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Proposed Registration Decision

PRD2020-16

Beauveria bassiana **strain ANT-03, BioCeres** **F WP, BioCeres F GR,** **and BioCeres D GR**

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Overview

Proposed registration decision for *Beauveria bassiana* strain ANT-03

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the [Pest Control Products Act](#), is proposing registration for the sale and use of *Beauveria bassiana* strain ANT-03, BioCeres F WP, BioCeres F GR, and BioCeres D GR, containing the technical grade active ingredient *Beauveria bassiana* strain ANT-03, for reduction in numbers of Colorado potato beetle on potato, tomato, bell pepper, and eggplant; tarnished plant bug on spinach, Chinese cabbage, lettuce, celery, strawberry, raspberry, and blackberry; as well as chinch bug and European chafer and Japanese beetle larvae in turf.

Beauveria bassiana strain ANT-03 is currently registered for reduction in numbers of whiteflies, aphids, and thrips on greenhouse tomatoes, cucumbers and ornamentals. For details, see Proposed Registration Decision PRD2014-06, *Beauveria bassiana* strain ANT-03, and Registration Decision RD2014-16, *Beauveria bassiana* strain ANT-03.

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products are acceptable.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of *B. bassiana* strain ANT-03 and BioCeres F WP, BioCeres F GR, and BioCeres D GR.

What does Health Canada consider when making a registration decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable¹ if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value² when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the

¹ "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

² "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact."

impact of pesticides. For more information on how the Health Canada regulates pesticides, the assessment process and risk-reduction programs, please visit the [Pesticides section](#) of the Canada.ca website.

Before making a final registration decision on *B. bassiana* strain ANT-03 and BioCeres F WP, BioCeres F GR, and BioCeres D GR, Health Canada's PMRA will consider any comments received from the public in response to this consultation document.³ Health Canada will then publish a Registration Decision⁴ on *B. bassiana* strain ANT-03 and BioCeres F WP, BioCeres F GR, and BioCeres D GR, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and Health Canada's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What is *Beauveria bassiana* strain ANT-03?

Beauveria bassiana strain ANT-03 is a fungus that infects and kills insects. It is the active ingredient in BioCeres products, which are biological insecticides. BioCeres F WP is a commercial class product for use in certain agricultural crops and in turf. BioCeres F GR and BioCeres D GR are commercial and domestic class products, respectively, for use in turf.

Health considerations

Can approved uses of *Beauveria bassiana* strain ANT-03 affect human health?

***Beauveria bassiana* strain ANT-03 is unlikely to affect your health when BioCeres F WP, BioCeres F GR and BioCeres D GR are used according to the label directions.**

Potential exposure to *B. bassiana* strain ANT-03 may occur through the diet (food and water), through applications to turf, through drift resulting from agricultural field applications, or when handling and applying BioCeres F WP, BioCeres F GR and BioCeres D GR. When assessing health risks, several key factors are considered:

- the microorganism's biological properties (for example, infection cycle);
- reports of any adverse incidents;
- its potential to cause disease or toxicity as determined in toxicological studies; and
- the level to which people may be exposed relative to exposures already encountered in nature to other isolates of this microorganism.

³ "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

⁴ "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

The levels used to assess risks are established to protect the most sensitive human population (for example children and nursing mothers). As such, sex and gender are taken into account in the risk assessment. Only uses that are determined as having no health risks of concern are considered acceptable for registration.

Studies in laboratory animals describe potential health effects from large doses of exposure to a microorganism and identify any pathogenicity, infectivity and toxicity concerns. When *B. bassiana* strain ANT-03 was tested on laboratory animals, there was low toxicity following oral, pulmonary and dermal exposures, and no infectivity following oral, pulmonary or intravenous exposures. Furthermore, there was no sign that the microbial pest control agent (MPCA), *B. bassiana* strain ANT-03 caused any disease. However, recent evidence was found that dry fungal spore preparations could be toxic via the inhalation route. In the absence of an inhalation study, dry formulations containing this MPCA were considered to be toxic via the inhalation route. *Beauveria bassiana* strain ANT-03 was also moderately irritating to the eye.

Residues in Water and Food

Dietary risks from food and water are acceptable

Residues of *B. bassiana* strain ANT-03 on various treated agricultural crops are possible at the time of harvest. There are no known metabolites of toxicological significance present in BioCeres F WP, BioCeres F GR and BioCeres D GR. Furthermore, no signs of infectivity or toxicity were observed when *B. bassiana* strain ANT-03 was tested on laboratory animals. In addition, the likelihood of residues of *B. bassiana* strain ANT-03 contaminating drinking water supplies from the proposed applications of BioCeres F WP, BioCeres F GR and BioCeres D GR to various field grown crops and turf is low and therefore not a health concern. Consequently, dietary risks are acceptable for all segments of the population, including infants, children, adults and seniors.

Risks in residential and other non-occupational environments

Estimated risk for non-occupational exposure is acceptable.

BioCeres F WP, BioCeres F GR and BioCeres D GR are proposed for use as biological insecticides on various field grown crops and/or on turf. The product labels will include measures to reduce bystander and residential exposure such as reducing spray drift and preventing access to the treated areas for 4 hours or until sprays have dried or dusts have settled. Domestic users of BioCeres D GR must also wear a long-sleeved shirt, long pants, socks and shoes during application. Residential and non-occupational exposure to BioCeres F WP, BioCeres F GR and BioCeres D GR is therefore expected to be low when the label directions are observed. Consequently, the risk to residents and the general public is acceptable.

Occupational risks from handling BioCeres F WP, BioCeres F GR and BioCeres D GR

Occupational risks are acceptable when BioCeres F WP, BioCeres F GR and BioCeres D GR are used according to label directions, which include protective measures.

Workers handling BioCeres F WP and BioCeres F GR can come into direct contact with *B. bassiana* strain ANT-03 on the skin, in the eyes or by inhalation. To protect workers from exposure to BioCeres F WP and BioCeres F GR, the label will specify that mixers, loaders and applicators must wear waterproof gloves, a long-sleeved shirt, long pants, protective eyewear (goggles), a NIOSH-approved particulate filtering facepiece respirator, socks and shoes.

A restricted-entry interval of 4 hours or until sprays are dried is required for BioCeres F WP, and if re-entry into treated areas is necessary during this restricted-entry interval, workers must wear the above personal protective equipment. Following application of BioCeres F GR, unprotected workers are also prevented from entering treated areas for 4 hours or until dusts have settled. The occupational risks are acceptable when the precautionary statements on the label are observed.

Environmental considerations

What happens when *Beauveria bassiana* strain ANT-03 is introduced into the environment?

Environmental risks are acceptable.

Beauveria bassiana is a common microorganism that is widely distributed in the natural environment. It is an insect pathogen that causes white muscardine disease in insects. When spores of the fungus come into contact with a susceptible host insect, they germinate, enter the body of the insect and grow eventually killing the insect. This species is typically identified as a soil microorganism. However, it can be found on insects and plants. There are also reports of some isolates of *B. bassiana* with the ability to colonize plants without causing disease.

The proposed use expansion of *B. bassiana* strain ANT-03 to include various field agricultural crops and turf is expected to increase environmental exposure to this microorganism. While information suggests that *B. bassiana* strain ANT-03 will survive under field conditions, over time the populations should return to naturally occurring levels. The spores of this species are hydrophobic and are not expected to be readily transferred to groundwater by leaching. However, the species could enter aquatic environments via run-off from treated areas. *Beauveria bassiana* is not expected to grow in aquatic environments.

No overt adverse effects to birds and to an insect species were observed during testing. Acute testing on honey bees with spores of *B. bassiana* strain ANT-03 demonstrated significant toxicity/pathogenicity following contact and dietary exposures. However, no such effects were observed in semi-field trials with BioCeres F WP. No evidence of significant adverse effects on birds, fish, non-arthropod invertebrates and plants were found in the published scientific literature. Also, *B. bassiana* strain ANT-03 was not toxic or pathogenic to laboratory mammals through a variety of exposure routes.

Based on a critical review of studies, scientific rationales and information from public sources, the risks to birds, wild mammals, fish, non-target terrestrial and aquatic arthropods, and plants are acceptable when the BioCeres F WP, BioCeres F GR and BioCeres D GR are applied according to directions on the label. Since studies on beneficial arthropods (including honeybees) demonstrated toxic and/or pathogenic effects, BioCeres F WP, BioCeres F GR and BioCeres D GR labels will include statements identifying the potential harm to beneficial insects and bees and instruct applicators to limit exposure to beneficial insects.

Value considerations

What is the value of BioCeres F WP, BioCeres F GR and BioCeres D GR?

BioCeres F WP is suitable for use in organic production of vegetable crops. All three products are suitable for use on turf in places where use of conventional chemical insecticides is restricted or not desired by the user.

BioCeres F WP reduces numbers of Colorado potato beetle in potato, tomato, bell pepper and eggplant crops and tarnished plant bug in spinach, Chinese cabbage, lettuce, celery, strawberry, raspberry and blackberry crops. Some of these uses have been identified as priorities for organic growers in Canada. All three products reduce numbers of chinch bug and of European chafer and Japanese beetle larvae in turf. These products provide a new mode of action for all of these uses.

Measures to minimize risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the labels of the technical grade active ingredient, *Beauveria bassiana* strain ANT-03, and the end-use products, BioCeres F WP, BioCeres F GR and BioCeres D GR, to address the potential risks identified in this assessment are as follows.

Key risk-reduction measures

Human health

The technical grade active ingredient, *Beauveria bassiana* strain ANT-03, and the end-use products, BioCeres F WP, BioCeres F GR and BioCeres D GR are considered to be toxic via the inhalation route and irritating to the eyes. In addition, all microorganisms, including *B. bassiana* strain ANT-03, contain substances that are potential sensitizers and thus, sensitivity may develop in individuals exposed repeatedly to large quantities of *B. bassiana* strain ANT-03. In turn, commercial workers handling or applying BioCeres F WP and BioCeres F GR must wear waterproof gloves, long-sleeved shirt, long pants, protective eyewear (goggles), a NIOSH-approved particulate filtering facepiece respirator, socks and shoes. Domestic users of BioCeres D GR must wear long-sleeved shirts, long pants, socks and shoes. Also, a restricted-entry

interval of 4 hours or until sprays are dried is required for BioCeres F WP, and if re-entry into treated areas is necessary during this restricted-entry interval, workers must wear waterproof gloves, long-sleeved shirt, long pants, protective eyewear (goggles), a NIOSH-approved particulate filtering facepiece respirator, socks and shoes. Unprotected commercial workers and domestic users applying BioCeres F GR and BioCeres D GR are also prevented from entering treated areas for 4 hours or until dusts have settled.

A standard statement is required on the end-use product labels to minimize the potential for drift to areas of human habitation or areas of human activity such as houses, cottages, schools and recreational areas as well as statements to limit contamination of water supplies through cleaning or waste disposal.

Environment

The end-use product label will include environmental precaution statements that reduce contamination of aquatic systems from the use of BioCeres F WP, BioCeres F GR and BioCeres D GR. The label for the end-use products will also include environmental precaution statements to minimize the risk to beneficial insects and pollinators.

Next steps

Before making a final registration decision on *B. bassiana* strain ANT-03 and BioCeres F WP, BioCeres F GR, and BioCeres D GR, Health Canada's PMRA will consider any comments received from the public in response to this consultation document. Health Canada will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). Health Canada will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed decision and Health Canada's response to these comments.

Other information

When the Health Canada makes its registration decision, it will publish a Registration Decision on *B. bassiana* strain ANT-03 and BioCeres F WP, BioCeres F GR, and BioCeres D GR (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science evaluation

***Beauveria bassiana* strain ANT-03 and BioCeres F WP, BioCeres F GR, and BioCeres D GR**

1.0 The active ingredient, its properties and uses

1.1 Identity of the active ingredient

Active microorganism	<i>Beauveria bassiana</i> strain ANT-03
Function	Insecticide – For the reduction in numbers of Colorado potato beetle and tarnished plant bug on various terrestrial crops as well as chinch bug and larvae of European chafer and Japanese beetle on turf
Binomial name⁵	<i>Beauveria bassiana</i> strain ANT-03
Kingdom	Fungi
Phylum	Ascomycota
Class	Sordariomycetes
Order	Hypocreales
Family	Cordyciptaceae
Genus	<i>Beauveria</i>
Species	<i>bassiana</i>
Strain	ANT-03
Patent Status information	None
Minimum purity of active	Technical grade active ingredient: 1×10^{10} conidia/g End-use Products: BioCeres F WP – 1.0×10^{10} conidia/g BioCeres F GR – 2×10^9 conidia/g BioCeres D GR – 2×10^9 conidia/g
Identity of relevant impurities of toxicological, environmental and/or significance.	The technical grade active ingredient does not contain any impurities or micro contaminants known to be Toxic Substances Management Policy Track 1 substances. The product must meet microbiological contaminants release standards. <i>Beauveria bassiana</i> strains are known to produce toxic secondary metabolites but the technical grade active ingredient is not expected to contain any of these metabolites.

⁵ National Center for Biotechnology Information - Taxonomy Browser
(<https://www.ncbi.nlm.nih.gov/taxonomy>)

1.2 Physical and chemical properties of the active ingredient and end-use product

Technical product—*Beauveria bassiana* strain ANT-03

Property	Result
Physical State	Powder
Colour	Cream White
Odour	Odourless
Specific gravity/bulk density	0.48–0.57 g/cm ³

End-use product—BioCeres F WP

Property	Result
Physical State	Powder
Colour	Cream White
Odour	Odourless
Specific gravity/bulk density	0.473–0.546 g/cm ³
Water Activity (mean±standard deviation)	0.453±0.118

End-use product—BioCeres F GR

Property	Result
Physical State	Granular
Colour	Cream White
Odour	Odourless
Specific gravity/bulk density	0.72–0.76 g/cm ³
Water Activity (mean±standard deviation)	0.453±0.118

End-use product—BioCeres D GR

Property	Result
Physical State	Granular
Colour	Cream White
Odour	Odourless
Specific gravity/bulk density	0.72–0.76 g/cm ³
Water Activity (mean±standard deviation)	0.453±0.118

1.3 Directions for use

BioCeres F WP is a wettable powder formulation that is diluted in water for foliar application to field vegetable and fruit crops and to turf. It is applied at concentrations of 4–8 g product per litre of water in sufficient volume to provide thorough coverage, with spray volumes of 500–1000

L/ha recommended. BioCeres F GR and BioCeres D GR have the same granular formulation and are applied directly to turf at rates of 10–20 g/m². All three products may be applied at intervals of 7 days, or 3–5 days under pest outbreak conditions, with no limit on the number of applications.

1.4 Mode of action

The active ingredient in BioCeres products, *B. bassiana* strain ANT-03, belongs to the Insecticide Resistance Action Committee’s Mode of Action Group UNF (fungal agents of unknown or uncertain mode of action). It is an entomopathogenic fungus, causing a lethal disease in insects. When spores of the fungus come into contact with a host insect, they germinate and the fungus grows into the body of the host, eventually killing it.

2.0 Methods of analysis

2.1 Methods for identification of the microorganisms

Refer to PRD2014-06, *Beauveria bassiana* strain ANT-03.

2.2 Methods for establishment of purity of seed stock

The strain has been deposited into the international depository authority in Illinois USA under the identification number NRRL# 50797. A stock culture of *B. bassiana* strain ANT-03 is maintained in the National Mycological Herbarium (DAOM) of Agriculture and Agri-Food Canada, and the private collection of Anatis Bioprotection Inc.

Acceptable methods for the establishment of the purity, viability and genetic stability of the stocks were described.

2.3 Methods to define the content of the microorganism in the manufactured material used for the production of formulated products

The potency (conidia/g) of the technical grade active ingredient is based on the percentage of viable spores and is determined using hemacytometry.

2.4 Methods to determine and quantify residues (viable or non-viable) of the active microorganism and relevant metabolites

As noted above, acceptable methods are available to enumerate the microorganism and to distinguish this MPCA from other *Beauveria* species.

2.5 Methods for determination of relevant impurities in the manufactured material

The quality assurance procedures used to limit contaminating microorganisms during the manufacture of *Beauveria bassiana* strain ANT-03 (technical grade active ingredient), BioCeres F WP, BioCeres F GR and BioCeres D GR are acceptable. These procedures include sterilization of all equipment and media as well as frequent sampling of the stock culture and production batches for purity and contamination.

The absence of human pathogens were shown in the microbial screening of batches of *Beauveria bassiana* strain ANT-03 (technical grade active ingredient) using standard methods for detecting and enumerating microbial contaminants of concern. All batches of *Beauveria bassiana* strain ANT-03 (technical grade active ingredient) conform to the human pathogen limits set out in the Organization for Economic Co-operation and Development (OECD) issue paper on microbial contaminants for microbial pest control products [ENV/JM/MONO(2011)43].

2.6 Methods to determine storage stability, shelf-life of the microorganism

Storage stability data were provided for BioCeres F WP, BioCeres F GR and BioCeres D GR. Results for BioCeres F WP support a storage period of 18 months if stored in the refrigerator at 4°C, 6 months at 21°C in an unopened package, or 3 months at 21°C in opened packages. Results for BioCeres F GR and BioCeres D GR support a storage period of 16 months at room temperature (20–25°C).

3.0 Impact on human and animal health

3.1 Toxicity and infectivity summary

3.1.1 Testing

A detailed review of an eye irritation study was conducted in support of *Beauveria bassiana* strain ANT-03 (technical grade active ingredient) and the associated end-use products, BioCeres F WP, BioCeres F GR and BioCeres D GR. In this eye irritation study, an aliquot (0.1 mL) of *B. bassiana* strain ANT-03 was instilled into the conjunctival sac of the right eye of three female New Zealand white rabbits. Following treatment, the eyes remained unwashed and the animals were observed for a period of 10 days. Irritation was scored by the method of Draize. All animals gained weight and appeared healthy throughout the study period. There was no iritis observed in any treated eye during this study. After 24 hours, two treated eyes exhibited corneal opacity and all treated eyes exhibited “positive” conjunctivitis. All animals recovered from ocular irritation by Day 10. In this study, *B. bassiana* strain ANT-03 was moderately irritating to the eye based on the noted ocular irritation and the reported time for recovery of 10 days.

No additional studies were required for the technical grade active ingredient since the new source of the technical grade active ingredient at the manufacturing site was considered to be equivalent to the existing source of the technical grade active ingredient. For details on the previously submitted toxicological studies in support of this technical grade active ingredient, see Proposed Registration Decision PRD2014-06, *Beauveria bassiana* strain ANT-03.

No additional end-use product studies were submitted in support of BioCeres F WP, BioCeres F GR and BioCeres D GR. Instead, end-use product testing was addressed through waiver rationales as described below in Section 3.1.2.

Test results are summarized in Appendix I, Table 1.

3.1.2 Additional information

Scientific rationales were submitted to waive all end-use product testing requirements. Rationales to waive acute dermal and dermal irritation testing were supported by the results of a combined acute dermal toxicity and irritation study on a surrogate product, Bioterra, which contains spores of *B. bassiana* strain ANT-03, and a discussion on the toxicological properties of the formulation ingredients. The cited acute dermal toxicity and irritation study was previously reviewed by Health Canada and found to be acceptable (see PRD2014-06 for details). According to this review, the spores of *B. bassiana* strain ANT-03 are of low toxicity and non-irritating to the skin of the rat. Furthermore, no toxicological concerns for any of the formulation ingredients were found in the Material Safety Data Sheets (MSDS) or in toxicological databases such as TOXNET. The untested formulants present in the proposed formulations do not pose any significant concerns with respect to toxicity or irritation. The requests to waive acute dermal toxicity and dermal irritation studies were accepted.

A scientific rationale was also submitted to waive acute inhalation testing of BioCeres D GR. Acute inhalation concerns have recently been identified for conidial spores of certain fungal species, including *B. bassiana* and related taxa due to their hydrophobic nature (Proposed Registration Decision PRD2017-19, *Beauveria bassiana* strain PPRI 5339). When inhaled in dried powder form, severe non-specific toxicological effects, including shortness of breath and mortality, are expected for hydrophobic fungal spores. This acute toxicity is not expected if the same spores are instilled intratracheally in an aqueous suspension. In the scientific rationale, the applicant indicated that the formulation was amended to reduce inhalation exposure following the proposed use of BioCeres D GR. Data were also provided demonstrating the efficacy of the formulation amendments in reducing dusts.

3.1.3 Incident reports related to human and animal health

As of 19 May 2020, no human or domestic animal incident reports involving *B. bassiana* strain ANT-03 had been submitted to the PMRA.

3.1.4 Hazard analysis

The available database in support of *Beauveria bassiana* strain ANT-03 (technical grade active ingredient), BioCeres F WP, BioCeres F GR and BioCeres D GR was reviewed from the viewpoint of human health and safety and was determined to be acceptable.

In a previous review, the technical grade active ingredient, *Beauveria bassiana* strain ANT-03, was found to be of low toxicity by the oral, pulmonary, and dermal routes, and was not pathogenic or infective by the oral, pulmonary or intraperitoneal routes. While the technical grade active ingredient was not considered to be irritating to the skin, it was found to be

minimally irritating to the eyes. Also, the MPCA was considered to be a potential sensitizer. Following the initial registration of *B. bassiana* strain ANT-03, additional information became available to Health Canada regarding the inhalation toxicity of dry fungal spores (PRD2017-19). Health Canada considers this finding to be relevant to all dry formulations containing fungal spores. Since no inhalation data were submitted in support of the technical grade active ingredient, the technical grade active ingredient is considered to be toxic via the inhalation route and as such the hazard statement “DANGER POISON” will be added to the principal display panel of the technical grade active ingredient. In addition, the new eye irritation study indicates that the technical grade active ingredient is moderately irritating to the eyes therefore the hazard statement, “WARNING EYE IRRITANT” will be added to the principal display panel of the technical grade active ingredient label.

Although no studies were provided for any of the end-use products, BioCeres F WP, BioCeres F GR and BioCeres D GR are considered to be of low toxicity by the oral and dermal routes. However, the end-use products are considered to be toxic via the inhalation route. While the formulation amendment to the BioCeres F GR and BioCeres D GR formulations greatly reduced inhalation exposure, it did not reduce the overall potential toxicity of the spores via the inhalation route. Since the spores are significantly diluted in the end-use product formulations, the toxicity category of BioCeres F WP, BioCeres F GR and BioCeres D GR via the inhalation route can be lowered to “WARNING POISON”. Also, the three end-use products are not considered to be irritating to the skin but are moderately irritating to the eyes. As noted for the technical grade active ingredient, the MPCA is considered to be a potential sensitizer. Consequently, the statements “POTENTIAL SENSITIZER”, “WARNING- EYE IRRITANT”, and “WARNING POISON” will be added to the principal display panel.

Notwithstanding the potential for inhalation toxicity, higher tier subchronic and chronic toxicity studies were not required because the technical grade active ingredient was not acutely toxic by the oral, dermal or pulmonary (intratracheal instillation) routes of administration. Furthermore, there were no indications of any infectivity or pathogenicity in any test animals tested with the MPCA at Tier I.

Within the available scientific literature, there are no reports that suggest *B. bassiana* has the potential to cause adverse effects on the endocrine system of animals. Based on the weight of evidence of available data, no adverse effects to the endocrine or immune systems are anticipated for this MPCA.

3.2 Occupational, residential and bystander risk assessment

3.2.1 Occupational and postapplication exposure and risk

When handled according to the label instructions, the potential for dermal, eye and inhalation exposure for applicators, mixer/loaders, and handlers exists, with primary exposure route being dermal. Since unbroken skin is a natural barrier to microbial invasion of the human body, dermal absorption could occur only if the skin were cut, if the microbe were a pathogen equipped with mechanisms for entry through or infection of the skin, or if metabolites were produced that could be dermally absorbed.

Beauveria bassiana has not been identified as a dermal wound pathogen and there is no indication that it could penetrate intact skin of healthy individuals. Furthermore, dermal toxicity studies in animals demonstrated no signs of systemic toxicity to the technical grade active ingredient.

The toxicity testing with the technical grade active ingredient showed no toxicity or infectivity via the oral, dermal, pulmonary, or intraperitoneal routes of exposure. The submitted dermal irritation studies using the MPCA showed no dermal irritation and the formulants contained in BioCeres F GR and BioCeres F WP are not dermal irritants. Since the end-use products are considered moderately irritating to the eyes, precautionary label statements will instruct all applicators to avoid contact of the end-use products with the eyes. Workers applying BioCeres F GR and BioCeres F WP must also wear eye goggles to mitigate occupational exposure concerns.

In addition to irritation concerns, the end-use products are potential sensitizers and are considered toxic via the inhalation route. For handlers of BioCeres F WP and BioCeres F GR, risk mitigation measures, including the wearing of personal protective equipment such as waterproof gloves, long-sleeved shirt, long pants, a NIOSH-approved particulate filtering facepiece respirator, socks and shoes are required to minimize exposure. Also, the formulation of BioCeres F GR has been amended to reduce the potential for inhalation exposure. Unprotected workers are also prohibited from entering treated areas (including turf) where the BioCeres formulations have been applied for 4 hours or until the sprays have dried or the dusts have settled.

Label warnings, restrictions and risk mitigation measures are adequate to protect users of BioCeres F WP, and BioCeres F GR. Overall, occupational risks to workers are acceptable when the precautionary statements on the label are followed, which include personal protective equipment.

3.2.2 Residential and bystander exposure and risk

The use of BioCeres F WP, BioCeres F GR and BioCeres D GR on outdoor field crops and/or on turf may result in bystander and residential exposure. To limit exposure, domestic users of BioCeres D GR must wear a long-sleeved shirt, long pants, socks and shoes during application. Bystander and residential exposure will also be mitigated by the inclusion of a spray drift statement on the label of BioCeres F WP, advising against application to areas of human habitation unless consideration has been given to the wind speed, wind direction, temperature inversions, application equipment, and sprayer settings. Statements on the labels of BioCeres F WP, BioCeres F GR and BioCeres D GR will also prevent unprotected bystanders and residents from entering treated areas where the BioCeres formulations have been applied for 4 hours or until the sprays have dried or the dusts have settled. The end-use products are of low toxicity via the oral and dermal routes and there were no signs that *B. bassiana* strain ANT-03 caused any disease in studies on laboratory animals. While these products are considered toxic via the inhalation route, BioCeres F WP is to be applied as a spray suspension and no inhalation toxicity is anticipated for aqueous suspensions.

Toxicity was only observed following inhalation of dry spores (see Section 3.1.2). Also, the formulations of BioCeres D GR and BioCeres F GR were amended to suppress dust formation. Consequently, the health risks to bystanders and individuals in residential areas are acceptable.

3.3 Dietary exposure and risk assessment

3.3.1 Food

While the proposed use pattern may result in dietary exposure with possible residues in or on agricultural commodities, the risks from consuming food crops treated with BioCeres F WP are acceptable because *B. bassiana* strain ANT-03 demonstrated no toxicity, pathogenicity or infectivity in Tier I acute oral and pulmonary studies. Although there are other strains of *B. bassiana* that are known to produce the secondary metabolites beauvericin, bassianolide, oosporein, bassiacridin, bassianin and tenellin, strain ANT-03 is not known to produce any of these metabolites. After application, *B. bassiana* strain ANT-03 is only expected to grow on susceptible insects. If toxic secondary metabolites are produced by the MPCA in insects, their occurrence in edible food commodities would be negligible due to common hygiene practices and standards that prevent insect parts from being contained in foodstuff. Consequently, there is no health risk for the general population, including infants and children, or animals.

3.3.2 Drinking water

Dietary exposure from drinking water is expected to be low as the label will include mitigative measures to limit contamination of drinking water from the proposed uses of *B. bassiana* strain ANT-03. The end-use product labels will instruct users not to contaminate irrigation or drinking water supplies or aquatic habitats through equipment cleaning or waste disposal. The labels will also limit runoff containing this product from entering lakes, streams, ponds or other waters. In addition, municipal treatment of drinking water is expected to reduce the transfer of residues to drinking water. Furthermore, there were no harmful effects observed in Tier I acute oral and pulmonary studies. Consequently, the risks from residues of *B. bassiana* strain ANT-03 in drinking water are acceptable.

3.3.3 Acute and chronic dietary risks for sensitive subpopulations

Calculations of acute reference doses and acceptable daily intakes are not usually possible for predicting acute and long-term effects of microbial agents in the general population or to potentially sensitive subpopulations, particularly infants and children. The single (maximum hazard) dose approach to testing MPCAs is sufficient for conducting a reasonable general assessment of risk if no significant adverse effects (in other words, no acute toxicity, infectivity or pathogenicity endpoints of concern) are noted in acute toxicity and infectivity tests. Based on all the available information and hazard data, the PMRA concludes that *B. bassiana* strain ANT-03 is of low oral toxicity, is not pathogenic or infective to mammals, and that infants and children are likely to be no more sensitive to the MPCAs than the general population. Thus, there are no threshold effects of concern and, as a result, there is no need to require definitive (multiple dose) testing or apply uncertainty factors to account for intra and interspecies variability, safety factors or margins of exposure. Further factoring of consumption patterns among infants and

children, special susceptibility in these subpopulations to the effects of the MPCA, including neurological effects from pre- or post-natal exposures, and cumulative effects on infants and children of the MPCA and other registered microorganisms that have a common mechanism of toxicity, does not apply to this MPCA. As a result, the PMRA has not used a margin of exposure (safety) approach to assess the risks of *B. bassiana* strain ANT-03 to human health.

3.3.4 Aggregate exposure and risk

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation).

In an aggregate risk assessment, the combined potential risk associated with food, drinking water and various residential exposure pathways is assessed. A major consideration is the likelihood of co-occurrence of exposures. Additionally, only exposures from routes that share common toxicological endpoints can be aggregated.

BioCeres F WP, BioCeres F GR, and BioCeres D GR are considered to be of low toxicity by the oral and dermal routes and end-use products will not be applied near or to drinking water. Label statements have been added to minimize non-occupational exposure (inhalation) in residential and commercial areas to the general Canadian population, including infants and children. When the end-use products are used as labelled, there is reasonable certainty that no harm will result from aggregate exposure of residues of *B. bassiana* strain ANT-03.

3.3.5 Maximum residue limits

As part of the assessment process prior to the registration of a pesticide, Health Canada must determine whether the consumption of the maximum amount of residues, that are expected to remain on food products when a pesticide is used according to label directions, will not be a concern to human health. This maximum amount of residues expected is then legally specified as a maximum residue limit (MRL) under the *Pest Control Products Act* for the purposes of the adulteration provision of the *Food and Drugs Act*. Health Canada specifies science-based MRLs to ensure the food Canadians eat is safe.

Residues of *B. bassiana* strain ANT-03 on treated food crops are possible at the time of harvest. Dietary risk to humans from the proposed use of BioCeres F WP is acceptable due to the low acute oral toxicity of *B. bassiana* strain ANT-03 and that metabolites of toxicological significance are not known to be produced by this MPCA. In addition, the likelihood of residues contaminating drinking water supplies is low. Therefore, the PMRA has determined that specification of an MRL under the *Pest Control Products Act* is not required for *B. bassiana* strain ANT-03.

3.4 Cumulative assessment

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with a common mechanism of toxicity. In its assessment of common mechanism of toxicity, the PMRA considers both the taxonomy of MPCAs and the production of any

potentially toxic metabolites. For the current evaluation, the PMRA has determined that *B. bassiana* strain ANT-03 shares a common mechanism of toxicity with the MPCAs; *B. bassiana* strain HF23, *B. bassiana* strain GHA, and *B. bassiana* strain PPRI 5339. The potential health risks from cumulative exposure of *B. bassiana* strain ANT-03 and these other MPCAs are acceptable when used as labelled given their low toxicity and pathogenicity.

4.0 Impact on the environment

4.1 Fate and behaviour in the environment

No new environmental fate data were submitted in support of the new end-use products and the proposed use expansion of *B. bassiana* strain ANT-03; however, environmental fate data (Tier II/III) are not normally required at Tier I, and are only triggered if significant toxicological effects in non-target organisms are noted in Tier I testing.

According to published information, *B. bassiana* is a generalist entomopathogen that causes white muscardine disease in insects of various orders. When spores of the fungus come into contact with an insect host, they germinate, enter the body of the insect and grow hyphae, eventually killing the insect. Although the fungus is a generalist, individual strains may be specific to select species. Isolates of this species can be naturally found on all continents with the exception of Antarctica. In Canada, isolates of this species can be found in all provinces. While this species is typically identified as a soil microorganism, conidia of *B. bassiana* can also be naturally found on insects and plants. There are also reports of some isolates of *B. bassiana* that demonstrate the ability to colonize plants endophytically.

In the environment, *B. bassiana* typically grows at temperatures of 20–30°C but some variability has been observed in isolates. On solid media, strain ANT-03 could grow at 25–30°C whereas growth at 33°C was poor. *Beauveria bassiana* is also sensitive to ultra violet (UV) radiation.

While the proposed use expansion of *B. bassiana* strain ANT-03 to include various field agricultural crops and turf is expected to increase environmental exposures to this microorganism, the organism is expected to behave as it would in nature, in other words, survive in environments with suitable conditions. As a ubiquitous soil microorganism, it is likely that *B. bassiana* would settle in the soil. Large scale applications of *B. bassiana*, however, could also temporarily increase levels of this microorganism in other habitats with suitable environmental conditions away from UV light. Evidence in soil suggests that *B. bassiana* strain ANT-03 could survive under field conditions, but that over time the populations of *B. bassiana* strain ANT-03 should return to naturally occurring levels. While the end-use products are not intended to be applied directly to water, field applications from the commercial use of BioCeres F WP could also cause some surface water exposure. Aquatic exposure, however, will be limited by label instructions that limit drift and run-off. Furthermore, *B. bassiana* is not considered an aquatic species and the spores of this microorganism are hydrophobic and thus unlikely to suspend in aquatic environments. In addition, the spores of this species are not likely to percolate through soil or transfer significantly to water bodies unless soil erosion has occurred.

4.2 Effects on non-target species

The PMRA has a four-tiered approach to environmental testing of microbial pesticides. Tier I studies consist of acute studies on up to seven broad taxonomic groups of non-target organisms exposed to a maximum hazard or Maximum Challenge Concentration of the MPCA. The Maximum Challenge Concentration is generally derived from the amount of the MPCA, or its toxin, expected to be available following application at the maximum recommended label rate multiplied by a safety factor. Tier II studies consist of environmental fate (persistence and dispersal) studies as well as additional acute toxicity testing of MPCAs. Tier III studies consist of chronic toxicity studies (life cycle studies), as well as definitive toxicity testing (for example, LC₅₀, LD₅₀). Tier IV studies consist of experimental field studies on toxicity and fate, and are required to determine whether adverse effects are realized under actual use conditions.

The type of environmental risk assessment conducted on MPCAs varies depending on the tier level that was triggered during testing. For many MPCAs, Tier I studies are sufficient to conduct environmental risk assessments. Tier I studies are designed to represent “worst-case” scenarios where the exposure conditions greatly exceed the expected environmental concentrations. The absence of adverse effects in Tier I studies are interpreted as minimal risk to the group of non-target organisms. However, higher tiered studies will be triggered if significant adverse effects on non-target organisms are identified in Tier I studies. These studies provide additional information that allows PMRA to refine the environmental risk assessments. In the absence of adequate environmental fate and/or field studies, a screening level risk assessment can be performed to determine if the MPCA is likely to pose a risk to a group of non-target organisms.

The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum application rate) and sensitive toxicity endpoints. A risk quotient is calculated by dividing the exposure estimate by an appropriate toxicity value (risk quotient = exposure/toxicity), and the risk quotient is then compared to the level of concern (level of concern = 1 for most species, 0.4 for acute risk to pollinators, and 2 for glass plate studies using the standard beneficial arthropod test species, *Typhlodromus pyri* and *Aphidius rhopalosiphi*; level of concern = 1 is used for higher tier tests of the standard arthropod test species and for other arthropod test species).

If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (environmental fate and/or field testing results). Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Effects on terrestrial organisms

Two honey bee studies were submitted to support the current submission to register new end-use products and to extend the use of *B. bassiana* strain ANT-03 to include various field crops and turf. Scientific rationales were also submitted in support of requests to waive further testing on remaining groups of non-target organisms. Data submitted under human and animal health toxicity testing were considered to assess the risk of harm to wild mammals. For details on the previously submitted environmental studies in support of this technical grade active ingredient, see PRD2014-06.

In one acute honey bee study, young bees (900) aged 1–4 days were transferred to experimental cages where they were kept at 29°C or 33°C in the dark for the entire experimental period. After a period of acclimation, the bees were exposed to the spores of *B. bassiana* strain ANT-03 by topical and/or oral exposure. For the topical treatments, the bees were exposed to different doses of the spores for 5 consecutive days and then the treated bees were observed for 16 days. For the oral treatments, the bees were fed for a period of 1, 7 or 21 consecutive days with a 50% sucrose solution containing different doses of the spores and then observed for a total period of 30 days. Dead bees were counted and removed from the cages each day. Bees exposed to the spores of *B. bassiana* ANT-03 by the topical route died significantly faster than bees exposed to the control solution at both temperatures. At 33°C, the median survival time of bees exposed to spores of *B. bassiana* strain ANT-03 at a dose equivalent to 1×(0.8 g/L) was 12 days compared to 8 days when the bees were maintained at 29°C. Bees exposed to the spores of *B. bassiana* ANT-03 by the dietary route also died significantly faster than bees exposed to the control solution at both temperatures. At 33°C, the observed median survival time of bees exposed to *B. bassiana* in the diet was 9 days compared to 8 days when the bees were maintained at 29°C.

In the second honey bee study, the effects of BioCeres F WP (1.2×10^{10} conidia/g) were assessed in a field trial based on OECD's Guidance Document on the Honey Bee (*Apis mellifera* L.) Brood Test Under Semi-Field Conditions (Series on Testing and Assessment Number 75, ENV/JM/MONO(2007)22). In this study, twelve test tunnels were constructed over red and white clover, and a hive was placed in each tunnel. Each tunnel was treated with either water or BioCeres WP by spraying onto the clover crops (6 tunnels per treatment). The treatments were applied as recommended on BioCeres WP label, in other words, 6 g/L in 200–400 L water when honey bees were not active after sunset. Two treatment periods were made, each consisting of 3 applications. Following the treatment periods in the tunnels, the hives were placed outside their respective tunnel and were free to forage in the field. After the final assessment in November 2018, the hives were wintered in a heated and ventilated indoor wintering facility. In April 2019, hives were removed from hibernation for final evaluations. Few statistical differences were found between treatments for all recorded data; primarily in behavioural observations. Foraging behaviour and flight activity was significantly reduced in tunnels treated with BioCeres F WP. This finding was attributed to a lower density of open flowers in BioCeres F WP-treated tunnels and a punctual bias resulting from a short observation interval. No statistically significant effect on mortality compared to control was observed during treatment periods, after treatment periods and after overwintering.

Also, collected specimens from the BioCeres F WP-treated tunnels during treatments did not show the presence of *B. bassiana* following incubation in a moist chamber at 27°C over 6 days. Overall, the BioCeres F WP treatments had no obvious effects on behaviour, mortality or overwintering of honey bees under the conditions of this study.

No new studies were provided to address the hazards of this MPCA to birds, other terrestrial arthropods, and terrestrial plants. Instead, the applicant provided scientific rationales based on the biological properties of *B. bassiana* and the results of previously reviewed studies as summarized in PRD2014-06.

In addition to the above information, no reports of adverse effects to birds, non-arthropod invertebrates or plants were found in the [PubMed database](#). Also, no adverse effects were identified in any of the supplementary information provided by the applicant on other strains of *B. bassiana*. Adverse effects to various terrestrial arthropods are described in published scientific literature. These findings were expected since the MPCA is an entomopathogen.

In mammalian studies conducted to satisfy the human health and safety requirements, it was determined that the three end-use products are of low toxicity by the oral and pulmonary routes and *B. bassiana* strain ANT-03 was not pathogenic by the oral, pulmonary, or intravenous routes (for details, see PRD2014-06). While the three end-use products are considered toxic via the inhalation route, toxicity is only anticipated following inhalation of dry spores and limited exposure to dry spores is expected by this route. The formulations of BioCeres F GR and BioCeres D GR were amended to significantly reduce dusts. Also, BioCeres F WP is applied as an aqueous suspension.

Based on all the available information, no harm to birds, wild mammals, non-arthropod invertebrates, and terrestrial plants is anticipated. However, the proposed use expansion could potentially harm non-target terrestrial arthropods. Label instructions will be added to the end-use product labels to alert users to this risk and to reduce adverse effects to terrestrial non-target arthropods. Overall, the risks to birds, terrestrial arthropods, non-arthropod invertebrates and terrestrial plants are acceptable and the formulants are not expected to contribute to the potential toxicity of the BioCeres F WP, BioCeres F GR and BioCeres D GR.

Test results are summarized in Appendix I, Table 2.

4.2.2 Effects on aquatic organisms

No new studies were submitted to evaluate the risk to non-target aquatic organisms resulting from the proposed use expansion to outdoor applications. Instead, scientific rationales were provided to waive testing on freshwater fish, aquatic arthropods and aquatic plants. These scientific rationales were based on the biological properties of the MPCA as well as results of previously reviewed study reports on daphnids (*Daphnia magna*). For a review of previously submitted studies, see PRD2014-06.

As noted under Section 4.1, *B. bassiana* is not considered to be an aquatic species and is not considered to be a pathogen of fish. Searches in [PubMed](#) using the keywords “Beauveria bassiana AND fish” and “Beauveria bassiana AND aquatic arthropod” found two reports of adverse effects to developing inland silverside fish (*Menidia beryllina*), one report describing the use of *B. bassiana* to control the larval stages of *Anopheles gambiae* and *Anopheles stephensi* in laboratory assays and two reports of adverse effects to *Chironomus xanthus*.

In the two published fish studies, embryo rupture and death were observed after exposure to *B. bassiana* strain UF1 5789 and *B. bassiana* strain GH. Surviving larvae hatched from embryos treated with strain GH also displayed developmental defects (in other words, vertebral abnormalities). In both reports, there was substantial variability in the observed effects, in other words, many embryos that exhibited advanced hyphal growth did not rupture, and ruptured embryos often completed development and successfully hatched. Also, these effects did not always correlate with concentration. In both of these studies, the study authors postulated that the hydrophobicity of the spores allowed them to attach to the chorion and germinate. Since the studies were conducted under nutrient-free conditions, the study authors speculated that the spores may have utilized carbon sources associated with or excreted from the embryo. According to the author, this nutrient limitation may be one reason why spore concentrations greater than or equal to 9.6×10^6 failed to cause any effects. If too many spores were competing for the limiting nutrients, spore germination may have been inhibited. Another possibility why spore concentrations greater than or equal to 9.6×10^6 failed to cause any effects may be the presence of germination inhibitors that reach effective levels when high concentrations of spores are present. The authors believe that the proteinaceous nature of the chorion probably rendered the inland silverside embryo susceptible to digestion by the extracellular enzymes of *B. bassiana*. Since heat-killed spores did not cause any adverse effects, the authors concluded that germination and penetration were responsible for rupture of the chorion and the increased incidence of embryo death. The study authors suspected that, even if the fungus was effectively inhibited by the defense mechanisms of the embryo (in other words, not infectious), the penetration of the chorion by hyphae was sufficient to cause a rupture. The developmental effects noted for strain GH are not understood. The study authors did suspect that these effects were caused by toxins. In a separate study, strain GH was found to produce beauvericin in vitro. Strain ANT-03 does not produce this toxin or any other toxin.

Published scientific literature is available on the use of *B. bassiana* to control the larval stages of *A. gambiae* and *A. stephensi*. While the finding that *B. bassiana* can infect larvae is expected, the finding that *B. bassiana* could infect aquatic larvae was unexpected since this microorganism is not considered to be an aquatic species. Such infections, in the PMRA’s opinion, are likely limited in that it is unknown if this species can sporulate under aquatic conditions and, even if sporulation occurs, the spread is expected to be very limited since the spores of this microorganism are very hydrophobic and would not disperse in aquatic environments. Without the addition of surfactants, the spores would simply clump together thus greatly reducing its ability to infect other hosts.

In two reports detailing adverse effects to *C. xanthus*, mortality, impaired larval growth and delayed larval emergence were reported for *B. bassiana*. These reports involved commercial formulations which likely contained formulation ingredients which could be responsible for the observed effects. Additional information would be required for fully characterize the reported effects.

In addition to the above reported effects, BioCeres F GR and BioCeres D GR contain a formulation ingredient that could be toxic to aquatic organisms.

While direct applications to aquatic environments could harm aquatic arthropods and to some extent fish, the proposed use expansions of *B. bassiana* strain ANT-03 as a biological insecticide is not expected to harm freshwater fish, aquatic arthropods since standard PMRA label statements prohibit the contamination of aquatic systems. A “run-off” statement will also be added to the end-use product labels to further reduce aquatic exposure. These label statements should significantly reduce aquatic exposure and thus mitigate any potential effects to aquatic organisms. Consequently, the environmental risks to fish, aquatic arthropods, aquatic non-arthropod invertebrates and aquatic plants are acceptable.

4.3 Incident reports related to the environment

As of 19 May 2020, no environmental incident reports involving *B. bassiana* strain ANT-03 had been submitted to the PMRA.

5.0 Value

A total of 17 field trials, including three for Colorado potato beetle, seven for tarnished plant bug, three for chinch bug, three for European chafer and one for Japanese beetle all conducted in Quebec and Ontario between 2000 and 2015, yielded variable results. However, the majority of trials provided sufficient evidence of efficacy to support the proposed claim of reducing numbers of Colorado potato beetle in potato, tomato, bell pepper and eggplant crops, tarnished plant bug in spinach, Chinese cabbage, lettuce, celery, strawberry, raspberry and blackberry crops, and chinch bug and larvae of European chafer and Japanese beetle in turf.

These products provide a new mode of action for use against all of the listed pests, including a few uses with few or no registered alternatives (tarnished plant bug on Chinese cabbage, raspberry and blackberry), and may aid in management of resistance to the registered alternative pest control products. These products are suitable for use in organic production and may help to address some identified priorities for organic growers (Colorado potato beetle on potato and tarnished plant bug on various outdoor food crops, including spinach, lettuce, celery and strawberry) and also suitable for use on turf where cosmetic use of conventional chemical pest control products is restricted or not desired by the user.

6.0 Pest control product policy considerations

6.1 Toxic substances management policy considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances, in other words, those that meet all four criteria outlined in the policy: persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*. The *Pest Control Products Act* requires that the TSMP be given effect in evaluating the risks of a product.

During the review process, *Beauveria bassiana* strain ANT-03 (technical grade active ingredient), BioCeres F WP, BioCeres F GR and BioCeres D GR were assessed in accordance with the PMRA Regulatory Directive DIR99-03⁶ and evaluated against the Track 1 criteria. The PMRA has reached the conclusion that *Beauveria bassiana* strain ANT-03 (technical grade active ingredient), BioCeres F WP, BioCeres F GR and BioCeres D GR do not meet the Track 1 criteria because the active ingredients are biological organisms and hence are not subject to the criteria used to define persistence, bioaccumulation and toxicity properties of chemical control products.

6.2 Formulants and contaminants of health or environmental concern

During the review process, contaminants in the technical as well as formulants and contaminants in the end-use products are compared against Parts 1 and 3 of the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.⁷ The list is used as described in the PMRA Notice of Intent NOI2005-01⁸ and is based on existing policies and regulations, including the *Toxic Substances Management Policy*⁶ and *Formulants Policy*,⁹ and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

⁶ DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

⁷ SI/2005-114, last amended on June 25, 2008. See Justice Laws website, Consolidated Regulations, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

⁸ PMRA's Notice of Intent NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* under the New Pest Control Products Act.

⁹ DIR2006-02, *Formulants Policy and Implementation Guidance Document*.

- Technical grade *Beauveria bassiana* strain ANT-03, BioCeres F GR and BioCeres D GR do not contain any formulants or contaminants identified in the *List of Pest Control Product Formulants of Health or Environmental Concern*. The end-use product, BioCeres F WP, contains the allergen, soy, which is on the *List of Pest Control Product Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions*.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006–02.

7.0 Proposed regulatory decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act*, is proposing registration for the sale and use of *Beauveria bassiana* strain ANT-03, BioCeres F WP, BioCeres F GR, and BioCeres D GR, containing the technical grade active ingredient *Beauveria bassiana* strain ANT-03, for reduction in numbers of Colorado potato beetle on potato, tomato, bell pepper, and eggplant; tarnished plant bug on spinach, Chinese cabbage, lettuce, celery, strawberry, raspberry, and blackberry; as well as chinch bug and European chafer and Japanese beetle larvae in turf.

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products are acceptable.

List of abbreviations

°C	degree(s) Celsius
µg	micrograms
1/n	exponent for the Freundlich isotherm
a.i.	active ingredient
cm	Centimetres
g	Gram
ha	hectare(s)
L	Litre
LC ₅₀	lethal concentration 50%
LD ₅₀	lethal dose 50%
m ²	square metre
MAS	maximum average score
MIS	maximum irritation score
mL	Millilitre
mL	Milliliter
MPCA	microbial pest control agent
MRL	maximum residue limit
OECD	Organization for Economic Co-operation and Development
PMRA	Pest Management Regulatory Agency
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet

Appendix I Tables and figures

Table 1 Toxicity profile of *Beauveria bassiana* strain ANT-03 (technical grade active ingredient)

Study Type/Animal/PMRA#	Study Results
Eye irritation New Zealand white, female PMRA# 2619213	MIS ^a = 16.7/110 (at 24 h), MAS ^b = 9.6/110 Irritation cleared by Day 10. Moderately irritating to the eyes (MIS, 24 h = 16.7/110, MAS = 9.6/110)

^a MIS = Maximum Irritation Score (average)

^b MAS = Maximum Average Score for 24, 48, and 72 h

Table 2 Toxicity/pathogenicity of *Beauveria bassiana* strain ANT-03 to non-target species

Organism	Exposure	Significant Effect, Comments
Terrestrial Organisms		
Invertebrates		
Arthropods		
Honeybee (<i>Apis mellifera</i>), 1–4 days-old PMRA# 2686528	Spores of <i>Beauveria bassiana</i> strain ANT-03 Dietary exposure – 0.8, 1.6, 2.32, 4, 8 and 23.2 g/L in 50% sucrose/water solution Bees were fed over 1, 7 or 21 days Topical exposure – 0.8, 1.6, and 8 g/L over 5 days	By the dietary route, the median survival time of bees exposed to <i>B. bassiana</i> strain ANT-03 in the diet at 33°C was 9 days compared to 8 days when the bees were maintained at 29°C. By the topical route, the median survival time of bees exposed to live spores of <i>B. bassiana</i> strain ANT-03 at 33°C at a dose equivalent to 1× (0.8 g/L) was 12 days compared to 8 days when the bees were maintained at 29°C. TOXIC and/or PATHOGENIC under the conditions of the study
Honeybee (<i>Apis mellifera</i>) PMRA# 3020348	BioCeres F WP Semi Field Study - 6 g/L in 200–400 L/ha applied to red and white clover	Few statistical differences were found between treatments for all recorded data; foraging behaviour and flight activity were reduced. No statistically significant effect on mortality compared to control was observed during treatment periods, after treatment periods and after overwintering.

Organism	Exposure	Significant Effect, Comments
	Two treatment periods: 21 June 2018 to 1 July 2018 and 13 August 2018 to 23 August 2018; 3 treatments per period.	Collected specimens from the BioCeres F WP-treated tunnels during treatments did not show the presence of <i>B. bassiana</i> following incubation in a moist chamber at 27°C over 6 days. LOW TOXICITY under the conditions of the study.

References

A. List of Studies/Information Submitted by Registrant

1.0 Product Characterization and Analysis

PMRA

Document

Number	Reference
3017938	2019, manufacturing methods and quality assurance, DACO: M2.8 CBI
3017939	2018, manufacturing process and quality control <i>B. bassiana</i> ant-03, DACO: M2.8 CBI
3017940	2019, potency estimation and product guarantee, DACO: M2.9.2 CBI
3017941	2018, conidia concentration of <i>Beauveria bassiana</i> , DACO: M2.9.2 CBI
3017942	2018, germination assessment of <i>B. bassiana</i> conidia, DACO: M2.9.2 CBI
3017943	2019, analysis of microbial contaminant, DACO: M2.10.2
3017944	2018, total bacterial, yeasts and molds count, DACO: M2.10.2 CBI
3020198	2019, name and addresses, DACO: M2.1
3020199	2019, origin, derivation and identification of the TGAI, DACO: M2.7.1
3020200	2018, recovery of <i>B. bassiana</i> ant-03 from infected insect, DACO: M2.7.1 CBI
3020201	2018, fungal culture collection, DACO: M2.7.1 CBI
3020202	2017, identification of <i>B. bassiana</i> ant-03, DACO: M2.7.1 CBI
3020203	2019, biological properties of the MPCA, DACO: M2.7.2
3020204	2011, phylogeny and systematics of the genus <i>Beauveria</i> , DACO: M2.7.2
3020205	2007, review on safety of <i>B. bassiana</i> and <i>B. gronghiartii</i> , DACO: M2.7.2
3020206	2014, enzymes of entomopathogenic fungi, DACO: M2.7.2
3020207	2013, pathogenicity induced by <i>B. bassiana</i> and <i>M. anisopliae</i> , DACO: M2.7.2
3020208	2004, density-dependence and host competition in a parasite of ants, DACO: M2.7.2
3020209	2008, host specificity in <i>B. bassiana</i> , DACO: M2.7.2
3020210	2001, lutte biologique en serre: utilisation du <i>B. bassiana</i> et de la coccinelle maculée, DACO: M2.7.2
3020211	2001, <i>B. bassiana</i> et <i>bacillus</i> contre les ravageurs du celeri et de la laitue, DACO: M2.7.2
3020212	2010, insect-toxic proteins and virulence of the <i>B. bassiana</i> , DACO: M2.7.2
3020213	2013, analysis of beauvericin in <i>B. bassiana</i> ant-03, DACO: M2.7.2 CBI
3020214	1994, heterogeneity of <i>B. bassiana</i> strains, DACO: M2.7.2
3020215	1997, effect of temperature on growth of <i>B. bassiana</i> , DACO: M2.7.2
3020216	1995, influence of ultraviolet light on persistence of <i>B. bassiana</i> , DACO: M2.7.2
3020217	2001, influence of ultraviolet light on pathogenicity of <i>B. bassiana</i> , DACO: M2.7.2
3020218	2009, influence of fungicides on the germination, growth and virulence of entomopathogenic fungi, DACO: M2.7.2
3020220	2019, anatis strain registration, DACO: M2.7.2
3020221	2006, <i>B. bassiana</i> a biocontrol agent, DACO: M2.7.2
3020222	2002, human deep tissue infection with <i>Beauveria</i> species, DACO: M2.7.2
3020223	1985, <i>B. bassiana</i> keratitis, DACO: M2.7.2

3020224	2013, in vitro and in vivo induction of beauvericin isolated from <i>B. bassiana</i> , DACO: M2.7.2
3020225	2011, cytotoxic activity of fungal metabolites from <i>B. bassiana</i> , DACO: M2.7.2
3020226	2019, DNA alignment of <i>B. bassiana</i> ant-03, DACO: M2.7.2 CBI
3020227	2019, manufacturing process for bioceres GR, DACO: M2.8 CBI
3020228	2018, manufacturing process for conidiospores of <i>B. bassiana</i> ant-03, DACO: M2.8 CBI
3020229	2019, manufacturing process for BioCeres GR, DACO: M2.8 CBI
3020230	2019, product specifications, DACO: M2.9.1 CBI
3020231	2019, potency estimation and product guarantee, DACO: M2.9.2 CBI
3020232	2018, conidia concentration of <i>B. bassiana</i> , DACO: M2.9.2 CBI
3020233	2018, germination assessment of <i>Beauveria</i> conidia, DACO: M2.9.2 CBI
3020234	2019, analysis for microbial contaminant, DACO: M2.10.2 CBI
3020235	2018, total bacterial, yeasts and molds count, DACO: M2.10.2 CBI
3020236	2019, storage stability testing, DACO: M2.11 CBI
3020237	2019, summary of physical and chemical properties, DACO: M2.12 CBI
3020291	2019, name and addresses, DACO: M2.0
3020292	2019, origin, derivation and identification of the TGAI, DACO: M2.7.1
3020293	2018, recovery of <i>B. bassiana</i> ant-03 strain from infected insects, DACO: M2.7.1 CBI
3020294	2018, fungal culture collection, DACO: M2.7.1 CBI
3020295	2017, identification of <i>B. bassiana</i> , DACO: M2.7.1 CBI
3020296	2019, biological properties of the MPCA, DACO: M2.7.2
3020297	2011, phylogeny and systematic of genus <i>Beauveria</i> , DACO: M2.7.2
3020298	2007, review on safety <i>B. bassiana</i> and <i>B. bronghiartii</i> , DACO: M2.7.2
3020299	2014, enzymes of entomopathogenic fungi, DACO: M2.7.2
3020300	2013, pathogenicity induced by <i>B. bassiana</i> and <i>M. anisopliae</i> , DACO: M2.7.2
3020301	2004, density-dependence and host competition in parasite of ants, DACO: M2.7.2
3020302	2008, host specificity of <i>B. bassiana</i> , DACO: M2.7.2
3020303	2001, lutte biologique en serre: utilisation de <i>B. bassiana</i> et de la coccinelle maculée, DACO: M2.7.2
3020304	2001, <i>Beauveria bassiana</i> et <i>Bacillus</i> contre les ravageurs du celeri et de la laitue, DACO: M2.7.2

2.0 Human And Animal Health

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Document

Number	Reference
2619213	2015, Anatis Bioprotection Inc., <i>Beauveria bassiana</i> strain ANT-03: Primary Eye Irritation in Rabbits, DACO: M4.5
3020238	2019, acute dermal toxicity, DACO: M4.4
3020239	2019, dermal irritation study, DACO: M4.5.2
3020324	2019, acute dermal toxicity, DACO: M4.4

3020325	2019, dermal irritation study, DACO: M4.5.2
3024571	2019, acute toxicity by inhalation, DACO: M4.9
3024572	2019, manufacturing process for bioceres GR, DACO: M4.9

3.0 Environment

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Document

Number	Reference
2686528	2016, DACO M9.5.1-100 Etude de pathogenicite/toxicite chez l'abeille, DACO: M9.5.1
3020240	2019, environmental toxicity summary, DACO: M9.1
3020241	2019, avian oral toxicity, DACO: M9.2.1
3020242	2011, acute oral toxicity, DACO: M9.2.1
3020243	2015, antimicrobial activity of some honey against bacteria, DACO: M9.2.1
3020244	2007, scalling of body temperature in mammals birds, DACO: M9.2.1
3020245	2000, <i>Beauveria bassiana</i> strain GHA, DACO: M9.2.1
3020246	2000, <i>Beauveria bassiana</i> atcc 74040, DACO: M9.2.1
3020247	2006, <i>Beauveria bassiana</i> HF23, DACO: M9.2.1
3020248	2008, <i>Beauveria bassiana</i> HF23, DACO: M9.2.1
3020249	2019, freshwater fish, DACO: M9.4.1
3020250	2014, current ecological understanding of fungal-like pathogens of fish, DACO: M9.4.1
3020251	2012, working document to the environmental safety of microbial control agents, DACO: M9.4.1
3020252	2007, ecology of <i>B. bassiana</i> and <i>M. anisopliae</i> , DACO: M9.4.1
3020253	2005, adhesion of the fungus <i>B. bassiana</i> , DACO: M9.4.1
3020254	2016, density dynamics of <i>B. bassiana</i> , DACO: M9.4.1
3020255	1994, functions for fish mucus, DACO: M9.4.1
3020256	1992, effects of <i>B. bassiana</i> of the inland silverside, DACO: M9.4.1
3020257	2011, rainbow trout, DACO: M9.4.1
3020258	2001, assessment of techniques for rainbow trout, DACO: M9.4.1
3020259	2019, terrestrial arthropods-green lacewings, DACO: M9.5.1
3020260	2011, acute oral toxicity green lacewing, DACO: M9.5.1
3020261	2017, comments to the draft protocol, DACO: M9.5.1
3020262	2019, semi-field trials of BioCeres WP on the honeybees, DACO: M9.5.1
3020263	2019, aquatic arthropods, DACO: M9.5.2
3020264	2011, <i>Daphnia magna</i> , DACO: M9.5.2
3020265	2019, terrestrial plants, DACO: M9.8.1
3020266	2015, <i>Beauveria bassiana</i> ant-03, DACO: M9.8.1
3020267	2019, aquatic plants, DACO: M9.8.2
3020326	2019, avian oral toxicity, DACO: M9.2.1
3020327	2011, acute oral toxicity bobwhite quail, DACO: M9.2.1
3020328	2015, antimicrobial activity of some honey against bacteria, DACO: M9.2.1
3020329	2007, scalling of body temperature in mammals birds, DACO: M9.2.1
3020330	2000, <i>Beauveria bassiana</i> GHA, DACO: M9.2.1
3020331	2000, <i>Beauveria bassiana</i> atcc 74040, DACO: M9.2.1

- 3020332 2006, *Beauveria bassiana* HF23, DACO: M9.2.1
- 3020333 2008, *Beauveria bassiana*, DACO: M9.2.1
- 3020334 2019, freshwater fish, DACO: M9.4.1
- 3020335 2014, current ecological understanding of fungal-like pathogens of fish, DACO: M9.4.1
- 3020336 2012, working document to the environmental safety of microbial biocontrol agents, DACO: M9.4.1
- 3020337 2007, ecology of *B. bassiana* and *M. anisopliae*, DACO: M9.4.1
- 3020338 2005, adhesion of the fungus *B. bassiana*, DACO: M9.4.1
- 3020339 2006, density dynamics of *B. bassiana*, DACO: M9.4.1
- 3020340 1992, effects of *B. bassiana* on the inland silverside fish, DACO: M9.4.1
- 3020341 1994, functions for fish mucus, DACO: M9.4.1
- 3020342 2011, rainbow trout, DACO: M9.4.1
- 3020343 2001, assessment techniques for rainbow trout, DACO: M9.4.1
- 3020344 2019, terrestrial arthropods-green lacewings, DACO: M9.5.1
- 3020346 2011, acute oral toxicity green lacewing, DACO: M9.5.1
- 3020347 2017, comments to the draft protocol, DACO: M9.5.1
- 3020348 2019, semi-field trials of BioCeres WP on the honeybees, DACO: M9.5.1
- 3020349 2019, aquatic arthropods, DACO: M9.5.2
- 3020350 2011, *Daphnia magna*, DACO: M9.5.2
- 3020351 2019, terrestrial plants, DACO: M9.8.1
- 3020352 2015, *Beauveria bassiana* ant-03, DACO: M9.8.1
- 3020353 2019, aquatic plants, DACO: M9.8.2
- 3024570 2019, name and address of applicant, DACO: M2.1
- 3024571 2019, acute toxicity by inhalation, DACO: M4.9
- 3024572 2019, manufacturing process for bioceres GR, DACO: M4.9
- 3124829 2020, answer M9.2.1, DACO: M9.2.1
- 3124830 2020, answer M9.5.1, DACO: M9.5.1

4.0 Value

- 3020271 2019, Field Studies (summary), DACO: M10.2.2
- 3020273 2012, Efficacy of Bioceres WP against the Chinch bug on turfgrass, DACO: M10.2.2
- 3020274 2014, Field Assessment of *Beauveria bassiana* (BioCeres) for Chinch Bug Control in Lawn Turf, DACO: M10.2.2
- 3020275 2013, Efficacy of Bioceres WP and GR against chafer white grubs on turfgrass, DACO: M10.2.2
- 3020276 2015, Efficacy of Bioceres-GR against chafer white grubs on turfgrass, DACO: M10.2.2
- 3020277 2015, Field testing of *Steinernema scarabei*, BioCeres WP and BioCeres Granular against white grubs, DACO: M10.2.2
- 3020278 2019, Statistical analysis of the trials with BioCeres controlling white grubs in grass- Vineland 2015, DACO: M10.2.2

- 3020358 2011, Efficacy of strain ANT-03, a.i. of Bioceres-WDB, for control of the tarnished plant bug, *Lygus lineolaris* (P. de B.) (Hemiptera: Miridae) in field of lettuce in Quebec, DACO: M10.2.2
- 3020359 2000, Persistence and infectivity of isolate MK 2001 of *B. bassiana* conidia in celery and lettuce crops, DACO: M10.2.2
- 3020360 2011, Efficacy of BIOCERES-WDB for control of Tarnished Plant Bug (*Lygus lineolaris*) on Strawberry in Quebec, Canada, DACO: M10.2.2
- 3020361 2011, Testing of Bioterra-WDB bio-insecticide against important pests in field strawberry and greenhouse vegetables, DACO: M10.2.2
- 3020362 2012, Essai d'efficacité de l'insecticide BioCérès (*Beauveria bassiana* ANT-03) contre la punaise terne (*Lygus lineolaris*) dans de tonnelles de fraisier (*Fragaria*), DACO: M10.2.2
- 3020363 2014, Efficacité de BioCeres contre la punaise terne dans la culture des framboises, DACO: M10.2.2
- 3020364 2004, Efficacité Bioceres WP contre le doryphore de la pomme de terre, DACO: M10.2.2
- 3020365 2005, Efficacité BioCeres WP contre le doryphore de la pomme de terre, DACO: M10.2.2
- 3020366 2015, Efficacité Bioceres WP contre le doryphore de la pomme de terre, DACO: M10.2.2

B. Additional Information Considered

None