Proposed Registration Decision PRD2024-09

# *Beauveria bassiana* strain ANT-03 and BioTitan WP

(*publié aussi en français*)

**5 December 2024**

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

Publications
Pest Management Regulatory Agency
Health Canada
2 Constellation Drive
8th floor, A.L. 2608 A
Ottawa, Ontario K1A 0K9

Internet: canada.ca/pesticides
pmra.publications-arla@hc-sc.gc.ca

Information Service:
1-800-267-6315
pmra.info-arla@hc-sc.gc.ca

Canada

ISSN: 1925-0878 (print)
1925-0886 (online)

Catalogue number: H113-9/2024-9E (print version)
H113-9/2024-9E-PDF (PDF version)

**© His Majesty the King in Right of Canada, as represented by the Minister of Health Canada, 2024**

All rights reserved. No part of this information (publication or product) may be reproduced or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, or stored in a retrieval system, without prior written permission of Health Canada, Ottawa, Ontario K1A 0K9.

# Table of Contents


Overview ..... 1
Proposed Registration Decision for *Beauveria bassiana* strain ANT-03 ..... 1
What does Health Canada consider when making a registration decision? ..... 1
What is *Beauveria bassiana* strain ANT-03? ..... 2
Health considerations ..... 3
Environmental considerations ..... 5
Value considerations ..... 6
Measures to minimize risk ..... 6
Next steps ..... 7
Other information ..... 7
Science evaluation ..... 8
1.0 The active ingredient, its properties and uses ..... 8
1.1 Directions for use ..... 8
1.2 Mode of action ..... 8
2.0 Methods of analysis ..... 8
3.0 Impact on human and animal health ..... 8
3.1 Toxicity and infectivity summary ..... 8
3.1.1 Testing ..... 8
3.1.2 Additional information ..... 9
3.1.3 Health incident reports ..... 9
3.1.4 Hazard analysis ..... 9
3.2 Occupational, residential and bystander risk assessment ..... 10
3.2.1 Occupational and postapplication exposure and risk ..... 10
3.2.2 Residential and bystander exposure and risk ..... 11
3.3 Dietary exposure and risk assessment ..... 11
3.3.1 Food ..... 11
3.3.2 Drinking water ..... 12
3.3.3 Acute and chronic dietary risks for sensitive subpopulations ..... 12
3.3.4 Aggregate exposure and risk ..... 12
3.3.5 Maximum residue limits ..... 12
3.4 Cumulative assessment ..... 13
4.0 Impact on the environment ..... 13
4.1 Fate and behaviour in the environment ..... 13
4.2 Effects on non-target species ..... 13
4.2.1 Effects on terrestrial organisms ..... 14
4.2.2 Effects on aquatic organisms ..... 14
4.3 Incident reports related to the environment ..... 15
5.0 Value ..... 15
6.0 Pest control product policy considerations ..... 15
6.1 Toxic substances management policy considerations ..... 15
6.2 Formulants and contaminants of health or environmental concern ..... 15
7.0 Proposed regulatory decision ..... 15

List of abbreviations ..... 16
Appendix I Tables and figures ..... 17
Table 1 Toxicity profile of Beauveria bassiana strain ANT-03 (technical grade active ingredient) ..... 17
References ..... 18

# 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 and BioTitan WP, containing the active ingredient *Beauveria bassiana* strain ANT-03, for reduction in numbers of tarnished plant bug on industrial hemp grown outdoors; and for the reduction in numbers of whiteflies, aphids, and thrips on outdoor ornamentals, including transplants.

*Beauveria bassiana* strain ANT-03 is currently registered for use on a variety of field crops as well as in turf. For details, see Proposed Registration Decision PRD2020-16, *Beauveria bassiana strain ANT-03, BioCeres F WP, BioCeres F GR, and BioCeres D GR*; and Registration Decision RD2021-02, *Beauveria bassiana strain ANT-03, BioCeres F WP, BioCeres F GR, and BioCeres D GR.*

*Beauveria bassiana* strain ANT-03 is also currently registered for use on a variety of greenhouse food crops 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 Section provides detailed technical information on the human health, environmental and value assessments of *Beauveria bassiana* strain ANT-03 and BioTitan WP.

## 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 individuals and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] 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.

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

The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include 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). They also consider the unique characteristics of organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the Health Canada regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Canada.ca.

Before making a final registration decision on *Beauveria bassiana* strain ANT-03 and BioTitan WP, Health Canada's PMRA will consider any written comments received from the public in response to this consultation document.[3] Health Canada will then publish a Registration Decision[4] on *Beauveria bassiana* strain ANT-03 and BioTitan WP, 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 Section 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 the biological insecticide BioTitan WP, which is a commercial class product registered for use in certain agricultural products and in turf.

---

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."

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*.

## 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 BioTitan WP is used according to the label directions.**

Potential exposure to *Beauveria bassiana* strain ANT-03 may occur through the diet (food and water) or when handling and applying BioTitan WP. When assessing health risks, several key factors are considered:

- the microorganism's biological properties (for example, production of toxic byproducts);
- 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.

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 *Beauveria 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), *Beauveria bassiana* strain ANT-03, caused any disease. The technical grade of the active ingredient, *Beauveria bassiana* strain ANT-03, is of moderate acute toxicity by the inhalation route of exposure. *Beauveria bassiana* strain ANT-03 is also moderately irritating to the eye.

All microorganisms, including *Beauveria bassiana* strain ANT-03, contain substances that are potential sensitizers and thus, sensitivity may develop in individuals exposed to potentially large quantities of *Beauveria bassiana* strain ANT-03.

### Residues in water and food

**Dietary risks from food and water are acceptable.**

Similar to currently registered uses of BioTitan WP on various food crops, the proposed new uses may result in residues of *Beauveria bassiana* strain ANT-03 on treated agricultural crops at the time of harvest. However, no signs of infectivity or toxicity were observed when *Beauveria bassiana* strain ANT-03 was tested on laboratory animals by the oral route, and metabolites of toxicological significance are not expected to occur on edible portions of the crops above

naturally occurring levels. In addition, the likelihood of residues of *Beauveria bassiana* strain ANT-03 contaminating drinking water supplies is expected to be low as the label has the necessary mitigation measures to limit contamination of drinking water from the proposed uses of BioTitan WP. Consequently, health risks from dietary exposure are acceptable for all segments of the population, including infants, children, adults and seniors.

**Occupational risks from handling BioTitan WP**

**Occupational risks are acceptable when BioTitan WP is used according to label directions, which include protective measures.**

BioTitan WP is currently registered as a commercial insecticide for terrestrial food crops and turf. Workers handling BioTitan WP can be exposed to *Beauveria bassiana* strain ANT-03 through direct skin or eye contact or through inhalation. While the technical grade active ingredient was of moderate acute toxicity by the inhalation route of exposure, BioTitan WP is applied as a spray suspension and no inhalation toxicity is anticipated for aqueous suspensions. To protect workers from exposure to BioTitan WP, the label states that workers must wear personal protective equipment, including a long-sleeved shirt, long pants, protective eyewear (goggles), waterproof gloves, socks and shoes, and a NIOSH-approved particulate filtering facepiece respirator with any N, R or P filter. The product label includes measures to restrict access to the treated area for four hours or until sprays have dried. The proposed new uses do not pose any additional occupational exposure concerns.

The health risks to workers are acceptable when the precautionary statements on the label are observed.

**Risks in residential and other non-occupational environments**

**Estimated risk for non-occupational exposure acceptable.**

BioTitan WP is currently registered as a commercial insecticide for terrestrial food crops and turf. The new uses for BioTitan WP include commercially-grown outdoor ornamentals and industrial hemp grown outdoors. There are no residential uses. The existing label includes mitigation measures to prevent bystander exposure such as reducing spray drift. The proposed new uses do not pose any additional residential and non-occupational exposure concerns. Residential and non-occupational exposure to BioTitan WP is therefore expected to be low when the label directions are observed. Consequently, the health risk to residents and the general public is acceptable.

## 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. The 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 *Beauveria bassiana* with the ability to colonize plants without causing disease.

The proposed use expansion of *Beauveria bassiana* strain ANT-03 to include outdoor ornamentals and industrial hemp grown outdoors is expected to increase environmental exposure to this microorganism. While information suggests that *Beauveria 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 *Beauveria bassiana* strain ANT-03 demonstrated significant toxicity/pathogenicity following contact and dietary exposures. However, no such effects were observed in semi-field trials with BioTitan WP. No evidence of significant adverse effects on birds, fish, non-arthropod invertebrates and plants were found in the published scientific literature. Also, *Beauveria bassiana* strain ANT-03 was not toxic or pathogenic to laboratory mammals through oral, pulmonary, and dermal routes. While the technical grade active ingredient is moderately acutely toxic by the inhalation route of exposure, BioTitan WP is applied as a spray suspension and no inhalation toxicity is anticipated for aqueous suspensions.

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 BioTitan WP is applied according to directions on the label. Since acute studies on beneficial arthropods (including honey bees) previously demonstrated toxic and/or pathogenic effects, the BioTitan WP label already includes statements identifying the potential harm to beneficial insects and bees and instructs applicators to limit exposure to beneficial insects.

## Value considerations

### What is the value of BioTitan WP?

**BioTitan WP is suitable for use in organic production of crops.**

BioTitan WP reduces numbers of tarnished plant bug in industrial hemp grown outdoors, which has been identified as a priority for Canadian growers, and also reduces numbers of whiteflies, aphids and thrips in outdoor ornamental plants, including transplants. BioTitan WP provides a new mode of action for 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 Beauveria bassiana strain ANT-03 (technical grade of the active ingredient) and BioTitan WP to address the potential risks identified in this assessment are as follows.

### Key risk-reduction measures

### Human health

The end-use product and technical grade active ingredient are considered to be irritating to the eyes, and are considered potential sensitizers. The signal words “POTENTIAL SENSITIZER” and “WARNING EYE IRRITANT” appear on the primary display panel of the labels. The technical grade active ingredient, Beauveria bassiana strain ANT-03, is moderately acutely toxic by the inhalation route of exposure, and the end-use product, BioTitan WP, is considered slightly acutely toxic by inhalation. Therefore, “WARNING POISON” and “CAUTION POISON” are required on the principal display panels of the technical grade active ingredient and end-use product labels, respectively.

Workers handling or applying BioTitan WP must wear a long-sleeved shirt, long pants, protective eyewear (goggles), waterproof gloves, socks and shoes and a NIOSH-approved particulate filtering facepiece respirator with any N, R or P filter. Furthermore, all unprotected workers are restricted from entering treated areas during application and for four hours following application or until sprays have dried.

### Environment

The end-use product label already includes standard environmental precaution statements to prohibit aerial application, limit drift, and reduce contamination of aquatic systems from the use of BioTitan WP. The label for the end-use product also includes environmental precaution statements to minimize the risk to beneficial insects and pollinators.

## Next steps

Before making a final registration decision on *Beauveria bassiana* strain ANT-03 and BioTitan WP, Health Canada's PMRA will consider any written comments received from the public in response to this consultation document up to 45 days from the date of publication (5 December, 2024) 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 *Beauveria bassiana* strain ANT-03 and BioTitan WP (based on the Science evaluation Section 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. For more information, please contact the PMRA's Pest Management Information Service.

# Science evaluation

## *Beauveria bassiana* strain ANT-03 and BioTitan WP

## 1.0 The active ingredient, its properties and uses

Refer to PRD2014-06, *Beauveria bassiana strain ANT-03*, and to PRD2020-16, *Beauveria bassiana strain ANT-03, BioCeres F WP, BioCeres F GR and BioCeres D GR*, for details regarding the product characterization and analysis of Beauveria bassiana strain ANT-03 and BioTitan WP (formerly BioCeres F WP).

### 1.1 Directions for use

BioTitan WP is a wettable powder formulation that is diluted in water for foliar application to industrial hemp grown outdoors and to outdoor ornamentals at application rates of 2–4 kg/ha, or as a suspension of 4–8 g product per litre of water for dip application to ornamental transplants. Foliar applications may be reapplied at intervals of 7 days, or 3–5 days under pest outbreak conditions. Applications may be repeated as necessary as determined by pest monitoring. Foliar applications to industrial hemp are limited to the vegetative/preflowering stages of the crop.

### 1.2 Mode of action

The active ingredient in BioTitan WP, *Beauveria bassiana* strain ANT-03, belongs to the Insecticide Resistance Action Committee (IRAC) 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

Refer to PRD2014-06, *Beauveria bassiana* strain ANT-03, and to PRD2020-16, *Beauveria bassiana* strain ANT-03, BioCeres F WP, BioCeres F GR and BioCeres D GR.

## 3.0 Impact on human and animal health

### 3.1 Toxicity and infectivity summary

#### 3.1.1 Testing

A detailed review of inhalation toxicity information and data was conducted in support of Beauveria bassiana strain ANT-03 (technical grade active ingredient) and the associated end-use product, BioTitan WP.

For details on the previously submitted toxicological studies in support of this technical grade active ingredient and end-use product, refer to PRD2014-06, *Beauveria bassiana strain ANT-03*, and to PRD2020-16, *Beauveria bassiana strain ANT-03, BioCeres F WP, BioCeres F GR and BioCeres D GR.*

An acute inhalation toxicity study with the technical grade active ingredient was conducted. In this study, 9-week-old Sprague-Dawley rats (5/sex/concentration) were exposed by the nose-only inhalation route to the technical grade active ingredient, Beauveria bassiana strain ANT-03 ($6.4 \times 10^{10}$ viable conidia/g) both with and without carboxymethylcellulose vehicle for 4 hours. The tested concentrations of technical grade active ingredient alone were 2.03, 0.52, and 0.054 mg/L. The tested concentrations of technical grade active ingredient with vehicle were 0.319 and 0.081 mg/L. Animals were observed for 15 days. A vehicle control group was concurrently tested. No mortality was observed in the vehicle control. For the technical grade active ingredient tested in vehicle, the number of dead animals was 0 at 0.081 mg/L and 4 (3/5 males and 1/5 females) at 0.319 mg/L. For the technical grade active ingredient tested alone, mortality at 0.054, 0.52, and 2.03 mg/L was 0, 2 (2/5 males), and 3 (2/5 males and 1/5 females), respectively. Deaths occurred on Days 4–5. The 4-hour inhalation $LC_{50}$ for males is $0.081 < LC_{50} < 0.319$ mg/L, the $LC_{50}$ for females is >2.03 mg/L, and the combined $LC_{50}$ is >2.03 mg/L. Treatment-related clinical signs (abdominal breathing) were observed in all animals and persisted until Days 5–9, except for the vehicle control group and the 0.054 mg/L technical grade active ingredient group where no clinical signs were observed. Greater test item concentration was associated with a longer duration and greater magnitude of body weight loss for animals treated with the technical grade active ingredient both alone and with vehicle. No body weight loss was observed at 0.054 mg/L.

Test results are summarized in Appendix I, Table 1.

No new information or data were submitted relating to the inhalation toxicity of the end-use product.

### 3.1.2 Additional information

Refer to PRD2020-16, *Beauveria bassiana* strain ANT-03, BioCeres F WP, BioCeres F GR, and BioCeres D GR for details.

### 3.1.3 Health incident reports

As of 21 May 2024, no human or domestic animal incident reports involving *Beauveria bassiana* strain ANT-03 have 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) and BioTitan WP was previously reviewed from the viewpoint of human health and safety and was determined to be acceptable. Refer to PRD2020-16, *Beauveria bassiana strain ANT-03, BioCeres F WP, BioCeres F GR, and BioCeres D GR* for details.

Previously, evidence was found that dry fungal spore preparations could be toxic via the inhalation route, and in the absence of an inhalation study, dry formulations containing this MPCA were considered to be highly acutely toxic via the inhalation route. However, the submitted acute inhalation toxicity study with Beauveria bassiana strain ANT-03 indicates that it is moderately acutely toxic to males via the inhalation route. Based on the results of the submitted inhalation study, the hazard statement on the label for the technical grade active ingredient will be downgraded to "WARNING POISON" (with accompanying precautionary statements).

No new information was submitted relating to the inhalation toxicity of BioTitan WP. However, because the toxicity category of the technical grade active ingredient can be lowered to "WARNING POISON", and as the toxicity category for the end-use product was previously lowered relative to the technical grade active ingredient due to the dilution of spores in the end-use product formulation, the toxicity category of BioTitan WP can now be similarly lowered to "CAUTION POISON" (with accompanying precautionary statements).

## 3.2 Occupational, residential and bystander risk assessment

### 3.2.1 Occupational and postapplication exposure and risk

BioTitan WP is currently registered as a commercial insecticide for terrestrial food crops and turf. The maximum application rate and application interval for industrial hemp grown outdoors and outdoor ornamentals are encompassed by the registered use pattern for BioTitan WP. The proposed new application method (dip) is not expected to result in greater occupational exposure relative to the currently-approved spray methods. Occupational exposure from uses on industrial hemp grown outdoors and outdoor ornamentals is, therefore, not expected to be substantially different than that associated with the currently registered use.

While the technical grade active ingredient is considered moderately acutely toxic via the inhalation route, BioTitan WP is applied as a spray suspension, and no inhalation toxicity is anticipated for aqueous suspensions. Toxicity was only observed following inhalation of dry spores and thus occupational concerns are greatest for workers handling the end-use product (see PRD2020-16, Section 3.1.2).

Like all microbial products, BioTitan WP is considered a potential sensitizer. While the label warning can be downgraded to "CAUTION POISON" for inhalation toxicity, the personal protective equipment (PPE) required for handlers of BioTitan WP remains unchanged due to the sensitization potential of the MPCA. For handlers of BioTitan WP, 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. Unprotected workers are also prohibited from entering treated areas (including turf) where BioTitan WP has been applied for 4 hours or until the sprays have dried.

Overall, occupational risks to workers are acceptable when the precautionary statements on the labels are followed, which include PPE.

Refer to PRD2020-16, *Beauveria bassiana* strain ANT-03, BioCeres F WP, BioCeres F GR, and BioCeres D GR, for details.

### 3.2.2 Residential and bystander exposure and risk

BioTitan WP is currently registered as a commercial insecticide for terrestrial food crops and turf. There are no residential uses. The product label already includes mitigation measures to prevent bystander exposure such as reducing spray drift, and requiring all unprotected workers to remain out of treated areas until sprays have dried. The end-use product is 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 the technical grade active ingredient was moderately acutely toxic via the inhalation route, BioTitan WP is applied as a spray suspension, and no inhalation toxicity is anticipated for aqueous suspensions.

The maximum application rate and application interval are unchanged. Residential and bystander exposure and risk from the proposed uses on industrial hemp grown outdoors and outdoor ornamentals, including the proposed new application method (dip), are not expected to be substantially different than that associated with the currently registered uses. Therefore, the existing label restrictions and risk mitigation measures to prevent bystander exposure are appropriate to mitigate the risk from the proposed use expansion.

## 3.3 Dietary exposure and risk assessment

### 3.3.1 Food

BioTitan WP is already registered for use on terrestrial food crops. While the proposed expanded use pattern on industrial hemp grown outdoors may result in dietary exposure with possible residues in or on agricultural commodities, the risks from consuming crops treated with BioTitan WP are acceptable because *B. bassiana* strain ANT-03 demonstrated no toxicity, pathogenicity or infectivity in Tier I acute oral testing.

Application of BioTitan WP is not expected to increase levels of beauvericin on treated crops beyond existing levels produced by naturally-occurring fungi. 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.

When the end-use product is applied to industrial hemp grown outdoors during the pre-flower stage, the health risk from consumer exposure is acceptable.

Consequently, there is no health risk to the general population, including infants and children, or animals.

### 3.3.2 Drinking water

BioTitan WP is currently registered for use on terrestrial food crops and turf. Dietary exposure from drinking water due to the proposed use on industrial hemp grown outdoors and outdoor ornamentals is not expected to be substantially different than that associated with the currently registered uses. Refer to PRD2020-16, *Beauveria bassiana strain ANT-03, BioCeres F WP, BioCeres F GR, and BioCeres D GR*, for details. Health risks from residues of *B. bassiana* strain ANT-03 in drinking water as a result of the proposed use expansion of BioTitan WP are acceptable.

### 3.3.3 Acute and chronic dietary risks for sensitive subpopulations

As noted above, when the end-use product is applied as directed by the label, the health risk is acceptable for the general population, including infants and children, and domestic animals.

### 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.

BioTitan WP is considered to be of low toxicity by the oral and dermal routes and the end-use product will not be applied near or to drinking water. The label includes statements to minimize non-occupational exposure in residential and commercial areas to the general Canadian population, including infants and children. Also, the observed inhalation toxicity was for dry spores only. Inhalation toxicity is not anticipated from mists resulting from the application of aqueous suspensions. When the end-use product is 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 dietary risks are acceptable from the consumption of foods treated with the pesticide when used according to the supported label directions. If acceptable, this means food containing that amount of residue is safe to eat, and maximum residue limits (MRLs) may be proposed. MRLs are the maximum amount of pesticide residue legally permitted to remain in/on food sold in Canada and are specified under the *Pest Control Products Act* for the purposes of the adulteration provision of the *Food and Drugs Act.*

Residues of *B. bassiana* strain ANT-03 on treated food crops are possible at the time of harvest. Dietary risk to humans from existing and new uses is acceptable due to the low acute oral toxicity of *B. bassiana* strain ANT-03 and because application of BioTitan WP is not expected to increase levels of beauvericin on treated crops beyond existing levels produced by naturally-occurring fungi. 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 non-occupational exposure to pesticides with a common mechanism of toxicity, based on the likelihood that people may be exposed to more than one of these pesticides at the same time. 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 other strains of *B. bassiana* that are used as MPCAs: *B. bassiana* strain R444, *B. bassiana* strain PPRI 5339, *B. bassiana* strain GHA, *B. bassiana* strain CFL-A, and *B. bassiana* strain HF23. The potential health risks from cumulative exposure of *B. bassiana* strain ANT-03 and these other MPCAs are acceptable when used as labelled given that they are naturally occurring and that pesticidal uses will not result in sustained increases over background, and they are not pathogenic. As well, application of BioTitan WP is not expected to increase levels of beauvericin on treated crops beyond existing levels produced by naturally-occurring fungi.

## 4.0 Impact on the environment

### 4.1 Fate and behaviour in the environment

Refer to PRD2014-06, *Beauveria bassiana* strain ANT-03, and PRD2020-16, *Beauveria bassiana* strain ANT-03, BioCeres F WP, BioCeres F GR, and BioCeres D GR.

### 4.2 Effects on non-target species

The PMRA has a four-level 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 (MCC) of the MPCA. The MCC 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, $LC_{50}$, $LD_{50}$). 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 is 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 (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC).

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 LOC, 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 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

No new studies were required to address the potential for effects on terrestrial organisms from exposure to *B. bassiana* strain ANT-03. Terrestrial exposure from the proposed use on industrial hemp grown outdoors and outdoor ornamentals and the proposed new application method (transplant dip) is not expected to be substantially different than that associated with the currently registered use. Refer to PRD2014-06, *Beauveria bassiana strain ANT-03,* and to PRD2020-16, *Beauveria bassiana strain ANT-03, BioCeres F WP, BioCeres F GR and BioCeres D GR,* for details.

### 4.2.2 Effects on aquatic organisms

No new studies were required to address the potential for effects on aquatic organisms from exposure to *B. bassiana* strain ANT-03. Aquatic exposure from the proposed use on industrial hemp grown outdoors and outdoor ornamentals and the proposed new application method (transplant dip) is not expected to be substantially different than that associated with the currently registered use. Refer to PRD2014-06, *Beauveria bassiana strain ANT-03,* and to PRD2020-16, *Beauveria bassiana strain ANT-03, BioCeres F WP, BioCeres F GR and BioCeres D GR,* for details.

### 4.3 Incident reports related to the environment

As of 21 May 2024, no environment incident reports involving *Beauveria bassiana* strain ANT-03 have been submitted to the PMRA or identified in the USEPA's Ecological Information System database.

## 5.0 Value

Scientific rationales were submitted to support extrapolation of the proposed new uses for tarnished plant bug on industrial hemp grown outdoors from registered uses of BioTitan WP for tarnished plant bug on various field vegetable and berry crops, and for whiteflies, aphids and thrips on outdoor ornamentals from registered uses of the similar product BioCeres G WP for whiteflies, aphids and thrips on a wide variety of greenhouse crops including ornamentals.

BioTitan WP provides a new mode of action for the above uses and can be incorporated into Integrated Pest Management programmes to help manage insecticide resistance in these pests. BioTitan WP has value in aiding in the management of tarnished plant bug on industrial hemp grown outdoors, which has been identified as a priority pest issue by Canadian growers. In addition, BioTitan WP is suitable for use in organic production.

## 6.0 Pest control product policy considerations

### 6.1 Toxic substances management policy considerations

Refer to PRD2020-16, *Beauveria bassiana strain ANT-03*, BioCeres F WP, BioCeres F GR, and BioCeres D GR, for details.

### 6.2 Formulants and contaminants of health or environmental concern

Refer to PRD2020-16, *Beauveria bassiana strain* ANT-03, BioCeres F WP, BioCeres F GR, and BioCeres D GR, for details.

## 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 and BioTitan WP, containing the active ingredient *Beauveria bassiana* strain ANT-03, for reduction in numbers of tarnished plant bug on industrial hemp grown outdoors; and for reduction in numbers of whiteflies, aphids, and thrips on outdoor ornamentals, including transplants.

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

| | |
|---|---|
| µm | micrometre |
| g | gram(s) |
| ha | hectare(s) |
| IRAC | Insecticide Resistance Action Committee |
| kg | kilogram(s) |
| L | litre |
| $LC_{50}$ | median lethal concentration |
| $LD_{50}$ | median lethal dose |
| LOC | level of concern |
| MCC | maximum challenge concentration |
| mg | milligram |
| MMAD | median mass aerodynamic diameter |
| MPCA | microbial pest control agent |
| MRL | maximum residue limit |
| NIOSH | National Institute for Occupational Safety and Health |
| OMAFRA | Ontario Ministry of Agriculture, Food and Rural Affairs |
| PMRA | Pest Management Regulatory Agency |
| PPE | personal protective equipment |
| RQ | risk quotient |

# Appendix I Tables and figures

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

| Study type, animal, and PMRA No. | Purity, group size, and exposure | Study results |
|---|---|---|
| Acute Inhalation Toxicity (nose-only)<br><br>Sprague-Dawley rat<br><br>PMRA No. 3458799 | $6.4 \times 10^{10}$ viable conidia/g<br><br>5/sex/group<br><br>0.054, 0.52, 2.03 mg/L (technical grade active ingredient alone)<br>0.081, 0.319 mg/L (technical grade active ingredient+vehicle)<br><br>MMAD = 2.62 – 3.26 μm<br><br>4-hour exposure, 15-day observation | $LC_{50}$ : $0.081 < LC_{50} < 0.319$ mg/L (♂)<br><br>Deaths occurred between 4 and 5 days postexposure. No mortality observed for vehicle control.<br>Clinical signs were abdominal breathing and body weight loss.<br><br>**Moderate acute toxicity** |

# References

## A. List of studies/Information submitted by registrant

### 1.0 Human and Animal Health

| PMRA Document Number | Reference |
|---|---|
| 3352563 | 2022, Acute Inhalation Toxicity and Eye Irritation, DACO: M4.9 |
| 3352567 | 2021, Acute Inhalation Study in Rat Bioceres WP, DACO: M4.9 |
| 3377979 | 2022, Use Description Scenario, DACO: 5.2 |
| 3377986 | 2022, Pyrolysis Study, DACO: 7.8 |
| 3458799 | 2023, Acute Inhalation Toxicity Study of Beauveria Bassiana Dry Conidia (TGAI) Strain ANT-03 in Sprague Dawley Rats (As per Acute Inhalation Toxicity and EPA OCSPP 870.1300), DACO: M4.9 |

### 2.0 Value

| PMRA Document Number | Reference |
|---|---|
| 3352560 | 2022, Part 1: Label Product Profile and Proposed Use Pattern, DACO: M1.2 |
| 3352575 | 2022, Part 10: Value (Including Efficacy), DACO: M10.2 |
| 3352576 | 2021, OMAFRA Support Letter for Tarnished Plant Bug, DACO: M10.2 |
| 3582446 | 2024, Response to PMRA Deficiency Dated 26 Jan 2024, DACO: 1.1.1, 10.2 |

## B. Additional Information Considered

None.