BIOPESTICIDES REGISTRATION ACTION DOCUMENT

Trichoderma gamsii strain ICC 080

PC Code: 119207

U.S. Environmental Protection Agency
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division

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I. EXECUTIVE SUMMARY

The Biopesticides and Pollution Prevention Division (BPPD) received applications to register, under Section 3(c)(5) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), two products containing the active ingredient, *Trichoderma gamsii* strain ICC 080, as a microbial fungicide. The manufacturing-use product (MP; *Trichoderma gamsii* strain ICC 080 Technical, EPA File Symbol 80289RN) is intended to be used to formulate end-use pesticide products with *Trichoderma gamsii* strain ICC 080. The end-use product (EP; Tenet WP, Bioten WP, Remedier WP; Tenet T&O; EPA File Symbol 80289-O) contains 2% *Trichoderma gamsii* strain ICC 080, as well as 2% of another similar microbial active ingredient, *Trichoderma asperellum* strain ICC 012. The EP is intended to control pathogenic fungi on several food and non-food crops, including ornamentals, fruiting vegetables, leafy vegetables, cole crops, legumes, aromatic herbs, cucurbits, berries and small fruits, and turf. Depending on the use, the EP may be applied as a cutting and bare root application, substrate mix, greenhouse and nursery drench, broadcast application, or through chemigation.

The active ingredient, *Trichoderma gamsii* strain ICC 080 is a strain of asexual fungi that was originally classified as *Trichoderma viride,* and subsequently recharacterized*. Trichoderma* species are asexual fungi that are isolated primarily from soil and decomposing matter.

Trichoderma gamsii strain ICC 080 was isolated from a soil in Sardinia, Italy that was found to suppress plant disease. *Trichoderma gamsii* strain ICC 080 is intended to be used for control of many soil-borne fungal plant pathogens [e.g., *Pythium* species (spp.), *Phytophthora* spp., *Sclerotinia* spp., *Sclerotium* spp., *Thielaviopsis basicola*, *Rhizoctonia* spp., *Verticillium* spp.]. *Trichoderma gamsii* strain ICC 080 acts as a pathogen antagonist, colonizing in soil and around plant roots to compete with plant pathogenic fungi for living space and nutrients. Moreover, *Trichoderma gamsii* strain ICC 080 also uses enzymes to attack the cell walls of pathogenic fungi.

Adequate mammalian toxicology data, data waivers and other information were submitted to fulfill the Tier I acute toxicity data requirements for the registration of *Trichoderma gamsii* strain ICC 080 as a microbial fungicide.

The toxicological data demonstrated that *Trichoderma gamsii* strain ICC 080 is not toxic, infective, or pathogenic to mammals. No acute, sub-chronic, chronic, immune, endocrine, or non-dietary exposure issues were identified. The intended uses of this microbial fungicide do not pose a dietary risk to the U.S. population in general, including infants and children. Dietary exposure via drinking water is also not expected to pose harm to populations, because the microbial fungicide is not known to grow or thrive in aquatic environments, nor would be expected to survive municipal treatment of drinking water. Further, in the unlikely event that humans are exposed to *Trichoderma gamsii* strain ICC 080 from drinking water, the toxicological data base indicates no adverse effects would be expected.

The potential for aggregate, non-occupational exposure from agricultural applications of *Trichoderma gamsii* strain ICC 080 is unlikely, because the intended use sites are not expected to be in close proximity to residential areas. However, the product is also intended to be used in residential settings, and if inadvertent residential exposures occur from agricultural applications, the low toxicity of the active ingredient would not be expected to cause adverse effects to humans.

A final rule establishing an exemption from the requirement of a tolerance was signed on February 5, 2010, and published in the Federal Register (75 FR, 8504, February 25, 2010).

Exposure of non-target organisms to *Trichoderma gamsii* strain ICC 080 is possible from the intended uses of this organism as a microbial fungicide. Isagro, S.p.A. submitted studies and data waiver rationales to satisfy data requirements for non-target organism risk assessment with the active ingredient (TGAI). BPPD has evaluated the information available and has determined that additional studies are not necessary for *Trichoderma gamsii* strain ICC 080. An extensive literature search did not produce reports of *Trichoderma gamsii* or *Trichoderma viride* having adverse effects on insects, including bees. Additionally, Gouli, et al. (2008) report a lack of adverse effects of a strain of *Trichoderma viride* in insects (thrips). Therefore, BPPD has determined that adverse effects of the proposed uses of *Trichoderma gamsii strain ICC* 080 to honey bees and other insects are unlikely.

Adverse effects are not anticipated to non-target species, including threatened or endangered species, exposed to the microbial fungicide *Trichoderma gamsii* strain ICC 080, when used in accordance with the label directions. Therefore, the Agency has made a "No Effect" determination for threatened or endangered species from the fungicidal use of Trichoderma *gamsii* strain ICC 080.

The information provided is sufficient to satisfy the Tier I non-target organism data requirements for the active ingredient, *Trichoderma gamsii* strain ICC 080, contained in the proposed MP and EP products. Further testing of non-target organisms at higher tier levels is not required.

Consistent with OPP's new transparency policy, EPA announced its preliminary registration decision on *Trichoderma gamsii* strain ICC 080 on December 30, 2009, and opened a 30-day comment period on this product as a "new active ingredient." EPA did not receive any comments on this proposed action during the comment period.

EPA concludes, based on the risk assessment and information submitted in support of the registration of *Trichoderma gamsii* strain ICC 080, that it is in the best interests of the public and the environment to issue the registration for *Trichoderma gamsii* strain ICC 012. The basis for this determination can be found in the risk assessment for *Trichoderma gamsii* strain ICC 080, which is characterized in this BRAD. Acute toxicity and pathogenicity data demonstrate that it has low toxicity (category III and IV). EPA has no concerns for non-target organisms, included threatened or endangered species,

exposed to *Trichoderma gamsii* strain ICC 012 when it is used in accordance with approved label directions. EPA has not identified any toxic endpoints for non-target mammals, birds, plants, aquatic, or soil organisms. Thus, EPA concludes that use of the microbial fungicide *Trichoderma gamsii* strain ICC 080 in accordance with the proposed label directions will not cause any unreasonable adverse effects on the environment.

II. ACTIVE INGREDIENT OVERVIEW

Biological Name:	*Trichoderma gamsii* strain ICC 080
Culture Deposit:	**CABI Bioscience International Mycological Institute- Egham, UK under IMI CC No. 392151**
Trade/Other Names:	**Bioten WP; Tenet WP; Remedier WP**
Office of Pesticide Programs (OPP) Chemical Code:	119207
Type of Pesticide:	Microbial Pesticide, fungicide See Appendix B for specific information (i.e., use sites, application rate, method of application, formulation type, and target pests)

III. REGULATORY BACKGROUND

On February 8, 2008, Mel Graben of Isagro, USA (address: 430 Davis Drive, Suite 240, Morrisville, NC 27560), acting as the United States authorized agent for Isagro S.p.A., (address: Centro Uffici San-Edifico D-ala 3, Via Caldera, 21-20153 Milan, Italy) submitted an application to register Bioten WP (EPA File Symbol 80289-O) and *Trichoderma gamsii* strain ICC 080 (EPA File Symbol 80289- RN) under Section 3 of the Federal Insecticide, Fungicide, and Rodenticide Act. On October 29, 2008, EPA announced receipt of this application to register a pesticide product containing a new active ingredient [73 Federal Register (FR) 64325], and opened a 60-day public comment period on the receipt of this application. We did not receive any substantive comments relevant to the subject *Trichoderma* pesticide products.

Concurrent with their registration application, and under the Federal Food, Drug, and Cosmetic Act (FFDCA), Isagro S.p.A. submitted a petition to establish an exemption from the requirement of a tolerance for *Trichoderma gamsii* strain ICC 080 [Pesticide Petition (PP) 8F 7327]. In the Federal Register dated November 12, 2008 (73 FR 66897), the EPA announced that Isagro, S.p.A., proposed to establish an exemption from the requirement of a tolerance for residues of the microbial pesticide, *Trichoderma gamsii* strain ICC 080. The Agency received one comment following the publication of a notice of filing of a petition under the FFDCA. This comment did not provide

substantive input into the determination as to whether to grant the subject petition.

IV. RISK ASSESSMENT

On October 26, 2007, the Agency issued a Final Rule in the Federal Register on the data requirements to support registration of biochemical and microbial pesticides, and updated the definitions for biochemical and microbial pesticides (72 FR 61002). The rule became effective on December 26, 2007. The data and information evaluated for this Biopesticides Registration Action Document (BRAD) were considered in light of these requirements.

The classifications that are found for each data submission are assigned by EPA science reviewers and are an indication of the usefulness of the information contained in the documents for risk assessment. A rating of "ACCEPTABLE" indicates the study is scientifically sound and is useful for risk assessment. A "SUPPLEMENTAL" rating indicates the data provide some information that can be useful for risk assessment. The studies may have certain aspects determined not to be scientifically acceptable ("SUPPLEMENTAL: UPGRADABLE"). If a study is rated as "SUPPLEMENTAL: UPGRADABLE," the Environmental Protection Agency always provides an indication of what is lacking or what can be provided to change the rating to "ACCEPTABLE." If there is simply a "SUPPLEMENTAL" rating, the reviewer will often state that the study is not required by the current 40 CFR Part 158. Both "ACCEPTABLE" and "SUPPLEMENTAL" studies may be used in the risk assessment process as appropriate. An "UNACCEPTABLE" rating indicates that new data must be submitted.

For product-specific acute toxicity data requirements, toxicity categories are assigned based on the hazard(s) identified from studies and/or information submitted to the Agency. The product is classified into Toxicity Category I, II, III, or IV, where Toxicity Category I indicates the highest toxicity and Toxicity Category IV indicates the lowest toxicity.

A. Product Analysis Assessment

All product analysis data requirements (40 CFR § 158.2120) for Section 3(c)(5) registration of *Trichoderma gamsii* strain ICC 080 Technical and Tenet WP, containing *Trichoderma gamsii* strain ICC 080 as an active ingredient, have been satisfied by either acceptable guideline studies or waiver rationales. For a comprehensive guideline-by-guideline summary of the product analysis data requirements described in sections IV(A)(1), IV(A)(2), and IV(A)(3), refer to Table 1 in Appendix A.

1. Product Chemistry and Composition

Trichoderma gamsii strain ICC 080 Technical is an MPCA soil fungicide for manufacturing use only. The product contains 99.9% w/w *Trichoderma gamsii* strain ICC 080 as active ingredient with a minimum and nominal content of 1 x 10^9 and 2.5 x 10^9 conida cfu/g dry weight, respectively. The label indicates that the product also

contains 0.10% other ingredients. The strain ICC 080, originally characterized as *Trichoderma viride*, has been reclassified as *Trichoderma gamsii,* and has been characterized by molecular biology techniques. *Trichoderma gamsii* strain ICC 080 was isolated from a soil in Sardinia, Italy that was found to suppress plant disease. The strain has been deposited in the CABI Bioscience International Mycological Institute-Egham, UK IMI CC No. 392151. No relationships are known between the *Trichoderma* genus and any pathogen of man, animals, or plants. The extensive *Moniliaceae* family, which includes phytopathogenic genera *Botrytis* and *Verticillium*, and the human pathogenic genus *Blastomyces,* includes *Trichoderma*, but no *Trichoderma* or closely related genera are known to be pathogenic to mammals.

Submitted data satisfied the requirements for manufacturing process, and discussion of formation of unintentional ingredients. [(OPPTS) Guidelines 885.1100, 885.1200, and 885.1300]

2. Analysis and Certified Limits

Results of a five-batch preliminary analysis were provided, and the requirement for analysis of samples has been satisfied. The requirement for certified limits has also been satisfied.

3. Physical and Chemical Characteristics

Submitted data and waiver rationales satisfied the requirements for the physical and chemical characteristics, including color, physical state, odor, stability to normal and elevated temperatures, metals, and metal ions, storage stability, miscibility, corrosion characteristics, pH, viscosity, and density/relative density/bulk density (specific gravity).

B. Human Health Assessment

1. Toxicology

Acceptable Tier I mammalian toxicology data and data waivers information support the registration of the manufacturing product, *Trichoderma gamsii* strain ICC 080 Technical, and the end-use product, Bioten™ WP, which contains *Trichoderma gamsii* strain ICC 080. Tier II and Tier III studies were not required for *Trichoderma gamsii* strain ICC 080, based upon the lack of acute toxicity/pathogenicity in the Tier I studies.

For a comprehensive guideline-by-guideline summary of the toxicology data requirements and additional studies described in sections IV(B)(1)(a), IV(B)(1)(b), and IV(B)(1)(c), refer to Table 2 in Appendix A.

a. Acute Toxicity/Pathogenicity – Tier I (40 CFR § 158.2140)

Acute Oral Toxicity – Rat [OPPTS Guideline 885. 3550; (MRID# 47345801)
An acute oral toxicity study was performed on rats given a single oral dose of

Trichoderma gamsii strain ICC 080 of (7.5×10^8 CFU/g) in 0.9% NaCl solution at a dose of 2000 mg/kg of body weight in a limit test. The animals were observed for a period of up to 14 days. The Oral LD_{50} for males, females, and the combined test animals were: males > 2000 mg/kg of body weight, females > 2000 mg/kg of body weight, combined > 2000 mg/kg of body weight. No mortalities occurred during the study. Based on the results of this study, *Trichoderma gamsii* strain ICC 080 was found to be of low acute oral toxicity. Microbial enumeration was not done so it is unknown if *Trichoderma gamsii* is infective or pathogenic in the rat. There were no treatment related clinical signs, changes in body weight or pathological findings at necropsy. This study was rated "ACCEPTABLE" for risk assessment purposes.

Acute Intraperitoneal Injection Toxicity– Rat (OPPTS Guideline 885.3200; MRID# 47345802) An acute intraperitoneal injection toxicity study was submitted, in which groups of fasted, 41-48 days old rats (3/sex) were injected with *Trichoderma gamsii* strain ICC 080 (at 7.5×10^8 CFU/g) in 0.9% NaCl solution at a dose of 1×10^7 CFU/g. Animals were then observed for up to 21 days. Control animals (2/sex) were injected with 0.9% NaCl solution only. *Trichoderma gamsii* strain ICC 080 is not toxic based on the results of this study. There were no treatment-related necropsy findings or changes in body weight. Microbial enumeration was not done so it is unknown if *Trichoderma gamsii* is infective or pathogenic in the rat. All of the animals treated with the test material experienced slightly reduced mobility, slight ataxia, slightly reduced muscle tone, slight dyspnea, mydriasis, and writhing, observed 60 minutes after administration. All of these clinical signs were completely resolved within 24 hours. This study was rated "ACCEPTABLE" for risk assessment purposes.

Acute Pulmonary Toxicity/Pathogenicity Studies– Rats (OPPTS Guideline 885.3150; MRID# 47345803, 47345804) Acute pulmonary toxicity/pathogenicity studies were submitted, in which groups of fasted 43-56 days old rats (31/sex) were exposed by the intratracheal route to *Trichoderma gamsii* strain ICC 080 at a dose of 2.5×10^6 CFU/animal. Animals were observed for up to 22 days. Rats in the control group were administered the vehicle, [0.1% solution of Tween 20 in *aqua ad iniectabilia* (water for injection)] only. Rats in the reference groups were administered inactivated test item. Samples of feces, lungs, lymph nodes, kidneys, brain, liver, spleen, and blood were taken for microbial enumeration in those tissues. None of the administered *Trichoderma gamsii* conidia from lung tissue of the animals appeared in other organ tissue. Conidia could not be detected in blood samples at any time during the study. Conidia were detected in the feces up to 21 days post administration. Conidia density in the lung tissue decreased to 0 within 21 days post administration. This shows a pattern of clearance and lack of infectivity of *Trichoderma gamsii* strain ICC 080. The recorded pulmonary LD_{50} was greater than 2.5×10^6 CFU/animal in males, females and in the combined group of test animals. No mortality occurred. Based upon these results, *Trichoderma gamsii* strain ICC 080 is of low toxicity, and *Trichoderma gamsii* was not infective or pathogenic in the rat. There were no treatment related clinical signs, changes in body weight, or pathological changes observed at necropsy. This study was rated "ACCEPTABLE" for risk assessment purposes.

Acute Oral Toxicity/Pathogenicity– Rats (OPPTS Guideline 870.1100; MRID# 47346301). In an acute oral toxicity study (MRID 47346201), groups of fasted, 6-7 week old CD/CRL:CD rats (5/sex) were given a single oral dose of Bioten WP (originally referred to as Remedier WP in the acute studies below)(*Trichoderma conidia* (1.2×10^8 CFU/g); *Trichoderma asperellum strain* ICC 012 (originally classified as T. *harzianum)* (7.8×10^7 CFU/g); *Trichoderma gamsii* strain ICC 080 (4.2×10^7 CFU/g)) in 0.9% NaCl solution at a dose of 2000 mg/kg bw in a limit test. The animals were then observed for a period of up to 14 days. Oral LD_{50} were as follows: Males > 2000 mg/kg bw, Females > 2000 mg/kg bw , Combined > 2000 mg/kg bw. Limit test: no mortality occurred during the study. Based on the results of this study BiotenWP (*Trichoderma asperellum* 7.8×10^7 CFU/g; *Trichoderma gamsii* 4.2×10^7 CFU/g) is not toxic and has an LD_{50} greater than 2000 mg/kg bw.(EPA Toxicity Category III.) Microbial enumeration was not performed, therefore, the infectivity and pathogenicity of *Trichoderma conidia*, *Trichoderma asperellum* strain ICC 012, and *Trichoderma gamsii* strain ICC 080, are unknown. There were no treatment related clinical signs, necropsy findings or changes in body weight. This study was rated "ACCEPTABLE" for risk assessment purposes.

Acute Dermal Toxicity (OPPTS Guideline 870.1200; MRID# 47346302)
In an acute dermal toxicity study (MRID 43746302), groups of fasted, 6-7 week old CD/CRL:CD rats (5/sex) were given a single dermal dose of BiotenWP (*Trichoderma conidia* (1.2×10^8 CFU/g); *Trichoderma asperellum* strain ICC 012 (7.8×10^7 CFU/g); *Trichoderma gamsii* strain ICC 080 (4.2×10^7 CFU/g)) in 0.9% NaCl at a dose of 2000 mg/kg bw for 24 hours to an area of approximately 5 x 6 cm (~10% of body surface). Following exposure, the animals were observed for a period of 14 days. Dermal LD_{50} were as follows: Males > 2000 mg/kg bw,Females > 2000 mg/kg bw, Combined > 2000 mg/kg bw. Limit test; no mortality occurred during the study. Based on the results of this study Remedier WP (*Trichoderma asperellum* 7.8×10^7 CFU/g; *Trichoderma gamsii* 4.2×10^7 CFU/g) is of MODERATE Toxicity**,** EPA Toxicity Category III. This study was rated "ACCEPTABLE" for risk assessment purposes.

Acute Inhalation Toxicity (OPPTS Guideline 870.1300; MRID# 47346303)
In an acute inhalation toxicity study (MRID 47346303), groups of fasted, 44-55 day old CD/CRL:CD rats (5/sex) were exposed by the inhalation route to Bioten WP (*Trichoderma conidia* (1.2×10^8 CFU/g); *Trichoderma asperellum* strain ICC 012 (7.8×10^7 CFU/g); *Trichoderma gamsii* strain ICC 080 (4.2×10^7 CFU/g)) as supplied at a concentration of 5.20 mg/L. Animals then were observed for 14 days. The MMAD was 2.573 μm and the GDS was 11.375. Inhalation LC_{50}were as follows: Males > 5.20 mg/L, Females > 5.20 mg/ L, Combined > 5.20 mg/L. No mortality occurred during the study. Bioten WP (*Trichoderma asperellum* 7.8×10^7 CFU/g; *Trichoderma gamsii* 4.2×10^7 CFU/g) is of LOW Toxicity**,** EPA Toxicity Category IV, based on lack of mortality in male and female rats. There were no treatment related clinical signs, necropsy findings or changes in body weight. This study was rated "ACCEPTABLE" for risk assessment purposes. Toxicity Category IV.

Acute Eye Irritation – Rabbit (OPPTS Guideline 870.2400; MRID# 473463034)
In a primary eye irritation study (MRID 47346304), 100 mg of Bioten WP (*Trichoderma conidia* (1.2 x 10^8 CFU/g); *Trichoderma asperellum* ICC 012 (7.8 x 10^7 CFU/g); *Trichoderma gamsii* strain ICC 080 (4.2 x 10^7 CFU/g)), as supplied, was instilled into the right conjunctival sac of 3 male fasted young adult Himalayan rabbits for 24 hours. Animals then were observed for 72 hours. Irritation was scored by the method that was not named but similar to the method of Draize (1959). Conjunctival redness was observed in all animals 1 hour after instillation, and resolved by 24 hours. The cornea and the iris were not affected by instillation of the test item. In this study, Bioten WP (*Trichoderma asperellum* 7.8 x 10^7 CFU/g; *Trichoderma gamsii* 4.2 x 10^7 CFU/g) was not an eye irritant and is in EPA Toxicity Category IV. This study was rated "ACCEPTABLE" for risk assessment purposes.

Acute Dermal Irritation Toxicity - Rabbit (OPPTS 870.2500; MRID # 47346305)
In a primary dermal irritation study (MRID 47346305), fasted young adult Himalayan rabbits (3 males) were dermally exposed to 500 mg of Bioten WP (*Trichoderma conidia* (1.2 x 10^8 CFU/g); *Trichoderma asperellum* strain ICC 012 (7.8 x 10^7 CFU/g); *Trichoderma gamsii* strain ICC 080 (4.2 x 10^7 CFU/g)) in *aqua ad iniectabilia* (water for injection) for 4 hours on a shaved area of 6 cm^2. Animals then were observed for 6 days. Irritation was scored by the method that was not named but similar to the method of Draize (1944). Very slight erythema was observed on all three animals 24 hours through 5 days after patch removal. Very slight edema was observed on one animal 72 hours through 4 days after patch removal. The Primary Irritation Index (PII) was 0.8. In this study, Remedier WP (*Trichoderma asperellum* 7.8 x 10^7 CFU/g; *Trichoderma gamsii* 4.2 x 10^7 CFU/g) is slightly irritating and is in EPA Toxicity Category IV. This study was rated "ACCEPTABLE" for risk assessment purposes.

Skin Sensitization Study-Guinea Pigs OPPTS 870.2600; MRID # 47346306)
In a skin sensitization study (MRID 47346306) with Bioten WP (*Trichoderma conidia* (1.2 x 10^8 CFU/g); *Trichoderma asperellum* strain ICC 012 (7.8 x 10^7 CFU/g); *Trichoderma gamsii* strain ICC 080 (4.2 x 10^7 CFU/g)) in 0.9% NaCl, young adult Dunkin-Hartley guinea pigs (15 males) were tested using the method of Magnusson and Kligman (Maximization Test). The test substance was administered as a suspension for intradermal application and applied as a suspension for topical application. Benzocaine was used as a positive control. Discrete or patchy erythema was observed on all test animals exposed to the 10% suspension of Bioten WP (*Trichoderma asperellum* and *Trichoderma gamsii* wettable powder) in 0.9% NaCl solution 25 and 48 hours after the induction phase. Some animals exposed to a 50% suspension of Bioten WP (*Trichoderma asperellum* and *Trichoderma gamsii* wettable powder) in 0.9% NaCl solution had moderate, confluent erythema 49 and 72 hours after application. There were no skin reactions in the test animals 24, 48, or 72 hours after the final challenge using a 1% suspension of BiotenWP (*Trichoderma asperellum* and *Trichoderma gamsii* wettable powder) in 0.9% NaCl solution. In this study, (*Trichoderma asperellum* 7.8 x 10^7 CFU/g; *Trichoderma gamsii* 4.2 x 10^7 CFU/g) was not a dermal sensitizer. This study was rated "ACCEPTABLE" for risk assessment purposes.

b. Acute Toxicology and Subchronic Toxicity/Pathogenicity – Tier II; Reproductive Fertility Effects, Carcinogenicity, Immunotoxicity, and Infectivity/Pathogenicity Analysis – Tier III (40 CFR § 158.2140)

Tier II and Tier III studies were not required for *Trichoderma gamsii* strain ICC 080 based on the lack of acute toxicity/pathogenicity in the Tier I studies.

c. Effects on the Endocrine System

Section 408(p) of the Federal Food, Drug, and Cosmetic Act (FFDCA) requires EPA 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 such other endocrine effect as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there were scientific bases for including, as part of its program, androgen and thyroid hormone systems, in addition to the estrogen hormone system. The Environmental Protection Agency also adopted EDSTAC's recommendation that the Program include evaluations of potential effects on wildlife.

The Agency has no information to suggest that *Trichoderma gamsii* strain ICC 080 has an effect on the endocrine system. The submitted acute pulmonary toxicity/pathogenicity study in rodents indicated that following pulmonary exposure, the immune system is still intact and able to process and clear the active ingredient. *Trichoderma gamsii* strain ICC 080 is a ubiquitous organism in the environment and there have been no reports of the organism affecting endocrine systems. Therefore, it is unlikely that this organism would have estrogenic or endocrine effects and it is practically non-toxic to mammals. Additional data on possible endocrine effects of this microbial pesticide, are not required at this time.

2. Dietary Exposure and Risk Characterization

Dietary exposure to the microbial pesticide is likely to occur, but the lack of acute oral toxicity, infectivity, and pathogenicity support the establishment of an exemption from the requirement of a tolerance for *Trichoderma gamsii* strain ICC 080.

Dietary exposure to the microbial active ingredient is expected to be minimal. The product is typically applied to soil, but sometimes may be applied when the crops are growing in the field, resulting in residues on the crops. The Agency expects residues on food to be minimal because of the typical method used to apply the microbial fungicide to soils. Moreover, *Trichoderma* lives in soils and is unlikely to live on the plants because any spores that do end up on the plant due to application would decrease over time due to weathering, desiccation and ultraviolet radiation, which can kill even quiescent forms of the fungus. In the remote likelihood that the applied fungus grew on the edible portions of a treated crop, the results of the oral toxicity testing demonstrated

that no toxicity or pathogenicity in treated animals occurred, even when dosed with the fungus at high levels by the oral route of exposure. (See section IV(B)(1)(a).)

3. Drinking Water Exposure and Risk Characterization

Drinking water exposure is expected to be negligible because the microbial fungicide will not be applied to water. Further, *Trichoderma gamsii* is a soil microorganism, and would not proliferate in aquatic environments. Moreover, the Agency believes that *Trichoderma* within the soil will not likely percolate into water due to the large size of the fungal spores and the fact that they adhere to soil particles. Even in the unlikely event that dietary exposure occurs through drinking water, the Agency concludes that there is a reasonable certainty that no harm will result because of the lack of acute oral toxicity/pathogenicity to mammals as previously described.

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

Section 408(b)(2)(C) of the FFDCA provides that EPA shall assess the available information about consumption patterns among infants and children, the special susceptibility of infants and children to pesticide chemical residues, and the cumulative effects on infants and children from the residues and other substances with a common mechanism of toxicity. In addition, FFDCA section 408(b)(2)(C) also provides that EPA shall apply an additional tenfold margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database unless EPA determines that a different margin of 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.

Based on the acute toxicity and pathogenicity data discussed in section IV(B)(1)(a), the Environmental Protection Agency concludes that there is a reasonable certainty that no harm to sensitive subpopulations, including infants, children, and adults, will result from the use of *Trichoderma gamsii* strain ICC 080. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. The Agency has arrived at this conclusion because the data available on *Trichoderma gamsii* strain ICC 080 do not demonstrate toxic, pathogenic, or infective potential to mammals. Thus, there are no threshold effects of concern and, as a result, the provision requiring an additional margin of safety does not apply. Further, the considerations of consumption patterns, special susceptibility, and cumulative effects do not apply to pesticides without a demonstrated significant adverse effect.

5. Occupational, Residential, School, and Daycare Exposure and Risk Characterization

a. Occupational Exposure and Risk Characterization

In light of the Tier I acute toxicity/pathogenicity studies, which did not show any toxicity *via* the oral, pulmonary, or intraperitoneal injection routes of exposure (see section IV(B)(1)(a)), or pathogenic effects to rats *via* the pulmonary route of exposure, handler exposure to *Trichoderma gamsii* strain ICC 080 is not expected to pose any undue risk. Regardless, requirements for the use of appropriate personal protective equipment, and precautionary statements are required on the product label to mitigate any potential risks to pesticide handlers due to prolonged exposure. Handlers working with *Trichoderma gamsii* strain ICC 080 must wear a long-sleeved shirt, long pants, socks, shoes, waterproof gloves, and a dust/mist filtering respirator meeting NIOSH standards of at least N-95, R-95, or P-95 when mixing, loading, or applying the product.

b. Residential, School, and Daycare Exposure and Risk Characterization

Trichoderma gamsii strain ICC 080 is a naturally occurring microorganism and is ubiquitous in the environment. *Trichoderma gamsii* strain ICC 080 will be applied to substrate mixes, ornamental plants, agricultural fields, turf, and various plants grown in greenhouses. Although some applications to turf or ornamental plants may be in residential areas, non-dietary exposure would be expected to be below the Agency's level of concern because of its low toxicity classification, and because the lab results indicate *Trichoderma gamsii* strain ICC 080 is not pathogenic to mammals.

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

In examining aggregate exposure, Section 408 of the FFDCA directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures, including drinking water from ground water or surface water and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

Trichoderma gamsii strain ICC 080 will be applied to substrate mixes, ornamental plants, agricultural fields, turf, and various plants grown in greenhouses. Although some applications to turf or ornamental plants may be in residential areas, non-dietary exposure would be expected to be below the Agency's level of concern because of its low toxicity/pathogenicity to mammals.

7. Cumulative Effects

Section 408(b)(2)(D)(v) of the FFDCA requires the Agency to consider the cumulative effect of exposure to *Trichoderma gamsii* strain ICC 080 and to other substances that

have a common mechanism of toxicity. These considerations include the possible cumulative effects of such residues on infants and children. Based on tests in mammalian systems, *Trichoderma gamsii* strain ICC 080 does not appear to be toxic to humans via dietary and pulmonary exposure. Therefore, the requirement to consider cumulative effects does not apply.

8. Risk Characterization

The Agency considered human exposure to *Trichoderma gamsii* strain ICC 080 in light of the standard for registration and safety factors in FIFRA and FFDCA, as amended by the FQPA. A determination has been made that no unreasonable adverse effects to the United States population in general, and to infants and children in particular, will result from the use of *Trichoderma gamsii* strain ICC 080 when used in accordance with EPA-approved labeling.

C. Environmental Assessment

Exposure of non-target organisms to *Trichoderma gamsii* strain ICC 080 is possible from the proposed uses of microbial pesticides containing this active ingredient. Isagro, S.p.A. submitted studies and data waiver rationales to satisfy data requirements for non-target organism risk assessment with the active ingredient (TGAI). The following is a summary of the information submitted to support registration and an assessment of environmental risk.

1. Summary of Non-target Organism Testing and Waiver Rationales

The data and other information provided to the Agency in support of registrations of *Trichoderma gamsii* strain ICC 080 as a manufacturing product and an end use product is sufficient to satisfy the Tier I non-target organism data requirements for the active ingredient. Further testing of non-target organisms at higher tier levels is not required. The honey bee study that was provided for this active ingredient (MRID 473458-07) was acceptable for determination of toxicity, but was of too short a duration to determine the pathogenicity to these organisms; however, an extensive literature search did not produce reports of *Trichoderma gamsii* or *Trichoderma viride* having adverse effects on bees. A non-target insect study on one species was also submitted. BPPD has evaluated the information available and has determined that additional studies are not necessary for *Trichoderma gamsii* strain ICC 080. The rationale for this decision, as well as summaries of each study are presented in the section below. Table 3 in Appendix A provides the status of the data requirements for the TGAI.

.a. Avian Oral Toxicity/Pathogenicity (OPPTS Guideline 885.4050); Avian Inhalation Toxicity/Pathogenicity (OPPTS Guideline 885.4100)

A data waiver was requested in lieu of data requirements for avian testing. Justification for these waivers was largely based on the temperatures at which *Trichoderma* species can grow compared with higher avian body temperatures. The supporting rationale cited

data that showed that *Trichoderma* species grow at temperatures below 37°C, whereas normal bird body temperatures are typically above 38°C, with active body temperatures above 40°C (Prinzinger et al. 1991). As the registrant states, EPA has acknowledged the validity of this rationale in the past (USEPA 2008). The registrant also argued that no toxic or pathogenic effects to birds should be expected, since none were observed in the rat acute oral toxicity/pathogenicity tests with the active ingredient or the EP. EPA does not accept this argument, however, because the comparability of the effects between these two taxa for *Trichoderma gamsii* strain ICC 080 is not known. Nonetheless, the growth temperature rationale presented is sufficient to conclude that adverse effects to birds are not expected due to exposure to *T. gamsii* strain ICC 080. This rationale is sufficient to fulfill the data requirement.

b. Freshwater Fish Toxicity/Pathogenicity (OPPTS 885. 4200) and (MRID No.: 47345805)

In a 30-day toxicity/pathogenicity study, juvenile rainbow trout (*Oncorhynchus mykiss*) received an aqueous exposure to nominal concentrations of 6.25, 12.5, 25, 50, and 100 mg *Trichoderma gamsii* strain ICC 080 Technical/L (corresponding to measured concentrations of 1.1×10^9, 2.2×10^9, 5.0×10^9, 8.2×10^9, and 1.4×10^{10} cfu/L, respectively) under semi-static conditions. A dilution water control and an attenuated (sterile filtered) control were also included. There was no mortality in rainbow trout exposed to *Trichoderma gamsii* strain ICC 080 and no signs of sublethal effects were observed at any of the test substance concentrations. The 30-day LC_{50} was empirically estimated to be greater than the highest nominal concentration tested 100 mg/L (measured concentration of 1.4×10^{10} cfu/L). Likewise, the NOEC was ≥ 100 mg/L (≥ 1.4×10^{10} cfu/L, measured). The study is scientifically sound and acceptable for assessment of risk to freshwater fish from exposure to *Trichoderma gamsii* strain ICC 080. Based on these results, adverse effects to freshwater fish resulting from proposed label applications of *Trichoderma gamsii* strain ICC 080 are not expected. This study was classified as "ACCEPTABLE."

c. Freshwater Invertebrate Toxicity/Pathogenicity (OPPTS 885.4240) and (MRID Nos.: 47345806 and 47346307)

In a 21-day toxicity/pathogenicity study, **(MRID No.:** 47345806) neonate *Daphnia magna* received an aqueous exposure to nominal concentrations of 6.25, 12.5, 25, 50, and 100 mg *Trichoderma gamsii* strain ICC 080 Technical/L (corresponding to measured concentrations of 1.6×10^9, 2.9×10^9, 4.4×10^9, 1.0×10^{10}, and 2.1×10^{10} cfu/L, respectively) under semi-static conditions. A dilution water control and an attenuated control were also included. Daphnia survival was 95%, 90%, 85%, 70%, and 50% in the 6.25, 12.5, 25, 50 and 100 mg/L *Trichoderma gamsii* strain ICC 080 test concentrations, respectively, and was 100% and 80% in the negative and attenuated controls, respectively. Thus, the survival rate was considered to be significantly reduced only in the highest test concentration (100 mg/L). Statistical calculation of the mortality/immobility EC_{50} could not be performed, since no test concentration produced >50% mortality. Results of statistical analysis of the reproduction rates indicate

reproduction rate was reduced only in *Daphnia* exposed to the 100 mg/L test concentration (38% reduction). Based on the mortality/immobility and the reproduction rates of surviving *Daphnia*, the 21-day NOEC was determined to be 50 mg/L highest (1.0 $x10^{10}$ cfu/L, measured). Based on these results, adverse effects to freshwater invertebrates resulting from proposed label applications of *Trichoderma gamsii* strain ICC 080 are not expected. This study was classified as "ACCEPTABLE."

This 48-hour Immobilization test (**MRID No.:** 47346307) was performed with the end-use product. In a 48-hour immobilization study, *Daphnia magna* received an aqueous exposure to the nominal concentration of 100 mg/L of Remedier WP under semi-static conditions (test and control water was renewed at 24 hours). The active ingredients in Remedier WP are *Trichoderma asperellum* strain ICC 012 and *Trichoderma gamsii* strain ICC 080 (corresponding to 3.2 x 10^8 cfu/L total, measured) and are each contained in the product at 2% by weight. A dilution water control was also included. No adverse effects were observed in daphnids exposed to the 100 mg/L limit test concentration which indicates a 48-hour EC_{50} of >100 mg/L (3.2 x 10^8 cfu/L). This study is classified as unacceptable as a Tier I pathogenicity study for freshwater aquatic invertebrate with a microbial pesticide due to the 48-hour duration. The study was classified as "unacceptable". It cannot be upgraded and cannot be used to fulfill the pathogenicity data requirement for either TGAI.

d. Non-target Insect Testing (OPPTS 885.4340) (MRID No.: 47346308)

This dose response study is not a data requirement for microbial fungicides. However, the registrant submitted a 14-day contact toxicity/pathogenicity study using the predatory mite, *Typhlodromus pyri.* The test insects were exposed to nominal concentrations of 0.062, 0.185, 0.556, 1.670, and 5.0 kg Remedier WP/ha (corresponding to 0.002, 0.007, 0.022, 0.067, and 200 g total active ingredient/ha). Mite mortality was monitored for the first 7-days and the effects of Remedier WP on reproduction potential were monitored in adult mites from day 7 thru 14. The active ingredients in Remedier WP are *Trichoderma asperellum* strain ICC 012 and *Trichoderma gamsii* strain ICC 080 (corresponding to 1.2 x 10^8 cfu/L, total). A dilution water control and positive control were included in the study. Statistically significant mortality was not observed in mites exposed to any of the Remedier WP treatment concentrations. Thus the LD_{50} was determined to be > 5 kg/ha, which is higher than the highest broadcast application rate. Confirmation of infection by the *Trichoderma* active ingredients in dead mites was not performed. Reproduction was affected in the 0.062 kg, 0.185 kg and 5.0 kg Remedier WP/ha treatment groups, but no statistically significant effects on reproduction occurred in the 0.556 kg or 1.670 kg Remedier WP/ha treatment groups. The study authors concluded that effects observed on reproduction were not of biological significance and not due to exposure to the test item. However, these results are inconclusive and it appears that the study design is not sensitive enough to detect biologically significant reductions in reproduction in this species as a result of exposure to the test material. Because mortality is the primary endpoint of concern, this study is classified as acceptable.

e. Honey Bee Testing (OPPTS 885.4380) (MRID No.: 47345807)

Adult *Apis mellifera* L. were exposed to 50 µg per bee *Trichoderma gamsii* strain ICC 080 Technical (0.85 x 10^5 cfu/bee) in the contact toxicity test and 112.1 µg/bee *Trichoderma gamsii* strain ICC 080 Technical (1.9 x 10^5 cfu/bee) in an oral toxicity test. The duration of both tests was 48 hours. A negative control (contact: water plus Adhasit [an adhesive], oral: or water plus sugar) and positive control (dimeothate) were also included. Two percent mortality was observed in the contact toxicity test while 4% mortality was observed in the acute oral toxicity test. There were no signs of abnormal behavior in the surviving honey bees throughout the tests. The 24 and 48 hour contact LD_{50} of *Trichoderma gamsii* strain ICC 080 was >50 µg product (0.85 x 10^5 cfu/bee). The 24 and 48 hour oral LD_{50} of *Trichoderma gamsii* strain ICC 080 was >112.1 µg product (1.9 x 10^5 cfu/bee). This study is classified as acceptable for toxicity determination. It is not adequate for determination of pathogenicity because the study duration was only 48 hours, which is too short a duration to allow for detection of pathogenicity to honey bees.

a. Non-guideline Studies

i) Acute Toxicity (14 Days) of *Trichoderma gamsii* to the Earthworm *Eisenia fetida* in Artificial Soil **(MRID No.:** 47345810)

Adult earthworms (*Eisenia fetida*) were exposed to 198, 296, 444, 667, and 1000 mg *Trichoderma gamsii* strain ICC 080 Technical/kg soil dry weight in artificial soil corresponding to 3.37 x $10^{8,}$ 5.03 x10^8, 7.55 x 10^8, 1.13 x 10^9, and 1.7 x 10^9 cfu/kg soil dry weight. A negative control (untreated soil) was also included. The test duration was 14 days. No mortality was observed in any of the soil test groups with *Trichoderma gamsii* and there were no signs of abnormal behavior in the surviving worms throughout the test. Body weight gain in the treatment groups was not significantly different from the negative control at test termination. The 14-day contact LD_{50} and LOEC of *Trichoderma gamsii* was >1000 mg/kg soil (1.7 x 10^9 cfu/kg soil) corresponding to the highest concentration tested. The NOEC was 1000 mg/kg soil (1.7 x 10^9 cfu/kg soil). This non-guideline study is scientifically sound and acceptable for earthworm toxicity testing.

ii) Effects of *Trichoderma gamsii* to the Activity of Soil Microflora in the Laboratory **(MRID No.:** 47345809)

The effects of *Trichoderma gamsii* strain ICC 080 on the activity of soil microflora as determined by carbon and soil nitrogen transformation was assessed in a 28-day laboratory study. Test concentrations of *Trichoderma gamsii* strain ICC 080 were 0.07 and 0.67 mg/kg soil dry weight were applied to loamy, sandy soils collected from a fallow field. On Day 28 after application, the respiration rates of *Trichoderma gamsii strain* ICC 080 treated soils, as determined by CO_2 production, were 8.86% and 3.40%

higher than in the untreated control for the test concentrations of 0.07 mg and 0.67 mg *Trichoderma gamsii* strain ICC 080/kg soil dry weight, respectively. These values were not statistically different from the crontrol and did not exceed the 25% inhibition threshold according to OECD, EPPO and SETAC guidelines, indicating no long-term effects of the test substance on soil respiration. Nitrate content was 18.7% and 10.4% lower in the soils treated at 0.07 mg and 0.67 mg *Trichoderma gamsii* strain ICC 080/kg soil dry weight, respectively, compared to the negative control, which was statistically significant for the lower test concentration. A minor difference (-5.5% from the control) was observed for nitrate formation rate. The differences for the soil mineral nitrogen content were -18.6% and -10.0%, respectively, which was statistically significant for the 0.07 mg/kg soil test level. However, the soil nitrate content, nitrate rate of formation and soil mineral nitrogen content were all below the 25% trigger values indicating no long-term effects to soil microflora. This non-guideline study is scientifically sound and classified as acceptable for assessing hazard of the effects of *Trichoderma gamsii* strain ICC 080 on soil microflora. This study was classified as "ACCEPTABLE."

2. Environmental Effects Conclusions

a. Terrestrial Animals and Plants

Exposure is expected to terrestrial animals and plants as a result of some, but not all, proposed use patterns for the EP containing *Trichoderma gamsii* strain ICC 080. Greenhouse applications will limit environmental release of the active ingredient, and exposure to non-target organisms is not expected from these uses. Applications made to cuttings and bare roots, in substrate mixes, and through soil drenches would limit the presence of the active ingredient to the soil immediately around treated plants, which will significantly reduce the potential for non-target exposure to only those organisms that utilize those areas. This exposure will be limited even further if the treated plants are in containers (e.g., pots, flats, etc.). A greater potential for non-target exposure exists with broadcast applications and chemigation that result in residues of the active ingredient on foliar surfaces in addition to the soil. Exposure to terrestrial non-target organisms is anticipated as a result of these applications.

The supporting rationale to waive the non-target data requirement for avian wildlife study was sufficient to conclude that adverse effects are not expected in avian wildlife as a result of exposure to *Trichoderma gamsii* strain ICC 080, due to the growth temperatures required for the microbial active ingredient compared with the higher body temperature of birds.

The data submitted for toxicity/pathogenicity to honey bees (*Apis mellifera*) were unacceptable due to the short duration (48 hours) of the oral and contact tests that were performed in the study that was submitted. Honeybee studies should be long enough (e.g., 30 days) to allow for the observation of pathogenic effects. While BPPD recognizes that some strains of *Trichoderma harzianum* are known to affect non-target insects (e.g., Glinski and Buczek 2003, Santamarina et al. 2002), there are no reports in the scientific literature that *Trichoderma gamsii* or *Trichoderma viride* causes adverse

effects on bees. Therefore, BPPD has concluded that adverse effects of the proposed uses of *Trichoderma gamsii* strain ICC 080 to honey bees are unlikely.

Although not a data requirement for microbial fungicides, an insect toxicity/pathogenicity study with the predatory mite (*Typhlodromus pyri*, MRID 47346308) was submitted and reviewed. This study showed that adverse effects on these and related insects are not expected at field application rates Therefore, BPPD concluded that the adverse effects to non-target insects as a result of the proposed fungicidal uses of *Trichoderma gamsii* strain ICC 080 are not expected.

Non-target plant testing is not required because *Trichoderma gamsii* strain ICC 080 is not related to any known plant pathogen. Adverse effects on plants are not expected to result from proposed fungicidal uses of *Trichoderma gamsii* strain ICC 080.

Two non-guideline studies on earthworm toxicity/pathogenicity and effects on soil microflora activity were also submitted. While these studies are not required for registration of microbial pesticides, they provided information to allow BPPD to conclude that the proposed fungicidal uses of *Trichoderma gamsii* strain ICC 080 are not expected to have adverse effects in soil.

Based on the data and other information submitted by the applicant, adverse effects are not expected to occur to terrestrial animals or plants as a result of proposed labeled applications of *Trichoderma gamsii* strain ICC 080.

b. Aquatic Animals and Plants

Exposure of non-target organisms to *Trichoderma gamsii strain ICC* 080 in the aquatic environment is not expected to be significant. For example, an application made directly to a pond that is only 6 inches deep (a standard size used by OPP to estimate aquatic exposure) at the highest broadcast application rate (5 lbs/acre) would yield a concentration of 184 cfu/mL, so the amount reaching nearby aquatic environments due to runoff or drift would be expected to be less. This is far below the maximum hazard concentrations at which the aquatic testing was conducted. Furthermore, if *Trichoderma gamsii* strain ICC 080 enters the aquatic environment it is not expected to proliferate in the aquatic environment, since it is a soil-borne fungus.

Studies with the TGAI were submitted for the freshwater fish and freshwater invertebrate toxicity/pathogenicity testing data requirements. No significant adverse effects were observed in the subjects of either study. Both of their endpoint values were above the maximum hazard dose for aquatic testing with microbial pesticides, indicating a lack of effects above environmental concentrations that may occur in aquatic environments as a result of the proposed applications of *Trichoderma gamsii* strain ICC 080. A 48-hour *Daphnia* test with the EP was submitted but was determined to be unacceptable due to the inadequate study duration; however, the available data on the TGAI are adequate to assess the potential risk of *Trichoderma gamsii* strain ICC 080. *Trichoderma* species are ubiquitous in the environment, and do not proliferate in aquatic ecosystems, so significant

exposure in freshwater environments is not expected from the proposed applications of *Trichoderma gamsii* strain ICC 080. Therefore, adverse effects to freshwater aquatic animals are not anticipated.

Trichoderma species are not related to any known plant pathogens, and as determined above, *Trichoderma gamsii* strain ICC 080 is not expected to occur in freshwater environments in significant amounts. Therefore, data from aquatic plant testing are not required, and no effects are anticipated to this taxon as a result of the proposed applications. A study with the aquatic vascular plant, *Lemna gibba*, was submitted and reviewed, and results show that the 7-day growth inhibition NOEC for the aquatic vascular plant *Lemna gibba* is $2.1x10^7$ cfu/mL. These results confirm the conclusion of no anticipated adverse effects to aquatic plants.

As with freshwater environments, significant amounts of *Trichoderma gamsii* strain ICC 080 are not expected to reach marine/estuarine environments. Therefore data are not required for these taxa, and adverse effects in these environments are not anticipated.

Based on the data submitted and what is known about the nature of *Trichoderma* species in aquatic environments, adverse effects to freshwater and marine/estuarine fish, invertebrates, and plants are not expected as a result of the proposed label applications of *Trichoderma gamsii* strain ICC 080.

3. Threatened and Endangered Species Assessment

There are no listed endangered or threatened species related to the target pests. Since it is concluded that effects are not anticipated for non-target species exposed to *Trichoderma gamsii* strain ICC 080 as a result of proposed labeled applications, effects to listed species are also not expected. Therefore, a "No Effect" determination is made for use of *Trichoderma gamsii* strain ICC 080 as labeled.

For a comprehensive guideline-by-guideline summary of the non-target toxicity data requirements, refer to Table 3 in Appendix A.

V. ENVIRONMENTAL JUSTICE

EPA seeks to achieve environmental justice, the fair treatment and meaningful involvement of all people, regardless of race, color, national origin, or income, in the development, implementation, and enforcement of environmental laws, regulations, and policies. To help address potential environmental justice issues, the Agency seeks information on any groups or segments of the population who, as a result of their location, cultural practices, or other factors, may have atypical, unusually high exposure to *Trichoderma gamsii* strain ICC 080, compared to the general population. Please comment if you are aware of any sub-populations that may have atypical, unusually high exposure compared to the general population.

VI. RISK MANAGEMENT AND REGISTRATION DECISIONS

A. Determination of Eligibility

Section 3(c)(5) of FIFRA provides for the registration of new active ingredients if it is determined that (A) its composition is such as to warrant the proposed claims for it; (B) its labeling and other materials required to be submitted comply with the requirements of FIFRA; (C) it will perform its intended function without unreasonable adverse effects on the environment; and (D) when used in accordance with widespread and commonly recognized practice it will not generally cause unreasonable adverse effects on the environment.

The four criteria of the Eligibility Determination for Pesticidal Active Ingredients are satisfied by the science assessments supporting products containing *Trichoderma gamsii* strain ICC 080. Such products are not expected to cause unreasonable adverse effects, and are likely to provide protection as claimed when used according to label instructions. Therefore, *Trichoderma gamsii* strain ICC 080 is eligible for registration as a microbial fungicide.

B. Regulatory Decision

On October 1, 2009, EPA announced a new policy to provide a more meaningful opportunity for the public to participate on major registration decisions before they occur. According to this new policy, EPA intends to provide a public comment period prior to making a registration decision for, at minimum, the following types of applications: new active ingredients; first food use; first outdoor use; and first residential use. Accordingly, EPA announced its preliminary registration decision on *Trichoderma gamsii* strain ICC 080 on December 30, 2009, and opened a 30-day comment period on this product as a "new active ingredient." EPA did not receive any comments on this proposed action during the comment period.

At this time, EPA believes, the data submitted fulfill the requirements of registration for products containing *Trichoderma gamsii* strain ICC 080 as a microbial fungicide. Acute toxicity data for *Trichoderma gamsii* strain ICC 080 demonstrate that it has low toxicity (category III and IV). EPA has no concerns for any non-target organisms, including threatened or endangered species, exposed to *Trichoderma gamsii* strain ICC 080 when it is used in accordance with approved label directions. EPA has not identified any toxic endpoints for non-target mammals, birds, plants, aquatic, or soil organisms. EPA supports its registration under Section 3(c) (5) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). Refer to Appendix B for product-specific information.

1. Conditional/Unconditional Registration

The Environmental Protection Agency (EPA) considered information submitted for granting registration under Section 3(c)(5) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and determined that the data and information submitted in

support of *Trichoderma gamsii* strain ICC 012 adequately satisfy current data requirements (refer to 40 CFR Subpart U § 158.2000). If the Agency receives comments during the 30 day public comment period that inform EPA's initial decision, EPA will address such new information and take appropriate action.

C. Labeling

Before releasing pesticide products containing *Trichoderma gamsii* strain ICC 080 for shipment, the applicant is required to provide appropriate labels.

VII. ACTIONS REQUIRED BY THE APPLICANT

The Agency evaluated the data submitted in connection with the initial registration of *Trichoderma gamsii* strain ICC 080 and determined that these data fulfill current registration requirements. No additional data are required to be submitted to the Agency at this time. Additional data may be required for new uses and/or changes to existing uses.

Notwithstanding the information stated in the previous paragraph, it should be clearly understood that certain, specific, data are required to be reported to the Agency as a requirement for maintaining the Federal registration for a pesticide product. A brief summary of these types of data are listed below.

A. Reporting of Adverse Effects and Hypersensitivity Incidents

Reports of all incidents of adverse effects to the environment must be submitted to the Agency under the provisions stated in FIFRA, Section 6(a)(2).

Additionally, all incidents of hypersensitivity (including both suspected and confirmed incidents) must be reported to the Agency under the provisions of 40 CFR Part 158.2140 (Guideline reference number OPPTS 885.3400).

VIII. GLOSSARY OF ACRONYMS AND ABBREVIATIONS

BCCM	Belgian Coordinated Collections of Microorganisms
BPPD	Biopesticides and Pollution Prevention Division
BRAD	Biopesticides Registration Action Document
CFR	Code of Federal Regulations
cfu	colony-forming unit
cm^2	square centimeter
°C	degrees Celsius
EDSP	Endocrine Disruptor Screening Program
EDSTAC	Endocrine Disruptor Screening and Testing Advisory Committee
EP	end-use product
EPA	Environmental Protection Agency (the "Agency")
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FQPA	Food Quality Protection Act
FR	Federal Register
g	gram
kg	kilogram
L	Liter
LC_{50}	median lethal concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air, or feed (e.g., mg/L, mg/kg, or ppm).
LLC	limited liability company
LOEC	lowest observable effect concentration
MRID No.	Master Record Identification Number
µm	micrometer
mg	milligram
mL	milliliter
mm	millimeter
MUCL	Mycothèque de l'Université Catholique de Louvain
NIOSH	National Institute for Occupational Safety and Health
NOEC	no observable effect concentration
OPP	Office of Pesticide Programs
OPPTS	Office of Prevention, Pesticides, and Toxic Substances
PII	Primary Irritation Index
P.O. Box	Post Office Box
PP	Pesticide Petition
PPE	personal protective equipment
TGAI	technical grade of the active ingredient

IX. BIBLIOGRAPHY

A. Studies Submitted in Support of *Trichoderma gamsii Strain ICC 080*

MRID	Citation	Receipt Date
47345800	Isagro U.S.A. (2008) Submission of Product Chemistry and Toxicity Data in Support of the Application for Registration of Trichoderma ICC 080 gamsii. Transmittal of 13 Studies.	08-Feb-2008
47345801	Leuschner, P. (2004) Acute Toxicity Study of Trichoderma viride Strain ICC 080 By Oral Administration to Rats. Project Number: 17290/03. Unpublished study prepared by Laboratory of Pharmacology & Toxicology. 30 p.	08-Feb-2008
47345802	Leuschner, P. (2004) Acute Toxicity Study of Trichoderma viride by Intraperitoneal Injection to Rats. Project Number: 17472/03. Unpublished study prepared by Laboratory of Pharmacology & Toxicology. 32 p.	08-Feb-2008
47345803	Leuschner, P. (2004) Acute Pulmonary Toxicity / Pathogenicity of Trichoderma viride Strain ICC 080 by Intratracheal Administration to Rats. Project Number: 17291/03. Unpublished study prepared by Laboratory of Pharmacology & Toxicology. 48 p.	08-Feb-2008
47345804	Dengler, D. (2004) Analysis of the Occurrence of Test Substance Trichoderma viride Conidia in Animal Tissue. Project Number: 20031372/01/AMAT. Unpublished study prepared by GAB Biotechnologie Gmbh. 25 p.	08-Feb-2008
47345805	Pawlowski, S. (2004) Toxicity of Trichoderma viride Strain ICC 080 to Rainbow Trout (Oncorhynchus mykiss) in a Prolonged Toxicity Test. Project Number: 17113231. Unpublished study prepared by Institut fuer Biologische Analytik und Consulting IBACON. 67 p.	08-Feb-2008
47345806	Pawlowski, S. (2004) Influence of Trichoderma viride Strain ICC 080 to Daphnia magna in a Reproduction Test. Project Number: 17112221. Unpublished study prepared by Institut fuer Biologische Analytik und Consulting IBACON. 68 p.	08-Feb-2008
47345807	Schmitzer, S. (2004) Effects of Trichoderma viride (Acute Contact and Oral) on Honey Bees (Apis mellifera L.) in the Laboratory. Project Number: 17115035. Unpublished study prepared by Institut fuer Biologische Analytik und Consulting IBACON. 30 p.	08-Feb-2008
47345808	Spatz, B.; Pawlowski, S. (2004) Toxicity of Trichoderma viride Strain ICC 080 to the Aquatic Plant Lemna gibba in a Growth	08-Feb-2008

	Inhibition Test. Project Number: 17114240. Unpublished study prepared by Institut fuer Biologische Analytik und Consulting IBACON. 69 p.	
47345809	Reis, K. (2004) Effects of Trichoderma viride on the Activity of the Soil Microflora in the Laboratory. Project Number: 17119080. Unpublished study prepared by Institut fuer Biologische Analytik und Consulting IBACON. 47 p.	08-Feb-2008
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APPENDIX A – MICROBIAL PESTICIDE DATA REQUIREMENTS

TABLE 1. Product Analysis Data Requirements for the Technical Grade of the Active Ingredient (TGAI), *Trichoderma gamsii* strain ICC 080, and Its Associated End-Use Product (EP), Tenet WP (40 CFR § 158.2120)

Data Requirement (OPPTS Guideline)	Results		MRID Number
	TGAI	EP	
Product Chemistry and Composition			
Product Identity (885.1100)	*Trichoderma gamsii* strain ICC 080, originally characterized as *Trichoderma viride*, has been recharacterized as *Trichoderma gamsii* and also has been characterized by molecular biology techniques. *Trichoderma gamsii* strain ICC 080 was isolated from a suppressive soil in Sardinia, Italy. Submitted data satisfy the requirements **Classification: Acceptable**	Submitted data satisfy the requirements of Product Identity for the EP. **Classification: Acceptable**	47345811 47346309 47460901 47643901
Manufacturing Process (885.1200)	Submitted data satisfy the requirements of manufacturing process for both the TGAI and EP. **Classification: Acceptable**		47345811 47346309 47460901
Deposition of a Sample in a Nationally Recognized Culture Collection (Not applicable)	*Trichoderma gamsii* strain ICC 080 has been deposited in the CABI Bioscience International Mycological Institute-Egham, UK with the Accession Number IMI CC No. 392151.		
Discussion of Formation of Unintentional Ingredients (885.1300)	Submitted data satisfy the requirements of discussion of formation of unintentional ingredients for both the TGAI and EP. **Classification: Acceptable**		47345811 47346309 47460901 47802701
Analysis and Certified Limits			
Analysis of Samples (885.1400)	Submitted data satisfy the requirements of analysis of samples for both the TGAI and EP. **Classification: Acceptable**		47345811 47345813 47346309 47460901

Data Requirement (OPPTS Guideline)	Results		MRID Number
	TGAI	EP	
			47802701
Certification of Limits (885.1500)	The certified limits for the Active ingredient were within the specified range. **Classification: Acceptable**	The certified limits for the active ingredients exceed the OPPTS Guideline 830.1750 specified ranges, but an acceptable explanation was provided. **Classification: Acceptable**	47345811 47346309 47460901 47802701
Physical and Chemical Characteristics			
Color (830.6302)	Gray green	Not applicable	47345812 47346310
Physical State (830.6303)	Solid powder	Not applicable	47345812 47346310
Odor (830.6304)	Slight odor	Not applicable	47345812 47346310
Stability to Normal and Elevated Temperatures, Metals, and Metal Ions (830.6313)	Not required for MP	Not applicable	47345812 47346310
Storage Stability (830.6317)	Stable for 6 months at 20ºC, not stable at 54ºC	Active ingredient stable for 15 months at 20-25ºC	47345812 47346310
Miscibility (830.6319)	Product is not a suspension.	Product is not a suspension.	47345812
Corrosion Characteristics (830.6320)	Product is not corrosive.	Product is not corrosive.	47345812.
pH (830.7000)	6.6 (1% aqueous solution)	Not applicable	47345812.
Viscosity (830.7100)	Product is not a liquid.	Product is not a liquid.	47345812 47346310
Density/Relative Density/Bulk Density (830.7300)	0.2 g/mL.	Not applicable	47345812 47346310

TABLE 2. Toxicology Data Requirements for the Technical Grade of the Active Ingredient (TGAI), *Trichoderma gamsii* Strain ICC 080, and Its Associated End-Use Product (EP), Bioten WP(40 CFR § 158.2140)

Data Requirement (OPPTS Guideline)	Results		MRID Number
	TGAI	EP	
Tier I			
Acute Oral Toxicity/Pathogenicity (885.3050)	*Trichoderma gamsii* strain ICC 080 (7.5×10^8 CFU/g) in 0.9% NaCl solution was not toxic at a dose of 2000 mg/kg bw. *Trichoderma gamsii* strain ICC 080 was of Low Toxicity. Microbial enumeration was not done so it is unknown if *Trichoderma gamsii* is infective or pathogenic in the rat. This study is classified SUPPLEMENTAL, but is upgraded by the Pulmonary Toxicity study which has the clearance data. **Classification: Acceptable**	Not applicable	47345801
Acute Pulmonary Toxicity/Pathogenicity (885.3150)	Not toxic, infective, and/or pathogenic to rats by pulmonary dose of 2.5×10^6 cfu/animal. **Classification: Acceptable**	Not applicable	47345803 47345804
Acute Intraperitoneal Injection Toxicity/Pathogenicity (885.3200)	Not toxic to rats by injection at dose of 1×10^7 cfu/animal. This study is classified SUPPLEMENTAL, but is upgraded by the Pulmonary Toxicity study which has the clearance data.	Not applicable	47345802

Data Requirement (OPPTS Guideline)	Results		MRID Number
	TGAI	EP	
	Classification: Acceptable		
Hypersensitivity Incidents (885.3400)	Any hypersensitivity incidents must be reported per OPPTS Guideline 885.3400.		
Cell Culture (885.3500)	Not required because *Trichoderma gamsii* Strain ICC 080 is not a virus (refer to test note #4 of 40 CFR § 158.2140(d)).	Not applicable	Not applicable
Acute Oral Toxicity (870.1100)	Not applicable	Bioten WP/ Remedier WP (*Trichoderma asperellum* 7.8 x 10^7 CFU/g; *Trichoderma gamsii* 4.2 x 10^7 CFU/g) is not toxic 5.3.9) in the rat. Oral LD_{50} was > 2000 mg/kg bw Limit test; no mortality occurred during the study **Classification: Acceptable TOXICITY CATEGORY III**	47346301
Acute Dermal Toxicity (870.1200)	Not applicable	When dosed with Bioten WP/ Remedier WP in 0.9% NaCl at a dose of 2000 mg/kg bw is of MODERATE Toxicity. There were no treatment related clinical signs, necropsy findings or changes in body weight. **Classification: Acceptable TOXICITY CATEGORY III**	43746302
Acute Inhalation Toxicity (870.1300)	Not applicable	Bioten WP/ Remedier WP Inhalation LC_{50}were as follows: Males > 5.20 mg/L, Females > 5.20 mg/ L, Combined > 5.20 mg/L. Bioten WP/ Remedier WP is of **LOW Toxicity,** based on lack of mortality in male and female rats. There were no treatment related clinical signs, necropsy findings or changes in body weight. **Classification: Acceptable TOXICITY CATEGORY IV**	47346303
Acute Eye Irritation	Not applicable	Bioten WP was not an eye irritant.	47346304

Data Requirement (OPPTS Guideline)	Results		MRID Number
	TGAI	EP	
(870.2400)		**Classification: Acceptable** **TOXICITY CATEGORY** IV	
Primary Dermal Irritation (870.2500)	Not applicable	When dosed with 500 mg of Bioten WP/ Remedier WP (*Trichoderma conidia* (1.2 x 10^8 CFU/g); *Trichoderma asperellum* ICC 012 (7.8 x 10^7 CFU/g); *Trichoderma gamsii strain ICC* 080 (4.2 x 10^7 CFU/g)), the product is slightly irritating. **Classification: Acceptable** **TOXICITY CATEGORY IV**	47346305
Skin Sensitization (870.2600)	Not applicable	This study is not required Bioten WP was not a dermal sensitizer. **Classification: Acceptable**	47346306
Tiers II and III			
Not required for *Trichoderma gamsii* Strain ICC 080 based on the lack of acute toxicity/pathogenicity in the Tier I studies.			

TABLE 3. Summary of data submitted to comply with non-target organism data requirements published in 40 CFR § 158.2150 for support of the registration of *Trichoderma gamsii strain ICC* 080.

Data Requirement	OPPTS Guideline No.	Results Summary and Classification	MRID No.
Avian oral toxicity	885.4050	Data waiver rationale provides sufficient information to determine that toxicity/pathogenicity to avian wildlife is not expected. **Classification: Acceptable**	Contained in tolerance petition
Avian inhalation toxicity/pathogenicity	885.4100	Data are not required. Nature of microbial pesticide does not indicate potential pathogenicity to birds or relatedness to any known bird pathogens.	N/A
Wild mammal toxicity/pathogenicity	885.4150	Tests required by 40 CFR § 158.2140 are adequate and appropriate for assessment of hazards to wild mammals. Testing indicates no adverse effects to laboratory rats at 7.7 x 10^7 spores/mL (2000 mg TGAI/kg bw) when dosed orally. Testing with the EP indicates no adverse effects to laboratory rats dosed orally at 2.3 x 10^7 spores/mL (2000 mg EP/kg bw). **Classification: Acceptable for wild mammal risk assessment**	473458-01 473463-01
Freshwater fish toxicity/pathogenicity	885.4200	The 30-day LC_{50} for rainbow trout (*Oncorhynchus mykiss*) is >4.9 x 10^{10} cfu/L. **Classification: Acceptable**	47345805
Freshwater invertebrate toxicity/pathogenicity	885.4240	The 21-day NOEC for *Daphnia* based on mortality/immobility and reproduction was ≥ 1x10^7 cfu/mL. A 48-hour *Daphnia* test with the EP (containing *T. gamsii strain ICC* 080 and *T. asperellum* ICC 012) was also submitted but was determined to be unacceptable due to the inadequate study duration. **Classification: Acceptable**	47345806 47346307
Estuarine/marine fish and invertebrate testing	885.4280	Data are not required. *T. gamsii strain ICC* 080 will not be applied directly to water and is not expected to enter marine/estuarine environments in amounts that are significantly higher than naturally-occurring concentrations.	N/A
Non-target plant testing	885.4300	Data are not required, since *T. gamsii strain ICC* 080 is not related to known plant pathogens, and is not expected to have adverse effects on plants. Additionally, a 7-day growth inhibition NOEC for the aquatic vascular plant *Lemna gibba* was	473458-08

Data Requirement	OPPTS Guideline No.	Results Summary and Classification	MRID No.
		$2.1x10^7$ cfu/mL. **Classification: Acceptable**	
Non-target insect testing	885.4340	LD_{50} >5 kg/ha for EP (containing *T. gamsii strain ICC* 080 and *T. asperellum* ICC 012) for predatory mite (*Typhlodromus pyri*) and no significant effects on reproduction observed. **Classification: Acceptable**	47346308
Honey bee testing	885.4380	48-hour contact and oral LD_{50} were > 0.85 x 10^5 cfu/bee and >1.9 x 10^5 cfu/bee, respectively. The study was of too short a duration. **Classification: Acceptable for toxicity determination**	47345807
Non-guideline testing Earthworm (*Eisenia fetida*) testing	N/A	The 14-day earthworm (*Eisenia fetida*) contact LD_{50} was determined to be >1.7 x 10^9 cfu/kg soil. **Classification: Acceptable**	47345810
Non-guideline testing Effects on Soil Microflora Activity	N/A	Soil respiration, nitrate content, nitrogen formation rate, and mineral nitrogen content were below the 25 % threshold value, indicating no significant perturbation of the soil microflora community **Classification: Acceptable**	47345809

APPENDIX B – *Trichoderma gamsii strain ICC* 080 Products

EPA Registration Number	Registration Name	Percentage Active Ingredient	Formulation Type	Use Site	Method of Application	Application Rate	Target Pests
80289-9	Bioten WP (or TenetWP)	2.0% *T. gamsii* 2.0% *T asperellum*	Wettable Powder	Alfalfa Berries Cereal Grains Citrus: Clover Cole Crops Corn: Cotton Cucurbits Grass, Forage, Fodder, and Hay Fruiting Vegetables Ginseng Herbs (fresh, dried and for oil) Leafy Vegetables (except Brassica) Legume Vegetables Olive Onions Dry bulb Pineapple Peanut Pomegranate Root , Tuber, and Corm Vegetables Sunflower Tobacco Tree Fruits Tree Nuts Tropical Fruit At Greenhouse, nursery and field sites Vines: (table grapes, wine grapes, muscadines, hops, kiwi)	In-furrow and banded application. Broadcast application Cutting and bare root application Drip, drench and chemigation. Substrate mix.	Rates vary by crop and application method	*Armillaria sp., Fusarium spp., Phytophthora spp., Pythium spp., Rhizoctonia spp., Rosellinia sp., Sclerotinia spp. Sclerotium rolfsii, Thielaviopsis basicola, Verticillium* spp
80289-10	*Trichoderma gamsii strain ICC* 080	99.9%		Formulating use only	N/A	N/A	