pathogenicity associated with *B. bassiana* exposure to honeybees. While the data submission was sufficient to satisfy the condition of registration, it did not support the removal from the label of the Environmental Hazards statement regarding potential toxicity/pathogenicity of the pesticide to honeybees. (**See Label Requirements.**)

Data Waivers Granted:

4. **Avian Inhalation Testing, Guideline No. 885.4100:** This study was not required because the Avian Oral Toxicity/Pathogenicity Study in Northern Bobwhite with *B. bassiana* Strain ATCC 74040, TGAI fulfilled all avian data testing requirements.
 5. **Wild Mammal Testing, Guideline No. 885.4150:** Review of the nontarget organism effects information in the public literature and the studies submitted by the registration applicant indicate that the only ecological effect of some concern is effect on nontarget insects. This fungus does not typically grow at normal mammalian or bird body temperatures. This testing requirement has been waived.
 6. **Freshwater Fish Testing, Guideline No. 885.4200:** The study "Evaluation of Potential Embryo-Larval Toxicity/Pathogenicity to Fathead Minnow (*Pimephales promelas*) Under Static Renewal Conditions with *Beauveria bassiana* Strain ATCC 74040, TGAI" is considered an acceptable substitute for a freshwater fish test and a waiver is not required.
 7. **Estuarine and Marine Animal Testing, Guideline No. 885.4280:** This test is not required because the product is for terrestrial use and significant amounts are not expected to enter estuarine or marine environments when used according to label directions.
 8. **Nontarget Plant Testing, Guideline No. 885.4300:** *B. bassiana* is generally known to be nonpathogenic to plants. This testing requirement has been waived.
- a. **Ecological Risk**

This microbial active ingredient occurs ubiquitously in the environment. It demonstrates a low toxicity profile, and the potential exposure is limited to ground applications to terrestrial crops only. Based on these factors and the data submitted, the potential ecological risk due to exposure to this microorganism, if used as labeled, is not likely to be an undue hazard.

H. Summary of Data Gaps

- . The active ingredient and End-use product were conditionally registered pending resolution of three conditions. Data were provided to remove two of these conditions, as discussed above, under honey bee toxicity/pathogenicity and toxicity to *Daphnia*

The only remaining condition of registration is that further nontarget insect testing be conducted. The registrant's submissions are pending Agency review for acceptability.

- a. All hypersensitivity incidents must be reported to the Agency when/if they occur.

V. Regulatory Actions

Unacceptable adverse effects from the use of *Beauveria bassiana* ATCC 74040 are not expected. A conditional registration of the manufacturing use product and end-use product were issued on May 26, 1995. An exemption from tolerance for ground and foliar applications to terrestrial food/feed commodities was granted April 28, 1999.

VI. Label Requirements

. 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 during application of the sole registered End-use Product, mixer/loaders, applicators 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. In addition to the above PPE, early-entry workers must wear coveralls during post application activities. To comply with the Worker Protection Standards for other products, the Agency will recommend appropriate Personal Protective Equipment(PPE) and suitable Restricted-Entry Interval (REI) if required for early entry workers as determined during their registration.

A. Environmental Hazard Statements

- . **Technical Product labels**

"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."

a. **End-use Product Labels**

- . The label for Naturalis 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: "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."

VII. Additional Contact Information

[Ombudsman, Biopesticides and Pollution Prevention Division](#) (7511P)
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