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# **Biopesticide Registration Action Document**

***Beauveria bassiana* HF23**

**(PC Code 090305)**

**U.S. Environmental Protection Agency**

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**(PC Code 090305)**

**Biopesticides and Pollution Prevention Division**  
**Office of Pesticide Programs**  
**United States Environmental Protection Agency**

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*Beauveria bassiana* HF23  
(PC Code 090305)

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## I. EXECUTIVE SUMMARY/FACT SHEET

### Active Ingredient and Proposed Use

*Beauveria bassiana* HF23 (*B. bassiana* HF23, PC Code 090305) is a strain of the entomopathogenic fungi of the Genus *Beauveria*. Several strains of *Beauveria bassiana* occur naturally in the United States and worldwide. JABB of the Carolinas proposes to register two pesticide products containing *B. bassiana* HF23 as the active ingredient. The first proposed product is a manufacturing use product (MP), which is the Technical Active Ingredient (TGAI, EPA Registration Number or EPA Reg. No. 70787-R). It contains 95 percent w/w of the active ingredient, *B. bassiana* HF23 spores, corresponding to  $4.75.0 \times 10^{11}$  colony forming units per gram (cfu/g). The MP is to be formulated into end-use pesticide products (EPs). The second proposed product is an EP, (Trade name balEnce, EPA Reg. No. 70787-U) which contains 1.18 percent by weight of *B. bassiana* HF23 TGAI. The viability of the active ingredient in the EP is  $5.6 \times 10^9$  cfu/gram.

*Beauveria bassiana* HF23 is distinct from three other registered pesticidal strains of the fungus. *Beauveria bassiana* strain GHA and *B. bassiana* ATCC 74040 are registered for agricultural and other outdoor terrestrial uses. A third strain, *B. bassiana* strain 447, is registered as indoor bait for fire ants. The strain, *Beauveria bassiana* HF23, discussed in this Biopesticide Registration Action Document (BRAD), is to be used as a microbiological insecticide for controlling house fly in chicken manure and poultry production/livestock houses. While the treatment of chicken manure and poultry houses may be considered an indoor use, treated chicken manure is to be rendered into fertilizer and used outdoors on agricultural crops. Therefore, this outdoor terrestrial use poses the potential of inadvertent residues of the active ingredient on food/feed items. Consequently, an exemption from tolerance for residues of *Beauveria bassiana* HF23 on food/feed items is being established concurrently with this registration action.

### Toxicology, Human Exposure and Risks

Laboratory tests demonstrate that the TGAI, *Beauveria bassiana* HF23, is not toxic, infective, and/or pathogenic in rats via the oral or pulmonary routes. It is considered Toxicity Category IV for acute oral and pulmonary effects. A study in New Zealand white rabbits places the TGAI in acute dermal Toxicity Category III, with no toxic, infective or pathogenic dermal effects. The results of this study indicate primary dermal irritation effects are not expected and support a Toxicity Category IV for dermal irritation. An acute intraperitoneal injection test showed no clinically significant signs in rats. In a primary eye irritation study, *B. bassiana* HF23 was mildly irritating to rabbits, and is placed in Toxicity Category III. Requests to waive data requirements for acute inhalation, hypersensitivity and immune response studies for the MP were granted, based on the nature of the inert ingredients, low toxicity potential and clearance observed in the submitted Tier I acute toxicology studies [see **Table 2a: Toxicology - Health Effects**].

Rationales based on the toxicology studies for the TGAI, the nature of the inert ingredients, and low potential human exposure, justified the Agency's acceptance of the registrant's requests to waive the studies for the acute oral, acute inhalation, acute dermal toxicity, and hypersensitivity studies for the EP. A primary eye irritation study for the EP places it in toxicity Category III. Hypersensitivity incidents, should adverse effects occur, must be reported to comply with Section 6(a)(2) 40CFR159.152. The results of the Tier I tests were such that longer term Tier II studies (such as subchronic, oncogenicity or developmental studies) were not required. In addition, Tier III studies were not required. All other ingredients in the proposed end product are exempt from the requirement of a food tolerance.

### **Food Tolerances**

An exemption from the requirement of a tolerance is being established concurrently with this registration action for pesticide products containing *B. bassiana* HF23 when used in chicken manure treatment for controlling house fly. The database evaluated in connection with the exemption of *B. bassiana* HF23 from the requirement of a tolerance complies with the Food Quality Protection Act (FQPA) of 1996 for the proposed use on poultry houses as discussed in this document. This exemption from tolerance may be revised to allow more extensive uses following evaluation of analyses of five production batches confirming that unintentional ingredients are within regulatory levels.

### **FQPA Considerations**

The Agency has considered *Beauveria bassiana* HF23 in light of the safety factors of the Food Quality Protection Act (FQPA) of 1996 and has made a determination of reasonable certainty of no harm to the U.S. population in general, and to infants and children in particular. The ubiquitous occurrence of *Beauveria bassiana* HF23 suggests that the fungus is normally expected to be present, albeit at very low levels, in/on food commodities regardless of treatment with *Beauveria bassiana* HF23 [see **Section IIIB. FQPA Considerations**].

The viability of the active ingredient declines to approximately two percent about 56 days (eight weeks) after it is applied to chicken manure. Composting of chicken manure takes much longer than eight weeks to be rendered into fertilizer for agricultural use. Also, the pesticide active ingredient, *Beauveria bassiana* HF23, does not survive UV light and temperatures greater than 37°C. Compost piles reach a much higher temperature than this (approximately 40°C or greater). The EP is only to be applied on chicken manure with no direct application to food or feed items. There is no post-harvest use of food/feed items associated with *Beauveria bassiana* HF23 at this time.

Furthermore, no toxicity/pathogenicity or other adverse effects were observed in the avian oral toxicity/pathogenicity study for ecological effects which was conducted with chickens as the test organism. Thus, transfer of residues is not expected to food or feed commodities, meat, milk, poultry, and eggs, which are potentially exposed to the treated chicken manure. Analysis of preliminary batches demonstrate that beauvericin, a metabolite produced by some strains of *Beauveria*, and other unintentional ingredients, are within levels required for quality assurance and quality control (QA&QC). To ensure that these levels are not exceeded, the company must submit confirmatory analyses of five production batches of the TGAI. These

data will satisfy the QA&QC requirements for the EP. All batches with unintentional ingredients or human pathogens exceeding the QA&QC standards must be destroyed.

Dietary (including drinking water) exposure is not expected to pose any harm to human adults, infants and children, as discussed in Section III of this BRAD. Non-occupational dermal and inhalation exposures are not expected because the pesticide will not be applied in proximity to residential, day care and other non-agricultural settings. As shown in the toxicology assessments, the active ingredient is not toxic, pathogenic or infective to mammals. Because no mechanism of toxicity or pathogenicity for mammals and other vertebrates has been identified for this active ingredient, no cumulative effects from residues of this active ingredient with other related microbial pesticides are anticipated. Thus, aggregate and cumulative exposure to *Beauveria bassiana* HF23 is expected to be negligible to non-existent.

### **Occupational and Residential Exposure and Risk**

Mixer/loader, applicator, post application exposure and risks are not likely to pose any harm to workers. A Restricted Entry Interval of four (4) hours is proposed for the EP. Appropriate Personal Protective Equipment (PPE) will mitigate worker exposure to the pesticide. Residential, daycare and non-occupational exposure and risks are not expected from the proposed use on chicken houses, which are agricultural sites and not proximal to residences and daycares [**Section III.B**].

### **Ecological and Environmental Exposure and Risks**

An acute oral toxicity/pathogenicity study in chickens was considered acceptable and provided a basis to grant a request to waive a requirement for a study in bobwhite quail or mallard ducks for avian species. Requests to waive data requirements for testing Freshwater Aquatic Invertebrate, Non-Target Plants, Non-Target Insects, Honey Bee Toxicity, Estuarine/Marine Animal, and Wild Mammal were acceptable. The optimal growth temperature of *B. bassiana* HF23 is 28<sup>0</sup>C. As a result the active ingredient is not expected to proliferate in the environment at temperatures greater than the mammalian body temperature of 37<sup>0</sup>C. Thus, ecological and environmental effects are expected to be minimal to non-existent [**Section III.C**].

### **Data Gaps and Requirements/Labeling**

All deficiencies and labeling must meet Agency requirements (**Section IV.C**). Analysis of five production batches is required to ascertain that nominal and certified limits and unintentional ingredients meet regulatory levels.



## II. CASE OVERVIEW

### A. Pesticide Product Overview

The following active ingredient is covered by this BRAD.

|                               |  |
|-------------------------------|--|
| <b>Common Name:</b>           | <i>Beauveria bassiana</i> HF23   |
| <b>Biological Name:</b>       | <i>Beauveria bassiana</i> HF23   |
| <b>OPP Chemical Code:</b>     | 090305   |
| <b>Trade and Other Names:</b> | <i>Beauveria bassiana</i> HF23 Technical (Manufacturing Use Product or TGAI) and balEnce (End-use Product) |
| <b>Basic Manufacturer:</b>    | JABB of the Carolinas<br>456 E. Main Street,<br>P.O. Box 310<br>Pine Level, NC 27568                       |

### B. Use Profile

|   |   |
|---|---|
| <b>Type of Pesticide:</b>               | Insecticide Microbial Pesticide Control Agent (MPCA)  |
| <b>Use Sites:</b>                       | Walls, floors and manure piles in poultry houses. Treated chicken manure, after being rendered into fertilizer, is to be spread on agricultural fields  |
| <b>Target Pests:</b>                    | House fly   |
| <b>Formulation Types:</b>               | Solid – Manufacturing Product<br>Liquid - End-use Product   |
| <b>Method and Rates of Application:</b> | The suggested application rate of <i>B. bassiana</i> HF23 for the control of house fly is 1.5 to 2 ounces of a product containing 1.18% of the active ingredient per 5000 square feet. The spray is to be applied with conventional spray equipment to walls, floor, posts and manure in poultry houses concentrating on areas where the greatest numbers of pests are located. |
| <b>Timing:</b>                          | Reapply at intervals of 2 to 7 days as long as pest pressure persists, or as pest eggs hatch and mature. There is no restriction on the total maximum amount of the EP which may be applied in a year.  |

**Use Practice Limitations:** Filter or screen of application equipment must be greater than 50 microns to allow the active ingredient to pass through. Agitate well for dispersion of the active ingredient. Poultry can be present during application of the pesticide.

**C. Estimated Usage**

This is the first proposed use of this pesticide. No usage information is available.

**D. Data Requirements**

The Agency requires analyses of five production batches of the TGAI to confirm that QA&QC standards are not exceeded for nominal and certified limits, potential unintentional ingredients and contaminants.

**E. Regulatory History**

EPA received an application dated January 17, 2005 to register the new pesticide active ingredient *Beauveria bassiana* HF23 for use as an insecticide. The application was made by the consultant, SHB Scientific, P.O. Box 321, Chandler AZ, 85244-0321, on behalf of JABB of the Carolinas, P.O. Box 310, 456 E. Main Street, Pine Level, NC 27568. The pesticide is proposed for control of house fly on chicken manure in poultry production/livestock houses. The receipt of the application for the new active ingredient was published in the Federal Register [FR: February 15, 2006 (Volume 71, Number 31)] [Page 7954-7955].

Concomitant with the application for the Section 3c registration, the registrant filed a petition (PP 5F6960) requesting an exemption from the requirement of a tolerance for the active ingredient, *Beauveria bassiana* HF23, on all agricultural food commodities. A notice of filing of this petition was published in the Federal Register [FR: December 7, 2005 (Volume 70, Number 234)][Page 72831-72833]. One comment was received in response to this publication. The commenter inquired if Diquat was included in this pesticide. In the final rule to establish the exemption from tolerance, the Agency responded that Diquat is not included in the formulation. The exemption from tolerance for residues of *Beauveria bassiana* HF23 will be established concurrently with this conditional registration approval.

### III. SCIENCE ASSESSMENT

#### A. Physical and Chemical Properties Assessment

The data submitted in support of product identity requirements for *Beauveria bassiana* HF23, are sufficient for the proposed use patterns of the microbial pesticide, as discussed below.

##### 1. Product Identity and Mode of Action

*Beauveria bassiana* is a fungal entomopathogen. The active ingredient in this BRAD, *Beauveria bassiana* HF23, is characterized taxonomically as follows: *Mycota* kingdom, *Deuteromycota* phylum, *Hyphomycetes* class, *Moniliales* order, *Beauveria* genus, and *bassiana* species. This strain, *B. bassiana* HF23, was deposited in the ARSEF Collection in Ithaca, NY, USDA-ARS Plant Protection Research Unit U.S. Plant, Soil, and Nutrition Laboratory Tower Rd. Ithaca, New York 14853-2901. This Microbiological Pest Control Agent (MPCA) is for control of domestic house fly (*Musca domestica*) on chicken manure in high rise chicken house facilities. The fungal active ingredient kills the adult house fly pest by growing on the insect's exoskeleton and secreting enzymes into the pest's soft body parts to kill it.

##### 2. Product Characterization – TGAI

The active ingredient in the TGAI or MP, *Beauveria bassiana* HF23, is 95 percent w/w *Beauveria bassiana* HF23 spores which corresponds to  $4.75 \times 10^{11}$  cfu/g. *Beauveria bassiana* HF23 is a naturally occurring fungus which was isolated from a domestic house fly (*Musca domestica*) in the United States of America. This HF23 strain is quite specific for the control of house fly. This product is manufactured by a solid state fermentation process, such that the TGAI is a solid. All of the inert ingredients in the TGAI are food grade material, and are exempt from the requirement of a tolerance under 40 CFR 180.950 (a). Potential human pathogens for these inert ingredients are within acceptable levels for the study which supports product characterization.

Furthermore, it is expected that neither the active ingredient nor the unintentional ingredients will survive the high temperatures achieved during composting of the treated chicken manure. Because the pesticide is not to be directly applied to food/feed commodities, the potential risk posed by unintentional ingredients is negligible to non-existent. The potential metabolite, beauvericin, is within levels required for Quality Assurance and Quality Control (QA&QC) for food use pesticides containing this active ingredient. In addition, the pesticide is efficacious against a public health pest, house fly, and its use is in the public interest to reduce the risk of exposure to diseases caused by this pest. Nevertheless, the Agency is requiring submission of analyses of five production batches as a condition of registration to confirm that adequate QA&QC measures are in place during production. Any potential *Bacilli* as unintentional ingredients must not exceed  $10^4$  cfu/gram.

### 3. Product Chemistry and Manufacturing Process – TGAI

Results of studies evaluated by the Agency in support of product chemistry data requirements are summarized below (BPPD DERs dated 1/31/06, 2/1/06). **Table 1a** summarizes results of the product identity and manufacturing process (MRIDs 46449601, 46580501). **Table 1b** discusses the physical chemical properties for the TGAI from a submission MRID 46811101. Guideline data requirements (40 CFR §158.740(a)) for this TGAI for melting point, boiling point, solubility, vapor pressure, dissociation constant, octanol/water partition coefficient, viscosity, oxidizing or reducing potential, flammability/flash point, miscibility, and dielectric breakdown voltage were not required because of the nature of the microbial pesticide. Batches containing more than 10<sup>4</sup> cfu/g *Bacilli* contaminants, or other unintentional ingredients of toxicological levels and concern, must be destroyed.

**Table 1a: Product Identity & Manufacturing Process for *Beauveria bassiana* HF23 (TGAI)**

| Guideline           | Study  | Result   | **MRID #   |
|---------------------|--|--|--|
| 151-10<br>*885.1100 | Product Identity                                     | Determine the purity of the cultures by plating for aerobic, anaerobic, or enteric bacteria at the end of the fermentation procedure as part of the QC procedure.  | 46449601<br>46580501                                     |
| 151-11<br>*885.1200 | Manufacturing process                                | Determine the purity of the cultures by plating for aerobic, anaerobic, or enteric bacteria at the end of the fermentation procedure as part of the QC procedure.  | 46449601<br>46580501                                     |
| 151-12<br>*885.1300 | Discussion of Formation of Unintentional Ingredients | Beauvericin, a metabolite of the Genus <i>Beauveria</i> , and other unintentional ingredients, including human pathogens, are within regulatory levels, pending confirmatory data to show that five production batches meet Agency requirements. | 46449601<br>46580501                                     |
| 151-13<br>*885.1400 | Analysis of Samples                                  | Not required for magnitude of residues for exemption from tolerance. Microbial and biochemical methods required for product identity and quality assurance and quality control of pesticide active ingredient.                                   | 46449601<br>46580501<br>No MRID for magnitude of residue |
| 151-15<br>*885.1500 | Certification of limits                              | Acceptable   | 46449601<br>46580501                                     |

\*OPPTS Harmonized Guidelines      \*\*MRID = Master Record Identification Number

| <b>Table 1b: Physical Chemical Properties TGAI <i>Beauveria bassiana</i> HF23</b> |                           |  |                        |
|---|---------------------------|--|------------------------|
| <b>Guideline No.</b>  | <b>Property</b>           | <b>Result</b>  | <b>MRID/ Reference</b> |
| 151-26<br>*830.6302   | Color                     | White to light beige   | Letter 10/27/06        |
| 151-26<br>*830.6303   | Physical state            | Solid - powder   | 46811101               |
| 151-26<br>*830.6304   | Odor                      | Slight musty smell   | Letter 10/27/06        |
| 63-12<br>*830.7300  | pH                        | Does not disperse in water; pH cannot be measured  | 46811101               |
| 63-16<br>*830.6316  | Explosibility             | Not potentially explosible; only required if product is potentially explosible 40 CFR 158.190, footnote 7. | 46811101               |
| 63-17<br>*830.6317  | Storage stability         | Greater than or equal to 15 months @ 22-26°C   | 46811101               |
| 63-20<br>*830.6320  | Corrosion Characteristics | Not corrosive, based on nature of microbe and inert ingredients.   | 46811101               |
| *830.7300   | Bulk Density              | 0.181 g/cc   | 46811101               |
|   | Viability                 | 4.75 x 10 <sup>11</sup> cfu/g  | Letter 10/27/06        |

\*OPPTS Harmonized Guidelines

\*OPPTS Harmonized Guidelines

| <b>Table 1c: Physical Chemical Properties – EP</b> |                           |   |                              |
|--|---------------------------|---|------------------------------|
| <b>Guideline No.</b>                               | <b>Property</b>           | <b>Result</b>                             | <b>MRID/ Reference</b>       |
| 151-26<br>*830.6302                                | Color                     | Not required (PR Notice 92-5)             | None                         |
| 151-26<br>*830.6303                                | Physical state            | liquid                                    | 46449614                     |
| 151-26<br>*830.6304                                | Odor                      | Not required (PR Notice 92-5)             | None                         |
| 63-7<br>*830.7300                                  | Specific gravity          | 0.92                                      | 46449614                     |
| 63-12<br>*830.7000                                 | pH                        | Not dispersible in water; pH not measured | 46449614                     |
| 63-13<br>*830.6317                                 | Stability (Shelf life)    | Greater than 15 months at 22°C – 26°C     | 46580601                     |
| 63-16<br>*830.6316                                 | Explosibility             | Not potentially explosive                 | 46449614                     |
| 63-18<br>*830.7100                                 | Viscosity                 | 40.6 Centipoises at 29.4°C (85°F)         | 46449614                     |
| 63-20<br>*830.6320                                 | Corrosion Characteristics | Not corrosive; does not react with metals | 46449614                     |
|  | Viability                 | 5.6 x 10 <sup>9</sup> cfu/g               | Letter 10/27/06;<br>46580601 |

\*OPPTS Harmonized Guidelines

## 4. End-Use Product

### Manufacturing Process and Quality Control

**a. Product Identity (MRIDs 46449614, 46580601, 46526012; OPPTS Gdln 885.1300; Gdlns151-10 through 151-16)**

**b. Physical and Chemical Properties (MRID 46449614; see Gdlns Table 1c above).**

The End-Use Product in this registration action is an oil-based liquid suspension containing 1.18 percent spores of *Beauveria bassiana* HF23 (TGAI). No chemical reactions occur during the manufacturing process and the product chemistry data submitted are acceptable for the formulation (MRIDs 46526012, 46449614). In the EP, unintentional ingredients associated with the relative proportions (1.18 percent) of the active ingredient are present at no greater levels than those found in the TGAI. The requirement for confirmatory analyses of five production batches was discussed previously (see TGAI). The other ingredients in the formulation ingredients are exempt from the requirement of a tolerance for food use (MRIDs 46526012, 46449614; 46580601; BPPD DERs 2/01/06; 06/22/06). Product Chemistry data, as summarized in Table 1c, are acceptable.

Guideline data requirements (40 CFR §158.740(a)) for this EP for melting point, boiling point, dissociation constant, octanol/water partition coefficient, solubility, vapor pressure, stability, oxidizing or reducing potential, flammability/flash point, miscibility, and dielectric breakdown voltage were not required because of the nature of the microbial pesticide.

## B. Human Health Assessment

### 1. Food Clearances/Tolerances

The application included a petition for an exemption from tolerance for all food commodities which are grown in fields where processed chicken manure, treated with *Beauveria bassiana* HF23, is used as fertilizer. The submitted data support the exemption from the requirement of a tolerance and comply with the Food Quality Protection Act of 1996. The ubiquitous occurrence of *Beauveria bassiana* HF23 suggests that the fungus is expected to be present on food/feed commodities, regardless of the use of this pesticide as described herein. For this reason, and because of the low toxicity potential of this fungal MPCA as described in this BRAD, a final rule establishing the exemption from tolerance for *Beauveria bassiana* HF23 will be published in the Federal Register concurrent with this Section 3 conditional registration of this active ingredient.

### 2. Toxicology Assessment

Summaries of the acute toxicological studies and the rationales for data waiver requests (Table 2) are discussed below.

**a. Acute Oral Toxicity (MRID 46526003; OPPTS Gdln 885.3050)**

The Agency reviewed a study to ascertain acute oral toxicity/pathogenicity effects of the Technical Grade Active Ingredient (TGAI) *Beauveria bassiana* HF23 on rats ((BPPD Data Evaluation Record (DER), dated 1/31/06). Three groups of rats were treated by oral gavage with *Beauveria bassiana* HF23 at a dose of  $4.05 \times 10^9$  cfu/animal (using the hemacytometer method) or  $3.20 \times 10^8$  cfu/animal (using the dilution plate count method). Group 1 was a shelf control group of untreated rats housed in the same room as the treated rats. Group 2, the room control group, refers to untreated rats housed separately from the treated rats. Group 3 was treated with *Beauveria bassiana* HF23. All rats, treated and untreated, survived the study and gained weight during the study. One animal in Group 3 had soft feces at 2.5 hours after dosing with recovery by 4 hours, which indicates minimal or insignificant adverse effects.

The other rats in all groups appeared normal throughout the study. The test organism was detected in feces of all treated animals (Group 3) collected on the day of dosing (males:  $2.10\text{-}4.20 \times 10^4$  cfu/g; females:  $1.60\text{-}3.60 \times 10^4$  cfu/g). No test organisms were detected in the feces, tissues, blood, and cecum contents collected from Group 3 animals on days 3 and 7. No test organism was detected in untreated animals (Groups 1 and 2). The presented data show no clinically significant signs in rats. *Beauveria bassiana* HF23 was not detected in kidney, brain, liver, lungs, spleen, cervical and mesenteric lymph nodes, cecum contents, or blood samples and are cleared from the feces by day 3. Therefore, based on the presented/submitted data, the test organism was not toxic, infective, or pathogenic to rats. The active ingredient was considered Toxicity Category IV for acute oral toxicity/pathogenicity effects in mammals.

**b. Acute Dermal Toxicity Study (MRID 46526004; OPPTS Gdln 885. 3100)  
Primary Dermal Irritation (OPPTS 870.2500)**

A study for acute dermal toxicity effects was evaluated by the Agency (BPPD DER dated 1/31/06). Five male and five female New Zealand White rabbits were ear-tagged and were acclimated for 7 days. The test material (2000 mg/kg body weight) was applied to the clipped back. The application site was covered with a porous gauze patch and secured with hypoallergenic tape. The trunk was wrapped with a bandage. Collars were affixed to the rabbits. The coverings and collars were removed after 24 hours and the excess test material was removed with water moistened paper towels. The test animals were observed twice daily for mortality and morbidity for 14 days. The dermal irritation was examined and scored at approximately 1, 2.5, and 4 hours post treatment and thereafter for 14 days. The rabbits were weighed prior to treatment and on days 7 and 14. The rabbits were euthanized on day 14, but no necropsies were performed.

All rabbits survived the study. All animals had normal body weight gain. All application sites were normal during the study. The dermal LD<sub>50</sub> for males, females, and combined genders was greater than 2000 mg/kg [ $4.27 \times 10^{11}$  cfu/g (using the hemacytometer method) and  $5.10 \times 10^{10}$  cfu/g (using the dilution plate count method)]. The test organism produced no adverse reaction on the skin of the rabbits. This places *Beauveria bassiana* HF23 in Toxicity Category III. Based on the lack of toxicity

observed in the acute dermal toxicity study and the nature of the inert ingredients a primary dermal irritation study is not required (BPPD DER dated 1/31/06).

**c. Acute Pulmonary Toxicity/Pathogenicity (MRID 46526005; OPPTS 885.3150; Gdln 152-32)**

A study to evaluate the acute toxicity and pathogenicity of *B. bassiana* HF23 in rats was reviewed. Rats were ear-tagged, assigned to treatment groups and acclimated for 5 days prior to dosing. The dose was prepared by weighing 0.5 g of the test organism into a container and adding 4.5 ml of sterile purified water. The dose preparation contained  $1.06 \times 10^7$  cfu/0.1 ml. Each animal in Group 3 was dosed with a single dose of 0.1 ml of the test organism suspension by intratracheal instillation.

**Table 2: Tier I - Acute Mammalian Toxicity of *Beauveria bassiana* HF23 TGAI**

| Guideline           | Study                                      | Toxicity Category | Results  | MRID #     |
|---------------------|--|-------------------|--|------------|
| 152-10<br>*885.3050 | Acute oral toxicity/<br>pathogenicity      | IV                | Not infective or pathogenic to rats treated with dose of $4.05 \times 10^9$ cfu/animal           | 46526003   |
| 152-31<br>*885.3100 | Acute dermal toxicity                      | III               | Not toxic to New Zealand white rabbits at 2000mg/kg bw. LD <sub>50</sub> greater than 2000 mg/kg | 46526004   |
| 152-34<br>*870.2500 | Primary dermal irritation                  | III               | Not required based on results of acute dermal toxicity test.                                     | Waived     |
| 152-32<br>*885.3150 | Acute pulmonary toxicity/<br>pathogenicity | III               | No clinical signs in treated rats. Not toxic, infective, pathogenic via pulmonary route.         | 46526005   |
| 152-32<br>*885.3400 | Acute inhalation                           | III               | No respirable particles; not toxic/pathogenic via pulmonary route                                | Waived     |
| 152-33<br>*885.3200 | Acute intraperitoneal injection            |                   | Not toxic, infective, pathogenic   | 46526006   |
| 152-35<br>*870.2400 | Primary eye irritation                     | III               | Eye instillation in rabbits and 7 day observation. Not eye irritant.                             | 46526007   |
| 152-36              | Hypersensitivity study                     | N/A               | Waived on lack of reports of hypersensitivity incidents (see below).                             | Waived     |
| 152-37              | Hypersensitivity incidents                 | N/A               | None reported. Must report hypersensitivity effects if any to comply with section 6(a)(2)        | Not waived |
| 152-38<br>*880.3800 | Immune response                            | N/A               |  | Waived     |

\*885.xxxx, 870.xxxx and 880.xxxx = OPPTS Harmonized Guidelines

Body weights were recorded on the day of dosing, on day 3 for those animals sacrificed on day 3, and on day 7 for the remaining animals. The test animals were observed for mortality and morbidity twice daily and for clinical signs at 1, 2.5, and 4 hours post dosing and daily thereafter for 7 days. Lungs were collected from one animal per sex in Group 2 and three animals per sex in Group 3 one hour post dose and on day 3.



Lungs were also collected from one animal per sex in Groups 1 and 2 and three animals per sex in Group 3 on day 7 of the study. Lungs, kidney, brain, liver, lungs, spleen, cervical and mesenteric lymph nodes, cecum contents and a blood sample were collected from one animal per sex in Group 2 and three animals per sex in Group 3 on day 3, and from one animal per sex in Groups 1 and 2 and three animals per sex in Group 3 on day 7 of the study. The number of viable cfu of the test organism/g of tissues, blood, cecum contents, and feces was determined by the serial dilution plate count method.

One male in Group 3 and one female were dead on the day of dosing. The cause of death was likely due to the anesthesia. All other rats survived until scheduled sacrifice. All surviving animals gained weight. All treated animals (Group 3) were normal. Reduced feces were observed in one female each from Groups 1 and 2 for one day. All surviving animals were killed at the end of the observation period without necropsy. The test organism was detected in lungs of all treated animals (Group 3) collected on the day of dosing (males:  $2.10\text{-}3.70 \times 10^4$  cfu/g; females:  $4.70\text{-}7.60 \times 10^4$  cfu/g). No test organisms were detected in the tissues, blood, and cecum contents collected from Group 3 animals on days 3 and 7. No test organisms were detected in untreated animals (Groups 1 and 2). The presented data show no clinical signs in treated rats. *Beauveria bassiana* HF23 was detected only in lungs with clearance by day 3 after dosing. Therefore, based on the presented/submitted data, the test organism was not toxic, infective, or pathogenic to rats via the pulmonary route (BPPD DER dated 1/31/06).

**d. Acute Inhalation (Data Waiver Request; OPPTS 885.3050; Gdln 152-32)**

The Agency has decided to waive the requirement for an acute inhalation study based on the nature of the inert ingredients and the low toxicity potential demonstrated in the acute pulmonary toxicity/pathogenicity study (BPPD DER dated 1/31/06) as discussed above. The inert ingredients consist of a solid state matrix with particles which are not respirable. The Manufacturing Product is to be used for formulation into End-use products. The use of a respirator with the NIOSH prefix N-95, R-95 or P-95 will protect workers during formulation of the MP into EP and is required on the label for the MP. Acute inhalation requests for EPs will be considered on a case-by-case basis.

**e. Acute Intraperitoneal Injection (MRID 46526006; OPPTS 885.3200; Gdln 152-33)**

An acute intraperitoneal study in rats was reviewed to determine if *B. bassiana* HF23 was toxic or pathogenic in mammals (BPPD DER dated 1/31/06). Rats were ear-tagged, assigned to treatment groups and were acclimated for 5 days prior to dosing. The dose was prepared by weighing 0.1 g of the test organism into a container and adding 99.9 ml of sterile purified water. Each animal in Group 2 was dosed with a single dose of 1ml of the test organism suspension by intraperitoneal injection. Body weights were recorded on the day of dosing, weekly thereafter, and at the terminal sacrifice. The test animals were observed for mortality and morbidity twice daily. All animals were necropsied at the end of the study.

The presented data show no clinically significant signs in rats. All animals survived the study and gained weight during the study. One treated male and one treated female had a lump under the skin in the ventral abdomen. The test organism was not recovered from the lesions. One treated male had mottled kidneys and one treated female had red lungs. One untreated female and four treated females had red/enlarged ovaries/uterus. No lesions or other signs of infectivity were observed in the affected kidneys, lungs, ovaries, and uteruses. Based on the presented/submitted data, the test organism was not toxic or pathogenic to rats via intraperitoneal injection (BPPD DER dated 1/31/06).

**f. Primary eye irritation (MRID 46526007; OPPTS 870.2400; Gdln 152-35)**

A study was performed in rabbits to determine the potential for *B. bassiana* HF23 to cause eye irritation in mammals. Rabbits were ear-tagged and acclimated for 7 days (BPPD DER 1/31/06). The dose preparation (0.1 g sample + 9.9 ml 1 percent emulsifier) contained  $4.27 \times 10^{11}$  cfu/g and  $5.10 \times 10^{10}$  cfu/g. The test organism (0.07 g = 0.1 ml/eye/animal) was applied into the conjunctiva sac of one eye, and the eye held closed for approximately one second. The contra lateral eye served as control. The eyes were examined and scored 1, 24, 48 and 72 hours and 7 days after test material instillation.

All animals survived the study. No corneal opacity was noted in any animal during the study. One animal had iritis 24 hours after the instillation of the test organism. Positive irritation of the conjunctiva was noted on all animals one hour through 72 hours after instillation of the test organism, with resolution by day 7. The maximum average score was 15.7 at 24 hours after test material instillation. Corneal opacity was not noted on any animal during the study. Positive conjunctiva irritation was noted on all animals one hour through 72 hours after test organism instillation with resolution by day 7. The maximum average score was 15.7 at 24 hours after test material instillation. *Beauveria bassiana* HF23 was mildly irritating and is in Toxicity Category III. These data were considered Supplemental at first review (BPPD DER dated 1/31/06) and upgraded to acceptable following review of a submission of information about the source of the rats used in the study (BPPD DER 2/1/06).

**g. Hypersensitivity Study (Guideline 152-36)**

The registrant requested to waive a hypersensitivity study based on the following arguments. *Beauveria bassiana* HF23 is a well known entomopathogenic fungi with a mechanical mode of action, which is not expected to incite a hypersensitive response in humans. Footnote (iii) of 40 DFR 158.740(c) states that this guideline is required if commonly recognized practices will result in repeated human contact by inhalation and dermal routes. Even if such repeated contact occurs, the low toxicity potential of the active ingredient poses no harm to exposed populations.

The Agency also considered the submitted acute dermal study which indicated no potential adverse dermal reaction to exposure to the active ingredient at guideline levels (see above). Other acute toxicity/pathogenicity tests indicate a low toxicity potential for the active ingredient via oral, intraperitoneal and pulmonary studies in rodents. In

addition, to mitigate against dermal and inhalation exposure the Agency will include the applicant's following recommendations for Personal Protective Equipment (PPE) for workers: (a) a respirator/dusk mask with NIOSH prefix N-95, P-95 or R-95, long sleeved shirt and long pants and (b) washing of hands after application, to ensure that exposure to the product is limited. In addition, the solid matrix of the inert ingredients is not respirable. A hypersensitivity study is not required at this time, but may be required in the future, if there are reports of hypersensitivity incidents associated with this active ingredient used in pesticides (BPPD DER dated 12/14/06).

#### **h. Hypersensitivity Incidents (Guideline 152-37)**

No incidents of hypersensitivity associated with the TGAI or proposed components of the EP have been reported to date. This guideline requirement is satisfied at this time. However, in order to comply with FIFRA requirements under Section 6(a)(2), any incident of hypersensitivity associated with the use of this pesticide must be reported to the Agency. This data requirement is not waived (BPPD DER dated 12/14/06).

#### **i. Immune Response (OPPTS 880.3800; Gdln 152-38)**

The registrant's request to waive this data requirement is based on the following rationale: *Beauveria bassiana* HF23 is a well known entomopathogenic fungi with a mechanical mode of action which is not expected to incite an immune response in humans.

The Agency also considered the results of the acute toxicity/pathogenicity oral, pulmonary and intraperitoneal tests. These demonstrate that the active ingredient is not toxic/pathogenic when it is administered to test rodents by oral gavage, and intratracheal instillation or injected intraperitoneally (BPPD DER dated 1/31/06). Results from these supporting toxicology tests indicate that test mammalian immune systems can clear the organism. Based on these considerations and the justifications submitted by the registrant, this request to waive the data requirement for an immune response study is granted (BPPD DER dated 12/14/06).

#### **j. Subchronic, chronic toxicity and oncogenicity, and residue data**

Based on the data generated in accordance with the Tier I data requirements set forth in 40 CFR 158.740(c), Tier II tests (Guidelines 152B-40 through 152B-49) involving acute oral, acute inhalation, subchronic oral, acute intraperitoneal/intracerebral, primary dermal, primary eye, immune response, teratogenicity, virulence enhancement, and mammalian mutagenicity were not required. As a result, Tier III tests (Guidelines 152-50 through 53) involving chronic testing, oncogenicity testing, mutagenicity, and teratogenicity also were not required.

Residue data were not required based on the ubiquity of *Beauveria bassiana* HF23 and the non-infective, non-toxic, and non-pathogenic potential as demonstrated in the Tier I tests. This pesticide is also not to be applied directly to food commodities by pre-

or post-harvest applications. Thus residues greater than background levels are not expected on crops where treated chicken manure is used as fertilizer.

#### **k. Effects on the Endocrine Systems**

EPA is required under the FFDCFA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) “may have an effect in humans that is similar to an effect produced by a naturally-occurring estrogen, or other such endocrine effects as the Administrator may designate.” Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific basis for including, as part of the program, the androgen and thyroid systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC’s recommendation that the program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCFA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

The Agency is not requiring information on the endocrine effects of this active ingredient, *Beauveria bassiana* HF23, at this time. The Agency has considered, among other relevant factors, available information concerning whether the microorganism may have an effect in humans similar to an effect produced by a naturally occurring estrogen or other endocrine effects. There is no known metabolite that acts as an “endocrine disrupter” produced by this microorganism. The submitted toxicity/pathogenicity studies in the rodent (required for microbial pesticides) indicate that following acute oral, dermal, pulmonary, and intraperitoneal studies, the immune system is still intact and able to process and clear the active ingredient. In addition, based on the low potential exposure level associated with the proposed use of this pesticide, the Agency expects no incremental adverse effects to the endocrine or immune systems. Thus, there is no impact via endocrine-related effects on the Agency’s safety finding set forth in this BRAD for *Beauveria bassiana* HF23.

#### **l. Toxicology - EP**

##### **Primary Eye Irritation – Rabbit ( MRID 46526013)**

Three young female white New Zealand rabbits were treated with the test organism. A dose of 0.1 ml/eye was applied into the conjunctival sac of one eye of each animal, and the eye held closed for approximately one second. The contralateral eye served as control. The eyes were examined and scored 1, 24, 48, and 72 hours after test material instillation.

Corneal opacity, iritis, or positive conjunctival irritation was not noted on any animal during the study. The maximum average score was 5.3 one hour after test material instillation. *Beauveria bassiana* HF23 End-Use Product was minimally irritating

to the eyes of the rabbits. This study is ACCEPTABLE and the EP is in Toxicity Category IV for primary eye irritation.

#### **m. Data Waiver Requests EP**

The applicant's requests to waive data for the EP based on the results of the acute toxicity tests for the TGAI and the nature of the inert ingredients are justified (BPPD DERs dated 1/31/06 and 12/14/06).

### **Food Quality Protection Act Considerations**

#### **3. Dietary Exposure and Risk Characterization (includes drinking water)**

The microbial pesticide containing the active ingredient, *Beauveria bassiana* HF23, is not applied directly to food as discussed in this unit. Food or feed commodities are exposed to *Beauveria bassiana* HF23 as a result of treated chicken manure being used as fertilizer to agricultural crops.

##### **a. Food**

*Beauveria bassiana* HF23 is sensitive to warm temperatures (MRID 46526011) and UV light. Thus, the amount of viable *B. bassiana* HF23 spores present in manure to be spread on agricultural fields would greatly diminish once the fungus is exposed to sunlight. However, data show that viable *B. bassiana* HF23 spores will leave poultry production houses upon disposal of manure and litter. The treated chicken manure is processed into fertilizer for use on agricultural crops. The high temperatures of composting are very likely to destroy any potential residual *Beauveria bassiana* HF23 or other potential microbial contaminants. At the time of application of the treated chicken manure, *B. bassiana* HF23 colonies have declined to levels which are no greater than those observed of the naturally occurring microbe (BPPD DER June 20, 2006).

The active ingredient occurs naturally and is ubiquitous in the environment. Thus, regardless of treatment with the pesticide, residues of *Beauveria bassiana* species are likely to be found on food/feed commodities. Neither direct applications to agricultural food/feed crops, nor direct post-harvest of the pesticide to food/feed commodities, are proposed for this pesticide at this time. Thus, detectable residues of *Beauveria bassiana* HF23, are not expected on food/feed commodities as a sole result of the proposed use of this active ingredient. Moreover, washing, peeling and processing of foods and feed commodities before consumption would further mitigate any potential exposure and risk via dietary exposure.

Even if there were exposure to *Beauveria bassiana* HF23, and direct treatment of food commodities, the toxicological study discussed in **Section III B** above indicates no acute oral toxicity/pathogenicity effects of this active ingredient. Subchronic and chronic oral, or other toxicology studies, were not required for this active ingredient since the acute toxicology studies demonstrated a low toxicity potential for this active ingredient. Thus, no harm is expected to human adults, children or infants via acute, subchronic or

chronic dietary exposure to food or feed grown in fields fertilized with chicken manure which has been treated with *Beauveria bassiana* HF23.

#### **b. Drinking water exposure**

No exposure to drinking water is anticipated because of the use pattern and use sites. There are no aquatic use sites permitted for this pesticide. Thus, transfer of *Beauveria bassiana* HF23 from soil to groundwater is unlikely. Even if such a transfer were to occur, the fungus would not tolerate the conditions drinking water treatment would provide, e.g., chlorination, pH adjustments, and/or processing conditions. So exposure to drinking water is not expected. Further, there is no evidence of adverse effects from exposure to this organism. Exposure from the proposed use of *Beauveria bassiana* HF23 is not likely to pose any incremental risk to adult humans, infants and children via consumption of drinking water.

#### **4. Aggregate Exposure - Other Non-Occupational Exposure**

The proposed product is for use as a TGAI for formulation into end-use products. The EP in this registration packet is to be used for control of house flies on chicken manure which will be commercially used as fertilizer on agricultural crops. No non-occupational residential, school or day care exposure is anticipated because of the use patterns of these pesticide products. No indoor residential, school, or daycare uses are permitted on the label of this product. Thus, use of *Beauveria bassiana* HF23 should result in minimal to non-existent, non-occupational risk.

##### **a. Dermal exposure**

EPA has concluded that this pesticide poses minimal risk to human populations via non-occupational dermal exposure. This conclusion is based on the low toxicity potential observed in the acute dermal studies discussed in Unit III, and the low exposure potential based on non-viability of the active ingredient on treated chicken manure used as fertilizer on agricultural crops. Moreover, potential non-occupational dermal exposure to *Beauveria bassiana* HF23 is unlikely because the use sites are commercial and agricultural.

As previously discussed, hypersensitivity incidents associated with *Beauveria bassiana* HF23 have not been reported to date. Thus, the active ingredient poses minimal risk to populations via non-occupational dermal exposure. Therefore, the Agency does not expect pesticides containing *Beauveria bassiana* HF23 to pose a non-occupational dermal exposure risk.

##### **b. Inhalation exposure**

Non-occupational inhalation exposure to the active ingredient itself is not expected to pose an inhalation risk. No treatment-related effects associated with the active ingredient were observed in the pulmonary tests reported in Unit III. Based on the low potential for non-occupational inhalation exposure, the Agency does not expect *Beauveria bassiana* HF23 to pose an inhalation risk.

In summary, the potential aggregate exposure as a result of the use of the pesticidal active ingredient *Beauveria bassiana* HF23 is not likely to pose a hazard. This includes hazards derived from (a) dietary exposure from the treated food/feed commodities, (b) drinking water potentially exposed secondary to treatment of sites with this pesticide; and (c) dermal and inhalation non-occupational and occupational exposure of populations exposed to *Beauveria bassiana* HF23.

## 5. Cumulative Effects

The Agency has considered the potential for cumulative effects of *Beauveria bassiana* HF23 and other substances in relation to a common mechanism of toxicity. These considerations include the possible cumulative effects of such residues on infants and children. As demonstrated in the toxicity assessment, *Beauveria bassiana* HF23 is non-toxic and non-pathogenic to mammals. Because no mechanism of pathogenicity or toxicity in mammals has been identified for this organism, no cumulative effects from the residues of this product with other related microbial pesticides are anticipated.

## 6. Determination of Safety for U.S. Population, Infants and Children

There is reasonable certainty that no harm will result to the U.S. population, including infants and children, from aggregate exposures to residues of *Beauveria bassiana* HF23, as a result of its proposed uses. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. As discussed previously, there appears to be no potential for harm, from this fungus in its use as an insecticide via dietary exposure since the organism is non-toxic and non-pathogenic to animals and humans. The Agency has arrived at this conclusion based on the very low levels of mammalian toxicity for acute oral, pulmonary, and dermal effects with no toxicity or infectivity at the doses tested (see Unit III above).

Moreover, potential non-occupational inhalation or dermal exposure is not expected to pose any adverse effects to exposed populations via aggregate and cumulative exposure (see **Sections III.4 and 5**).

FFDCA section 408(b)(2)(C) provides that EPA shall apply an additional ten-fold margin of exposure (safety) for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database on toxicity and exposure, unless EPA determines that a different margin of exposure (safety) will be safe for infants and children. Margins of exposure (safety), which are often referred to as uncertainty factors, are incorporated into EPA risk assessment either directly, or through the use of a margin of exposure analysis, or by using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk. In this instance, based on all the available information (as discussed above), the Agency concludes that the fungus, *Beauveria bassiana* HF23, is non-toxic to mammals, including infants and children. Because there are no threshold effects of concern to infants, children and adults when *Beauveria bassiana* HF23 is used as a pesticidal active ingredient, the Agency has determined that the additional margin of safety is not necessary to protect infants and children, and that not adding any additional margin of safety will be safe for infants and

children. As a result, EPA has not used a margin of exposure (safety) approach to assess the safety of *Beauveria bassiana* HF23.

## **7. Other Considerations - Occupational and Residential Exposure and Risk Characterization**

### **a. Occupational Exposure**

Dermal exposure via the skin would be the primary route of exposure for mixer/loader applicators. Dermal and inhalation exposure would be the greatest route of exposure for workers. However, the acute dermal and pulmonary toxicity tests previously discussed in this BRAD demonstrate that this low toxicity active ingredient poses no harm to exposed populations. Personal Protective Equipment (PPE) will further mitigate exposure to workers formulating the pesticide into EPs and applying the EP to poultry houses. Such PPE includes long sleeve shirt, long pants, shoes, socks and dist/mist filtering respirators with the NIOSH prefix N-95, P-95 and R-95.

### **b. Residential, School and Day Care Exposure and Risk Characterization**

The evaluation of acute dermal and pulmonary toxicity mammalian data resulted in a categorization of the pesticide as Toxicity Category III for dermal and inhalation exposure [BPPD Review dated 1/31/06]. The pesticide is not to be applied in the vicinity of residences, schools, and daycares. It does not pose a risk to the environment or human health as discussed in **Section III** of this BRAD. Hence, the risk of residential, school and daycare exposure is expected to be minimal to negligible via the proposed uses of the active ingredient.

## **C. Environmental Assessment**

### **Ecological Effects Hazard Assessment**

Below is a summary of the ecological effects database evaluated in support of this action. The database for studies and information of toxicity of *Beauveria bassiana* HF23 to non-target organisms are sufficient to allow conditional registration as a microbial pesticide for use on chicken manure to control housefly.

#### **1. Non-guideline Studies**

##### **a. Evaluation of Viability Degradation Over Time of *B. bassiana* Conidia Applied to Poultry Manure and Litter (MRID 46526010)**

End-use formulations of Jabb DB2 ES and Jabb HF23 ES containing conidia of *B. bassiana* were applied at rates of  $2 \times 10^{11}$  or  $1 \times 10^{11}$  conidia/100 ft<sup>2</sup>, respectively, to containers holding either chicken manure or chicken house litter and monitored for viability over 56 days. Manure and litter material was placed in containers at a rate of  $35 \pm 2$  g/container. Test material was delivered by a spray system mounted on a tractor using a standard application rate of 1.3 gallons of water/1000 ft<sup>2</sup>. One hour after test material application, viability was measured in a laboratory. Viability was measured by staining filtered samples of manure/litter with a Molecular Probes Live/Dead Viability Kit and viewing samples with a fluorescence microscope. Viability analysis was repeated



at weekly intervals for 55 days post-application. *B. bassiana* HF23 viability in both manure and litter was greater than 94 percent one hour after application. Viability gradually decreased by day 21, particularly in manure. At day 56, viability was less than 2 percent in both manure and litter. These data indicate that some viable *B. bassiana* HF23 spores will leave poultry production houses upon disposal of manure and litter. This study is acceptable.

**Table 3. Summary of environmental effects studies and waiver justifications submitted for *Beauveria bassiana* HF23 to comply with 40 CFR § 158.740 data requirements**

| Guideline           | Study                                   | Results   | MRID            |
|---------------------|---|---|-----------------|
| Non-Gdln            | Growth at Different Temperatures        | <i>B. bassiana</i> strains DB, HF, and CT were unable to grow on Barley Start Slurry Agar at 35-37°C. The HF strain grew better than the DB or CT strains when incubated at 30°C.   | 46526011        |
| Non-Gdln            | Viability                               | Viability in poultry litter and manure was greater than 94 percent at one hour post-treatment and decreased over time to less than 2 percent at day 55.   | 46526010        |
| 154-16<br>*885.4050 | Avian Oral, Tier 1 (Broiler Chicken)    | No mortality or adverse effects were seen at the maximum hazard dose; therefore both the LD <sub>50</sub> and the ID <sub>50</sub> were greater than 0.91 g/kg body weight, and the NOEL is also 0.91 g/kg body weight                    | 46526008        |
| 154-16<br>*885.4050 | Avian Oral Toxicity                     | A waiver was requested based on MRID No. 46526008. Minimal exposure to wild birds is expected from use of this product.   | NA/waived study |
| 154-17<br>*885.4100 | Avian Injection                         | This study is required only for MPCAs related to known avian pathogens.   | NA/waived study |
| 154-18<br>*885.4150 | Wild Mammal Testing, Tier I             | The potential for exposure to wild mammals from use of this product is expected to be minimal; therefore wild mammal testing is not warranted. In addition, no adverse effects were reported in MRID 46526003 (rodent oral toxicity test) | NA/waived study |
| 154-17<br>*885.4200 | Freshwater Fish Toxicity                | The potential for exposure to freshwater fish from use of this product is expected to be minimal; therefore a freshwater fish toxicity test is not warranted.   | NA/waived study |
| 154-20<br>*885.4240 | Freshwater Aquatic Invertebrate Testing | The potential for exposure to freshwater aquatic invertebrates from use of this product is expected to be minimal; therefore a freshwater aquatic invertebrate toxicity test is not warranted.  | NA/waived study |
| 154-21<br>*885.4280 | Estuarine/Marine Animal Testing, Tier I | The potential for exposure to estuarine/marine animals from use of this product is expected to be non-existent, therefore minimal; an estuarine/marine animal toxicity test is not warranted.   | NA/waived study |
| 154-22<br>*885.4300 | Non-Target Plants                       | <i>B. bassiana</i> is generally known to be non-pathogenic to plants.   | NA/waived study |
| 154-23<br>*885.4340 | Non-Target Insects                      | The potential for increased exposure above background levels to non-target insects from use of this product is expected to be minimal; therefore a non-target insect toxicity test is not warranted.                                      | NA/waived study |
| 154-24<br>*885.4380 | Honey Bee Toxicity, Tier I              | Although some <i>B. bassiana</i> strains are known to be harmful to honey bees, the expected exposure from use of <i>B. bassiana</i> HF23 is not expected to be at levels that would be of concern.                                       | NA/waived study |

\* OPPTS Harmonized Guidelines

**b. Growth of *Beauveria bassiana* in Barley Start Slurry Agar at Two Temperatures (MRID 46526011)**

Dilutions of *B. bassiana* strain DB2 and strain HF23 at  $10^{-8}$ ,  $10^{-9}$ , and  $10^{-10}$  (representing 10,000 cfu/ml, 1,000 cfu/ml, and 100 cfu/ml, respectively) were inoculated onto plates of agar and incubated at 30°C or 35-37°C for 14 days. None of the plates incubated at 35-37° produced any fungal growth. All plates incubated at 30°C produced fungi resembling *B. bassiana*. This study is acceptable

**2. Guideline Requirements**

**a. Toxicity to Terrestrial animals**

**(i) Avian Oral Toxicity, Tier I (MRID 46526008; OPPTS 885.4050; Gdln 154-16)**

In a 30-day laboratory study, (MRID 46526008) 20-day old WW36 chickens (male and female) were administered TGAI *Beauveria bassiana* HF23 at a target dose level of 0.91 g/kg/body weight for five consecutive days. Three control groups were used, including a negative control (corn oil), sterile control (autoclaved *B. bassiana* HF23 spores), and sterile filtrate control (*B. bassiana* HF23 filtrate by-product of spore culture). For the treatment and sterile control solutions, dry spores were combined with corn oil to facilitate delivery by gavage. The sterile filtrate control birds were dosed with the undiluted sterile filtrate. The negative control birds were dosed with only corn oil. There were no deaths or adverse clinical signs, and no significant differences in body weight, feed consumption, gross necropsy, or histopathology among the test groups after the 5-day dosing period followed by a 26-day observation period (30-days total). The estimated LD<sub>50</sub> and ID<sub>50</sub> were greater than 0.91 g/kg/body weight and the NOEL was 0.91 g/kg/body weight. Therefore, no adverse effects to avian wildlife are expected from the proposed uses of *B. bassiana* HF23. The study was classified as acceptable.

**(ii) Avian Oral Toxicity (MRID 46526008; OPPTS 885.4050; Gdln 154-16)**

A request was submitted to waive this study based on the submitted avian oral toxicity study conducted with chickens using a maximum hazard dose (MRID 46526008). The proposed use of *B. bassiana* HF23 is in enclosed poultry production houses, resulting in no exposure to wild bird species. Therefore, chickens were used as the test animal instead of bobwhite quail. No adverse effects were observed in the study. In addition, *B. bassiana* HF23 does not grow at 37°C (MRID 46526011) and bird body temperature is usually around 40°C. Optimum growth temperature of *B. bassiana* HF23 is 28°C. The waiver justification for this study is acceptable.

**(iii) Avian Injection Test (OPPTS Gdln 885.4100; Gdln 154-17)**

A request was submitted to waive this study based on the relatively low levels of *B. bassiana* HF23 used to treat large manure pits in poultry production houses. The average size of such facilities is 1 acre (13,560 feet). Manure pits are generally 10 feet

deep and are recessed into the floor area of poultry houses. Poultry exposure to *B. bassiana* HF23 is expected to be minimal because of the distance between poultry cages and the manure pit and because applications of *B. bassiana* HF23 will be made directly to the manure. The waiver for this study is accepted because this study is required only for MPCAs related to known avian pathogens.

**(iv) Wild Mammal Testing (MRIDs 46526003, 46811101; Gdln 885.4150)**

A request was submitted to waive this study because increased environmental exposure to *B. bassiana* HF23 will be minimal, given that *B. bassiana* is naturally occurring. In addition, *B. bassiana* HF23 will be applied inside poultry production houses, minimizing direct exposure to wild mammals. Further, no adverse effects were seen in the Acute Oral Toxicity Study conducted with *B. bassiana* HF23 (MRID 46526003). A literature search was conducted as part of MRID 46811101. The literature search of the AGRICOLA and PubMed databases was conducted and no report of adverse mammalian reactions to *B. bassiana* was found. The waiver justification for this study is acceptable.

**b. Toxicity to Aquatic animals**

**(i) Freshwater Aquatic Vertebrate (MRIDs 46526010, 46526011; Gdln 885.4200)**

A request was submitted to waive this study based on the data included in MRID 46526010. This study shows that *B. bassiana* HF23 viability concentration in chicken manure and litter decreases from 94 percent ( $9.4 \times 10^8$  cfu/ft<sup>2</sup>) at 1 hour post treatment to less than 2 percent 56 days after treatment. The potential for water contamination by this fungus is further reduced due to its sensitivity to warm temperatures (MRID 46526011) and UV light. The amount of viable *B. bassiana* HF23 spores present in manure being spread would greatly diminish once it is exposed to sunlight. The waiver justification for this study is acceptable.

**(ii) Freshwater Aquatic Invertebrate Testing (MRIDs 46526010, 46526011; Gdln 885.4240)**

A request was submitted to waive this study requirement based on the data included in MRID 46526010. This study shows that *B. bassiana* HF23 viability concentration in chicken manure and litter decreases from 94 percent ( $9.4 \times 10^8$  cfu/ft<sup>2</sup>) at 1 hour post treatment to less than 2 percent 56 days after treatment. In addition, the potential for water contamination is further reduced by the sensitivity of *B. bassiana* HF23 to warm temperatures (MRID 46526011) and UV light. The amount of viable *B. bassiana* HF23 spores present in manure being spread would greatly diminish once it is exposed to sunlight. The waiver justification for this study is acceptable.

**(iii) Estuarine/Marine Animal Testing (MRIDs 46811101, 46786401; Gdln 885.4280)**

A request was submitted to waive this study requirement based on information provided in MRID 46811101. The waiver request provides rationale that the active ingredient is a naturally-occurring soil organism whose level in the aquatic environment will not significantly increase with the use of *B. bassiana* HF23. In addition, MRID 46786401 shows that even if manure treated with *B. bassiana* HF23 is used for fertilizer, the manure contains such low levels of *B. bassiana* HF23 that it would not introduce additional amounts of the fungus into the environment. MRID 46811101 also provided information and a literature search regarding no adverse effects in estuarine and marine animal testing using other strains of *B. bassiana*. The waiver justification is acceptable.

**c. Toxicity to Non-target Plants (Gdln 885.4300)**

A request was submitted to waive this study requirement based on the data included in MRID 46526010. This study shows that *B. bassiana* HF23 viability concentration in chicken manure and litter decreases from 94 percent ( $9.4 \times 10^8$  cfu/ft<sup>2</sup>) at 1 hour post treatment to less than 2 percent 56 days after treatment. In addition, the potential for water contamination is further reduced by the sensitivity of *B. bassiana* HF23 to warm temperatures (MRID 46526011) and UV light. Further, *B. bassiana* is generally known to be nonpathogenic to plants. The End-use Product, containing *B. bassiana* HF23, is formulated with inert ingredients which are exempt from the requirement of a tolerance. They are known to cause some phytotoxicity when **non-diluted concentrations** are applied directly to plants. However, this EP contains **low concentrations** of these inert ingredients. When the EP is further diluted and sprayed on to the manure the concentration of these inerts will be further diluted. Moreover, the sprays are not directly applied to agricultural crops. Even if it were applied to crops, the levels are not expected to reach those that would result in adverse effects to non-target plants (both terrestrial and aquatic). The waiver justification for this study is acceptable.

**d. Toxicity to Toxicity to Non-target Insects (Gdln 885.4340)**

A waiver is requested for this study based on the fact that minimal exposure that will result from use of *B. bassiana* HF23 in poultry production houses. In addition, MRID 46786401 shows that even if manure treated with *B. bassiana* HF23 is used for fertilizer, the manure contains such low levels of *B. bassiana* HF23 that it would not introduce additional amounts of the fungus into the environment. Supporting literature provided by the registrant demonstrates that use of *B. bassiana* containing composted poultry manure in rangeland and poultry house settings did not pose adverse effects to non-target and beneficial insects (MRIDs 46786401 and 46811101). The waiver justification for this study is acceptable.

**e. Toxicity to Beneficial Insects - Honey Bee Toxicity (Gdln 885.4380)**

A request was submitted to waive this study in MRID 46811101 based on the fact that exposure to *B. bassiana* HF23 will be minimal to honey bees. Although some strains of *B. bassiana* are known to be harmful to honey bees, the proposed use of *B. bassiana* in

poultry production houses is not expected to result in increased exposure or adverse effects to honey bees. The waiver justification for this study is acceptable.

### 3. Endangered Species Assessment

Information provided to the Agency shows that *B. bassiana* has the potential to be transported out of poultry production houses via removal of manure. However, information provided to the Agency (MRID 46786401) also shows that expected viability after transfer to an agricultural field is expected to be less than the background levels of *B. bassiana* (see discussions above). Therefore, the Agency has determined there will be NO AFFECT (NA) on endangered species or on critical habitat, based on reviewed data and proposed use patterns following the use of the active ingredient *B. bassiana* HF23. There is no evidence of toxicity to non-target taxa except for insect species. However, this environmental risk assessment has determined that the proposed use patterns of *B. bassiana* HF23 will not result in exposure to endangered insects.

#### D. Efficacy data

PR Notice 2002-1 lists housefly as a public health hazard, for which product performance or efficacy data are required according to 40CFR158.202(i). *Beauveria bassiana* is a wide spectrum entomopathogenic fungus. This HF23 strain has been shown to be specific for control of house fly.

The registrant submitted the published study “Evaluation of *Beauveria bassiana* Applications Against House Fly, *Musca domestica*, in Commercial Caged-Layer Poultry Facilities in New York State” to demonstrate their product’s efficacy against the target pest. The study compared applications of *B. bassiana* with pyrethrin insecticide treatments for control of adult house flies in high-rise poultry houses. The study was conducted in four high-rise poultry houses (two poultry houses on two farms) and manure was completely removed from each facility prior to initiating the study.

Once preset fly threshold levels were reached, one poultry house on each farm was treated with *B. bassiana* HF23. Applications were made using backpack mistblowers and were delivered at a rate of application equal to  $2 \times 10^8$  *B. bassiana* HF23 conidia/m<sup>2</sup>/week applied over four weeks. Producers did not use other pesticides in the houses treated with *B. bassiana*, while methomyl-based fly baits were used in all four houses. Other poultry houses were treated with pyrethrin-based insecticides to reduce adult fly numbers. In addition, the house fly parasitoids *Muscidifurax raptor* and *M. raptorellus* were purchased and released as biological controls into all poultry houses. Consistent with current integrated pest management programs, spot card and moving sticky ribbons counts were used to assess weekly abundances of adult house flies. House fly parasitism rates, house fly predators, darkling beetles, and house fly larvae were also monitored. Further, house fly breeding potential was determined weekly by measuring the number of centimeters from the manure cone peak to one edge of the pile. Within that zone the number of centimeters that contained first and second stage house fly larvae were determined.

Results of the study showed that successful house fly parasitism was low and was comparable to levels in poultry facilities where parasitoids were not released. *Carcinops pumilio*, an important predator of house fly larvae, was more prevalent in *B. bassiana*-treated houses, although a significant difference was not detected. During the spray period, larval house fly numbers were significantly lower in *B. bassiana*-treated facilities. In *B. bassiana*-treated houses, house fly breeding decreased from approximately 98 percent of the manure pile in the pre-spray period to 25 percent of the pile during the post-spray period. With respect to controlling adult house fly, the *B. bassiana* system (along with current IPM strategies) exceeded the control observed with the currently available best management program (pyrethrin applications plus IPM strategies). In conclusion, the submitted article demonstrates that *B. bassiana* HF23 can be used to adequately control house fly populations in high-rise poultry houses. Thus the pesticide can be considered as efficacious against house fly, while it does not harm human adults, infants, children and the environment.

#### IV. PUBLIC INTEREST FINDING

The Agency believes the use of *Beauveria bassiana* HF23 under this conditional registration would be in the public interest. The criteria for Agency evaluation of public interest findings are outlined in 51 FR No. 43, Wednesday March 5, 1986. Under part IV.A, the proposed product may qualify for an automatic presumptive finding that the proposed conditional registration is in the public interest if it is for a minor use, is a unique replacement for pesticides of concern, or is for use against a public health pest.

It has been suggested that this entomopathogenic fungus may be used as an alternative to malathion, an organophosphate, for house fly control in chicken manure. Fly resistance to organochlorine (OC) larvicides is common and widespread and resistance to organophosphorus (OP) larvicides is not unusual. Some effective OP larvicides against flies include permethrin, dimethoate (*O,O*-dimethyl *S*-(*N*-methyl carbamoylmethyl) phosphorodithioate), tetrachlorvinphos ((*Z*)-2-chloro-1-(2,4,5-trichlorophenyl) vinyl dimethylphosphate), dichlorvos (2,2-dichlorovinyl dimethyl phosphate), trichlorfon (dimethyl (2,2,2-trichloro-1-hydroxyethyl) phosphonate), and fenthion (*O,O*-dimethyl-*O*-[3-methyl-4-(methylthio)phenyl] phosphorothioate) all of which must be applied at 1–2 g/m<sup>2</sup>.

*Beauveria bassiana* HF23 fits well in an IPM program where conventional chemicals can be used as well, depending on the timing of applications in the program. This active ingredient also decreases adult house fly populations. Some strains of *Beauveria bassiana* have been reported in public literature from Netherlands and Greece to kill adults with 84-95 percent efficacy. IPM practices must include consideration of the fungal nature of the active ingredient which precludes tank mixes with fungicides. Control of larvae by other conventional chemical pesticides is not excluded.

The house fly can transport several diseases to human adult, infant and children populations from garbage and dung heaps such as these chicken manure piles. *Beauveria bassiana* HF23 is proposed for control of house fly, which is a public health pest. *Beauveria bassiana* HF23 is a fungal active ingredient with a non-toxic mode of action. It occurs naturally in the environment and is not toxic, infective or pathogenic to mammals or avian species. It will not be applied directly to agricultural crops. Rather, it can be considered as inadvertent residues if any appear on agricultural crops where composted chicken manure, treated with *Beauveria bassiana* HF23, is used as a fertilizer.

The human health and ecological data and information considered in this BRAD indicate that use of the pesticide during the period of conditional registration will not cause any unreasonable adverse effect on man and the environment or on wildlife, terrestrial and aquatic non-target organisms and beneficial insects (see **Section III.C**).

On the basis of all these considerations, it is in the public interest to register this active ingredient on the condition that the applicant provides confirmatory data to demonstrate that five production batches meet regulatory requirements for nominal and certified limits and formation of unintentional ingredients. These data must be provided within 18 months of this conditional registration to show that QA&QC measures are in place during production of the pesticide.

## **V. RISK MANAGEMENT AND REGISTRATION DECISION**

### **A. Determination of Eligibility**

Section {3(c)7}(c) of FIFRA provides for the conditional registration of a pesticide containing a new active ingredient (*i.e.*, not contained in any currently registered pesticide) “for a period reasonably sufficient for the generation and submission of required data . . . on the condition that by the end of such period the Administrator receives such data and the data do not meet or exceed risk criteria” identified in regulations issued under FIFRA “and on such other conditions as the Administrator may prescribe.” Such a conditional registration will be granted “only if the Administrator determines that use of the pesticide during such period will not cause any unreasonable adverse effect on the environment, and that use of the pesticide is in the public interest.”

Certain conditions apply to this eligibility and the applicant must take certain actions (*e.g.*, generate and provide certain data) within the time frames outlined in **Section VI** of this document. This active ingredient, *Beauveria bassiana* HF23, is eligible for conditional registration pending analyses of five production batches to ascertain that quality assurance and quality control measures for nominal limits and unintentional ingredients meet Agency requirements.

### **B. Regulatory Position - Conditional Registration**

#### **1. Eligible use**

Data submitted are sufficient for a conditional registration of *Beauveria bassiana* HF23 as a TGAI to be formulated into an EP for use on poultry houses. This EP is for control of house fly on chicken manure, which can be processed and used as fertilizer on agricultural food/feed items. An exemption from tolerance for residues of *Beauveria bassiana* HF23 in/on all food/feed items, as allowed herein, is being processed concurrently with this registration decision to allow this use.

#### **2. Ineligible Uses**

This pesticide cannot be applied directly, or used as post harvest applications, on agricultural food/feed items at this time. When the applicant requests further amendments and complies with Agency requirements for Quality Assurance and Quality Control for nominal and certified limits and unintentional ingredients in five production batches, this case will be re-evaluated. Any other application of this pesticide, not in compliance with Agency requirements, will constitute a misuse.

#### **3. CODEX Harmonization**

There are no Codex harmonization considerations since there is no Codex Maximum Residue Limits set for food use of this active ingredient.



#### 4. Reregistrations

This is a new active ingredient, to be registered after 1984, and, therefore, is not subject to reregistration.

#### 5. Risk Mitigation

There is minimal or negligible potential risk to non-target organisms (plants and wildlife), and to ground and surface water contamination through the proposed use of products containing *Beauveria bassiana* HF23 as discussed in this document. No mitigation measures are required at this time for dietary risk, including risk due to exposure via drinking water. Appropriate PPE is required for formulators who manufacture the TGAI into EPs and for pesticide handlers who apply this EP to poultry houses. These include long sleeve shirt, long pants, shoes, socks, gloves and a respirator with NIOSH prefix N-95, R-95, or P-95. The product label will also bear Environmental Hazards text to mitigate any potential risk as determined by reviewed data and use sites.

#### 6. Endangered Species Statement

The Agency has determined there will be NO AFFECT (NA) on endangered species or on critical habitat, based on reviewed data and proposed use patterns following the use of the active ingredient *B. bassiana* HF23 (see **Endangered Species Assessment, Section III.C.7** of this BRAD). Thus, no labeling is required for endangered species at this time.

### C. Labeling Rationale

It is the Agency's position that the labeling for manufacturing products containing *Beauveria bassiana* HF23 must comply with the pesticide labeling requirements in existence when such products are registered.

#### 1. Manufacturing Use Product Labeling

The label must include appropriate statements to indicate that the registered product is a Manufacturing-use Product (MP) if the intent is to use the product to formulate into end-use products (EP). Personal Protective equipment to be used during manufacture of the EP include long sleeve shirt, long pants, shoes, socks, and a dust/mist filtering respirator with the appropriate NIOSH prefix N-95, R-95 or P-95.

The following NPDES statement must be placed on the manufacturing use product for the active ingredient, *Beauveria bassiana* HF23, at this time.

“Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority have been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.”

## **2. End-use Product Labeling**

It is the Agency's position that the labeling for End-use Product products containing *Beauveria bassiana* HF23 must comply with the pesticide labeling requirements in existence when such products are registered.

### **a. Human Health Hazard**

#### **(i) Worker Protection Standard**

Any product whose labeling reasonably permits use in the production of an agricultural plant on any farm, forest, nursery, or greenhouse must comply with PR Notice 93-7, "Labeling Revisions required by the Worker Protection Standard (WPS), and PR Notice 93-11, "Supplemental Guidance for PR Notice 93-7", which reflect the WPS (40 CFR part 156, subpart K). These labeling revisions are necessary to implement the Worker Protection Standard for Agricultural Pesticides (40 CFR part 170). Unless otherwise specifically directed, all statements required by PR Notices 93-7 and 93-11 are to be on the product label exactly as instructed in those Notices.

The labels and labeling of all products must comply with EPA's current regulations and requirements as specified in 40 CFR 156.10 and other applicable notices, such as, and including the WPS labeling. Personal Protective Equipment required for the EP in this registration packet include long sleeve shirt, long pants, shoes and socks, waterproof gloves and a dust/mist filtering respirator with a NIOSH prefix N-95, R-95 or P-95 as appropriate. A Restricted Entry Interval of four hours is required for pesticide handlers entering treated areas.

#### **(ii) Other Precautionary Labeling**

The Agency has examined the toxicological database for *Beauveria bassiana* HF23 and concluded that the precautionary labeling required during this conditional registration process (i.e. Signal Word, First Aid Statements, WPS statements for pesticide handlers, and other label statements) adequately mitigates the risks associated with the proposed uses. Additional labeling may be required for other uses of products containing *Beauveria bassiana* HF23 on a case by case basis.

### **b. Environmental Hazards Labeling**

Standard Environmental Hazards labeling statements are required for this agricultural application to poultry houses. Provided the following statements are placed in the environmental hazards statement, the risk of exposure to *Beauveria bassiana* HF23 is minimal to nonexistent to ground water or drinking water, or to non-target organisms including endangered species:

"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 when disposing of rinsate or equipment wash waters."

## **3. Application Rate**

It is the Agency's position that the labeling for the pesticide products containing *Beauveria bassiana* HF23 must comply with existing pesticide labeling requirements relevant at

the time of registration. The EP is to be applied as a spray to the poultry houses and chicken manure piles.

**D. Labeling**

**a. Manufacturing Use Product**

The Manufacturing-use Product must clearly state that it is to be used for formulating End-use Products.

**Manufacturing-use Product name: *Beauveria bassiana* HF23**

|                                     |             |
|-------------------------------------|-------------|
| Ingredient Statement:               | w/w         |
| <i>Beauveria bassiana</i> HF23..... | 98 percent* |
| Inert Ingredients .....             | 2 percent   |

---

Total . . . . . 100.00 percent\*

\*viability of End-use Product is  $4.75 \times 10^{11}$  cfu/g

**b. End-use Product**

**End-use Product trade name: balEnce**

|                                     |               |
|-------------------------------------|---------------|
| Ingredient Statement:               | w/w           |
| <i>Beauveria bassiana</i> HF23..... | 1.18 percent* |
| Inert Ingredients .....             | 98.82 percent |

---

Total . . . . . 100.00 percent\*

\*viability of End-use Product is  $5.6 \times 10^9$  cfu/g

Based on the evaluation of the acute oral, acute dermal, and acute pulmonary toxicity/infectivity studies submitted in support of the conditional registration of the product, containing *Beauveria bassiana* HF23, the signal word is “**Caution**” for both the TGAI and the EP considered in this BRAD. Signal words for other end-use products containing this active ingredient will vary depending on the toxicity/pathogenicity evaluations of those products as determined by the inerts used in the EPs.

## VI. WHAT REGISTRANTS MUST DO

Reports of incidents of adverse effects to humans or domestic animals are required under FIFRA, Section 6(a)(2) and incidents of hypersensitivity under 40 CFR Part 158.690(c), guideline reference number 152-16. There are no data requirements, label changes and other responses necessary for the reregistration of the end-use product since the product is being registered after November 1984 and is, therefore, not subject to reregistration. For the same reason, there are also no existing stocks provisions at this time. Before releasing these products for shipment, the registrant is required to provide appropriate labels and other Agency requirements as discussed in this BRAD. The applicant must provide the following data within 18 months of the conditional registration date as shown below.

### **Guidelines 151-10 through 151-16 (OPPTS Gdln 885.1300): Product Identity, Manufacturing Process and Quality Control – *Beauveria bassiana* HF23 TGAI**

Analyses of 5 batches are required at production and must include data relevant to detection, identification, enumeration and rejection limits of metabolites and potential human pathogens (bacterial and fungal), using quality control and assurance methods to be used during large scale production. Batch analysis must also include:

- (i) certifications of limits;
- (ii) analysis and quantification of metabolites and other unintentional ingredients;
- (iii) identification and enumeration of potential human pathogens;
- (iv) storage stability; and
- (v) viability data.

Batches containing more than  $10^4$  cfu/g *Bacilli* contaminants, or other unintentional ingredients, or metabolites which are of toxicological levels and concern, and which exceed quality assurance and quality control levels, must be destroyed.

The data from production batches listed above will be a condition of registration and must be submitted within 18 months of the date of this conditional registration action.

## VII. APPENDICES

### APPENDIX A - Use sites

Table 4 lists the use sites for the product. The registrant must comply with the appropriate labeling requirements before releasing products containing *Beauveria bassiana* HF23 as the active ingredient for shipment.

**Table 4: Use Site Conditional registration**

| <b>Site registered</b>           | <b>Official date registered:</b> |
|----------------------------------|----------------------------------|
| Chicken Manure in poultry houses |                                  |

## **APPENDIX B – Citations Considered to be part of the Database Supporting the Conditional registration of *Beauveria bassiana* HF 23 and Pesticide Petition 5F6960**

### **GUIDE TO APPENDIX B**

1. CONTENTS OF BIBLIOGRAPHY. This bibliography contains citations of all studies considered relevant by EPA in arriving at the positions and conclusions stated elsewhere in the Reregistration Eligibility Document. Primary sources for studies in this bibliography have been the body of data submitted to EPA and its predecessor agencies in support of past regulatory decisions. Selections from other sources including the published literature, in those instances where they have been considered, are included.

2. UNITS OF ENTRY. The unit of entry in this bibliography is called a “study”. In the case of published materials, this corresponds closely to an article. In the case of unpublished materials submitted to the Agency, the Agency has sought to identify documents at a level parallel to the published article from within the typically larger volumes in which they were submitted. The resulting “studies” generally have a distinct title (or at least a single subject), can stand alone for purposes of review and can be described with a conventional bibliographic citation. The Agency has also attempted to unite basic documents and commentaries upon them, treating them as a single study.

3. IDENTIFICATION OF ENTRIES. The entries in this bibliography are sorted numerically by Master Record Identifier, or “MRID number”. This number is unique to the citation, and should be used whenever a specific reference is required. It is not related to the six-digit “Accession Number” which has been used to identify volumes of submitted studies (see paragraph 4(d)(4) below for further explanation). In a few cases, entries added to the bibliography late in the review may be preceded by a nine character temporary identifier. These entries are listed after all MRID entries. This temporary identifying number is also to be used whenever specific reference is needed.

4. FORM OF ENTRY. In addition to the Master Record Identifier (MRID), each entry consists of a citation containing standard elements followed, in the case of material submitted to EPA, by a description of the earliest known submission. Bibliographic conventions used reflect the standard of the American National Standards Institute (ANSI), expanded to provide for certain special needs.

a. Author. Whenever the author could confidently be identified, the Agency has chosen to show a personal author. When no individual was identified, the Agency has shown an identifiable laboratory or testing facility as the author. When no author or laboratory could be identified, the Agency has shown the first submitter as the author.

b. Document date. The date of the study is taken directly from the document. When the date is followed by a question mark, the bibliographer has deduced the date from the evidence contained in the document. When the date appears as (19??), the Agency was unable to determine or estimate the date of the document.

c. Title. In some cases, it has been necessary for the Agency bibliographers to create or enhance a document title. Any such editorial insertions are contained between square brackets.

d. Trailing parentheses. For studies submitted to the Agency in the past, the trailing parentheses include (in addition to any self-explanatory text) the following elements describing the earliest known submission:

(1) Submission date. The date of the earliest known submission appears immediately following the word “received.”

(2) Administrative number. The next element immediately following the word “under” is the registration number, experimental use permit number, petition number, or other administrative number associated with the earliest known submission.

(3) Submitter. The third element is the submitter. When authorship is defaulted to the submitter, this element is omitted.

(4) Volume Identification (Accession Numbers). The final element in the trailing parentheses identifies the EPA accession number of the volume in which the original submission of the study appears. The six-digit accession number follows the symbol “CDL,” which stands for “Company Data Library.” This accession number is in turn followed by an alphabetic suffix which shows the relative position of the study within the volume.

## Bibliography

| MRID     | Citation Reference  |
|----------|---|
| 46449600 | Jabb of the Carolinas, Inc. (2005) Submission of Product Chemistry Data in Support of the Application for Registration of <i>Beauveria bassiana</i> HF23 and BalEncE End Use Product. Transmittal of 2 Studies.   |
| 46449601 | Arends, J. (2005) <i>Beauveria bassiana</i> HF23: Product Chemistry. Unpublished study prepared by Jabb of the Carolinas, Inc. 29 p.  |
| 46526000 | Jabb of the Carolinas (2005) Submission of Product Chemistry, Toxicity, Environmental Fate and Safety Data in Support of the Applications for Registration of <i>Beauveria bassiana</i> HF23 and BalEncE End Use Product. Transmittal of 12 Studies.  |
| 46526002 | Hinz-Bridger, S. (2005) Request for Exemption from the Requirement of Tolerance: (BalEncE). Unpublished study prepared by SHB Scientific Enterprises. 16 p.   |
| 46526003 | O'Leary, A. (2004) Acute Oral Toxicity/Pathogenicity Study in Rats with <i>Beauveria bassiana</i> HF23. Project Number: 016545, 70787/TGAI/5, 016545/1. Unpublished study prepared by Ricerca Biosciences, LLC. 18 p.   |
| 46526004 | O'Leary, A. (2004) Acute Dermal Toxicity/Pathology Study in New Zealand White Rabbits with <i>Beauveria bassiana</i> HF23. Project Number: 70787/TGAI/6, 016544, 016544/1. Unpublished study prepared by Ricerca Biosciences, LLC. 16 p.  |
| 46526005 | O'Leary, A. (2004) Acute Pulmonary Toxicity/Pathogenicity Study in Rats with <i>Beauveria bassiana</i> HF23. Project Number: 016546, 70787/TGAI/7, 016546/1. Unpublished study prepared by Ricerca Biosciences, LLC. 19 p.  |
| 46526006 | O'Leary, A. (2004) Acute Injection Toxicity/Pathogenicity Study in Rats with <i>Beauveria bassiana</i> HF23. Project Number: 70787/TGAI/8, 016547, 016547/1. Unpublished study prepared by Ricerca Biosciences, LLC. 21 p.  |
| 46526007 | O'Leary, A. (2004) Acute Eye Irritation Study in New Zealand White Rabbits with <i>Beauveria bassiana</i> HF23. Project Number: 016298, 016298/1, 70787/TGAI/9. Unpublished study prepared by Ricerca Biosciences, LLC. 19 p.   |
| 46526008 | Stafford, J. (2004) <i>Beauveria bassiana</i> HF23 Conidia: Microbial Oral Toxicity and Pathogenicity Test (LD50 or ID50) with Chickens Using a Maximum Hazard Dose. Project Number: 13817/4100, 70787/TGAI/10, 81503/OPPTS/MICROBIAL/ACUTE/ORAL/CHICKEN. Unpublished study prepared by Springborn Smithers Laboratories. 65 p. |
| 46526009 | O'Leary, A. (2004) Effect of Milling on and Sensitivity of Detection of <i>Beauveria bassiana</i> HF23 in Fortified Rat Tissues. Project Number: 70787/TGAI/11, 016626, 016626/1. Unpublished study prepared by Ricerca Biosciences, LLC. 18 p.   |



**MRID**

**Citation Reference**

- 46526010 Arends, J.; Black, W. (2000) Evaluation of Viability Degradation Over Time of *Beauveria bassiana* Conidia Applied to Poultry Manure and Litter: Final Report. Project Number: JABB/02100, 70787/TGAI/12. Unpublished study prepared by Jabb of the Carolinas. 16 p.
- 46526011 Jabb of the Carolinas (2003) Growth of *Beauveria bassiana* in Barley Start Slurry Agar at Two Temperatures. Project Number: 70787/TGAI/13. 6 p.
- 46526012 Jabb of the Carolinas (2005) BalEnce: Product Chemistry. Project Number: 70787EP/2. 19 p.
- 46526013 O'Leary, A. (2004) Acute Eye Irritation Study in New Zealand White Rabbits with *Beauveria bassiana* End-Use Product. Project Number: 70787/EP/4, 016660, 016660/1. Unpublished study prepared by Ricerca Biosciences, LLC. 22 p.
- 46580500 Jabb of the Carolinas, Inc. (2005) Submission of Product Chemistry Data in Support of the Application for Registration of *Beauveria bassiana* HF23. Transmittal of 1 Study.
- 46580501 Jabb of the Carolinas (2005) *Beauveria bassiana* HF23: 5 Lot Analysis. Project Number: MCB/029/01, 02100. Unpublished study prepared by Jabb of the Carolinas, Inc., Kansas State University and Southern Testing & Research Labs., Inc. 57 p.
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## **APPENDIX C - Technical Support Documents**

### **Health Effects Data Evaluation Records and Documents**

Barsoum, Ibrahim and Kough, John. January 31, 2006. USEPA/OPP/BPPD. Memorandum to Shanaz Bacchus. USEPA/OPP/BPPD

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### **Ecological Effects Data Evaluation Records and Documents**

Hunter, Mika and Vaituzis, Zigfridas. June 20, 2006. USEPA/OPP/BPPD. Memorandum to Shanaz Bacchus. USEPA/OPP/BPPD

### **Public Literature**

A. Siri, A. C. Scorsetti, V. E. Dikgolz and C. C. López Lastra. December 2005. BioControl. "Natural Infections Caused by the Fungus *Beauveria bassiana* as a Pathogen of *Musca domestica*". Vol. 50., No. 6. pages 937-940. publ. Springer Netherlands.

Kaufman, P. E., Reasor, C., Rutz, D. A., Ketiz, J. K., and J. J. Arends. 2005. Evaluation of *Beauveria bassiana* Applications Against Adult House Fly, *Musca domestica*, in Commercial Caged-Layer Poultry Facilities in New York State. Biological Control 33: 360-367.

### **Federal Register Publications**

Federal Register [FR: February 15, 2006 (Volume 71, Number 31)] [Page 7954-7955]. Notice. Receipt of the application for the new active ingredient.

Federal Register [FR: December 7, 2005 (Volume 70, Number 234)][Page 72831-72833]. Notice of Filing a Pesticide Petition. PP Number 5F6960 proposing an Exemption from the Requirement of a Tolerance for Residues of *Beauveria bassiana* HF23 in/on all food commodities.

### **APPENDIX C - Technical Support Documents**

Additional documentation in support of this BRAD is maintained in the OPP records, which are subject to Freedom of Information Act (FOIA) inquiries and Confidential Business Information restrictions and exclusions. The docket, EPA OPP 2005-0316 also contains initial documents announcing the notices of receipt of the application to register pesticides and the notice of filing of the Pesticide Petition

The EPA considered comments and added the formal “Response to Comments” in the Final Rule to be published concurrent with this conditional registration document.

All documents, in hard copy form, may be viewed in the OPP docket room or downloaded or viewed via the Internet at the following site:

[www.epa.gov/pesticides/biopesticides](http://www.epa.gov/pesticides/biopesticides) BRAD or Technical Document

[www.fdms.gov](http://www.fdms.gov) for Docket (includes (a) Federal Register Notice of Receipt of application; (b) Notice of filing of Pesticide Petition; (c) Final Rule establishing Exemption from tolerance; (d) Federal Register Notice announcing registration of *Beauveria bassiana* HF23.