Proposed Re-evaluation Decision PRVD2018-11

# *Cydia pomonella* Granulovirus strain CMGv4 and Its Associated End-use Product

*Consultation Document*

*(publié aussi en français)*

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# Proposed Re-evaluation Decision

Under the authority of the *Pest Control Products Act*, all registered pesticides must be regularly re-evaluated by Health Canada's Pest Management Regulatory Agency (PMRA) to ensure that they continue to meet current health and environmental safety standards and continue to have value. The re-evaluation considers data and information from pesticide manufacturers, published scientific reports, and other regulatory agencies. The PMRA applies internationally accepted risk assessment methods as well as current risk management approaches and policies to all re-evaluations.

*Cydia pomonella* granulovirus (CpGV) strain CMGv4 is a naturally occurring baculovirus that is used as a microbial pest control agent for the control of codling moth on apple trees. The commercial end-use product is formulated as a suspension and is applied as a spray to the fruit and leaves of apple trees using ground application equipment.

This document presents the proposed regulatory decision for the re-evaluation of CpGV strain CMGv4 and includes the proposed label updates, as well as the science evaluation on which the proposed decision was based. All products containing CpGV strain CMGv4 registered in Canada are subject to this proposed re-evaluation decision. This document is subject to a 90-day public consultation period, during which the public, including the pesticide manufacturers and stakeholders, may submit written comments and additional information to the PMRA. The final re-evaluation decision will be published taking into consideration the comments and information received.

## Outcome of Science Evaluation

CpGV strain CMGv4 has value in providing an additional option for insect control and in resistance management practices for moths.

CpGV strain CMGv4 is a naturally occurring baculovirus and it is a member of the Baculoviridae family. Baculoviruses are widespread in the environment and have a long history of use with no attributed reports of adverse effects on people or environment. CpGV strain CMGv4 is considered to be of low toxicity and pathogencity via the oral, dermal and pulmonary routes of exposure, it is minimally irritating to the eyes and there is no evidence of hypersensitivity in laboratory animals.

When the current label directions are followed, occupational and residential exposures to all populations are not of concern. With current label directions, residues of CpGV strain CMGv4 are expected on treated apples; however, residues in drinking water are expected to be minimal. Based on a long history of dietary exposure from natural populations and the low toxicity and infectivity profile of CpGV strain CMGv4, dietary risk (from food and drinking water) is not expected to be of concern for all populations.

Baculoviruses are known to have a limited host range, with a pathogenicity specific for arthropods (insects). Based on the available baculovirus information, CpGV strain CMGv4 is not expected to adversely affect aquatic and terrestrial organisms. Under the current conditions of use, the potential risk to the environment is not expected to be of concern.

## Proposed Regulatory Decision for *Cydia pomonella* Granulovirus strain CMGv4

Under the authority of the *Pest Control Products Act* and based on the evaluation of currently available scientific information, Health Canada is proposing that products containing CpGV strain CMGv4 are acceptable for continued registration for use and sale in Canada, provided that the proposed updates to labels are in place.

Registered pesticide product labels include specific instructions for use. Directions include risk mitigation measures to protect human health and the environment that must be followed by law. As a result of the re-evaluation of CpGV strain CMGv4, no additional risk mitigation measures are proposed by the PMRA. To meet current labelling standards, the following label updates are proposed (Refer to the details in Appendix II):

- Personal protective equipment label statement;
- Environmental hazard label statements;
- Restricted entry interval label statement.

## International Context

CpGV strain CMGv4 is currently acceptable for use in other Organization for Economic Co-operation and Development (OECD) member countries, including Australia, Chile, the European Union, Israel, New Zealand, Turkey and the United States of America.

No decision by an OECD-member country to prohibit all uses of this microbial for health or environmental reasons has been identified.

## Next Steps

The public, including the registrants and stakeholders, are encouraged to submit comments during the 90-day public consultation period[1] upon publication of this proposed re-evaluation decision.

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

All comments received during the 90-day public consultation period will be taken into consideration in preparation of re-evaluation decision document[2]. The re-evaluation decision document will include the final re-evaluation decision, the reasons for it, and a summary of comments received on the proposed re-evaluation decision along with the PMRA's responses.

## Additional Scientific Information

No additional data are required.

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

# Science Evaluation

## 1.0 Introduction

*Cydia pomonella* granulovirus (CpGV) strain CMGv4 is a biological insecticide used to control codling moth damage in apple trees.

The end-use product is formulated as a suspension and is applied as a foliar spray using ground application equipment. The leaves and fruit of apple trees can be treated up to four times per year with a minimum two week interval between treatments.

Currently registered products are listed in Appendix I.

## 2.0 Identity of the Technical Grade Active Ingredient

| | |
|---|---|
| **Active microorganism** | *Cydia pomonella* Granulovirus strain CMGv4 |
| **Function** | Biological Insecticide |
| **Binomial name** | *Cydia pomonella* granulovirus strain CMGv4 |
| **Taxonomic designation** | |
| **Family** | Baculoviridae |
| **Genus** | Granulovirus |
| **Species** | *Cydia pomonella* granulovirus |
| **Strain** | CMGv4: a wild type isolated from codling moth larvae from Microbial Ecozone 4 of Canada, which encompasses the Great Lakes Region of both the U.S. and Canada, the Northeastern U.S., and the Canadian Maritimes |
| **Registration No. of the TGAI** | 26532 |
| **Nominal concentration of active ingredient** | $4 \times 10^{13}$ Occlusion Bodies (OBs) per liter |
| **Identity of relevant impurities of toxicological, environmental and/or significance.** | The technical grade active ingredient (TGAI) does not contain any impurities or micro contaminants known to be Toxic Substances Management Policy (TSMP) Track 1 substances. The product must meet microbiological contaminants release standards. |

The CpGV strain CMGv4 used in the pesticide products has not been genetically modified or engineered through recombinant nucleic acid procedures.

## 3.0 Human Health

Based on the registered use pattern, exposure to CpGV strain CMGv4 from use as an insecticide can occur through consuming food and drinking water, through working as commercial mixer, loader, applicator, or by entering treated sites. When assessing health risks of microorganisms, the following 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 the microorganism.

Studies in laboratory animals describe potential health effects from large doses of exposure to a microorganism, and they identify any potential pathogenicity, infectivity, and toxicity concerns. The levels used to assess human risks are established from these studies 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. Continued registration is only supported for uses that are determined as having no health risks of concern.

### 3.1 Toxicity and Infectivity Summary

CpGV strain CMGv4 is a naturally occurring baculovirus. Baculovirus pathogenicity is specific for arthropods, and they are known to have a limited host range.

CpGV strain CMGv4 is considered to be of low toxicity and pathogenicity via the oral and pulmonary routes of exposure. CpGV strain CMGv4 was not toxic when administered orally or dermally at maximum hazard doses and no signs of toxicity were found when it was administered through pulmonary exposure. CpGV strain CMGv4 is slightly irritating to the skin, minimally irritating to the eyes, and no evidence of hypersensitivity has been reported. For more details, refer to Regulatory Note REG2000-10, *Virosoft CP4* Cydia pomonella *granulosis virus*.

The PMRA's knowledge and familiarity with baculoviruses and the relevant published literature indicated that these insect viruses have a low potential to infect or transform mammalian cells.

Baculoviruses are widespread in the environment, and human exposures to naturally-occurring baculoviruses exist in populations with no adverse effects. However, the presence of insect debris in the end-use product may cause irritation, upon exposure to the skin and eyes. As such, the PMRA is proposing standard warning label statements be added to all products (Appendix II).

It is expected that CpGV strain CMGv4 will pose little or no risk of eliciting any adverse effects. No toxicological endpoints have been established for quantitative risk assessment by the PMRA, and, as such, the PMRA has used a qualitative approach to assess the potential risks of CpGV strain CMGv4 to human health.

## 3.2 Occupational Exposure and Risk

The CpGV strain CMGv4 end–use product is formulated as a commercial suspension that is applied as a spray to the foliage and fruit of apple trees using ground application equipment. Workers can be exposed to CpGV strain CMGv4 through mixing, loading, and/or applying the product as well as through clean-up and maintenance activities. Workers can also be exposed when entering a treated site to conduct activities such as scouting and harvesting.

Potential routes of occupational exposure to CpGV strain CMGv4 are pulmonary, dermal, and ocular. However, substantial dermal and occular exposure from the use of CpGV strain CMGv4 are not expected given current label directions and mitigative measures (for example, wearing a long-sleeved shirt, long pants, water-proof gloves, shoes, socks, and eye googles; and removing personal protection equipment immediately after handling the product). A NIOSH approved mist filtering mask or NIOSH approved mist filtering respirator is required as a standard precaution when handling microbial pest control products, however current label personal protection equipment precautions do not indicate to use a respirator when handling the end-use product. As such, update to the current PPE requirement is proposed (Appendix II). Provided that the end-use product is used with the proposed label updates and combined with the low toxicity/pathogenicity profile of CpGV strain CMGv4, the risk for workers handling and/or performing clean-up/repair activities with the CpGV strain CMGv4 end-use product is not expected to be of concern.

Postapplication and re-entry tasks for workers may include scouting, pruning treated trees, and/or harvesting treated crop. As such, dermal exposure to residues is considered to be the primary post-application exposure route. Nevertheless, exposure to re-entry workers is anticipated to be minimal given that the unbroken skin of workers will act as a natural barrier to microbial invasion of the human body, and CpGV strain CMGv4 is unlikely to be a dermal wound pathogen. Combined with the low toxicity/pathogenicity profile of CpGV strain CMGv4 and the current conditions of use, the risk to workers from early entry is not expected to be of concern. However, to meet current labelling standards, restricted-entry interval statements are proposed (Appendix II).

No additional risk mitigation measures are proposed.

## 3.3 Residential and Bystander Exposure and Risk

There are no domestic-class products containing CpGV strain CMGv4. Residential exposure to commercial products and potential risk is not expected to be of concern. There is a potential for residential bystander (all populations) exposure to spray drift from the commercial application of CpGV strain CMGv4. As the amount of virus that will be applied is small based on the current use pattern, a substantial increase in exposure from spray drift above natural exposure is not expected.

Combined with the low toxicity/infectivity profile of CpGV strain CMGv4, the risk to all bystander populations is not expected to be of concern. The current label does not contain standard precautionary statements for spray drift, and updates to the label are proposed to minimize bystander exposure to spray drift (Appendix II).

No additional risk mitigation measures are proposed.

### 3.4 Dietary Exposure and Risk

The acute oral toxicology data, the lack of production of known mammalian toxins, and a long history of research, use and safety testing of baculoviruses, suggest that there will not be any additional risk of adverse effects upon humans or animals under the current conditions of use of CpGV strain CMGv4 on food/feed crops for insect control. The CpGV virus is a naturally-occurring organism to which environmental and dietary exposure (food and water) exists for most individuals. Application of the product for control of codling moth is not expected to result in an appreciable increase in virus exposure to consumers. CpGV strain CMGv4 has a low toxicity and pathogenicity profile. Based on the above considerations, potential dietary risk (from food and water) is not expected to be of concern. To meet current labelling standard, a pre-harvest interval (PHI) statement is proposed (Appendix II).

### 3.5 Aggregate Exposure Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential, and other non-occupational sources from all known or plausible exposure routes (oral, dermal, and inhalation). For CpGV strain CMGv4, aggregate exposure is limited to residential bystander and dietary exposure; however, exposures of concern are not expected (See Section 3.3 and 3.4). As such, aggregate exposure is not expected to be of concern for all populations under the current conditions of use.

### 3.6 Cumulative Assessment

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with a common mechanism of toxicity. For the current evaluation, the PMRA has determined that CpGV shares a common mechanism of toxicity with other registered isolates of baculoviruses. The potential health risks from cumulative exposure of CpGV strain CMGv4 and these other registered baculoviruses are not of concern given the low toxicity and pathogenicity of baculoviruses.

## 4.0 Environment

CpGV strain CMGv4 is a naturally occurring baculovirus. Most baculoviruses have a narrow host range, never exceeding the order (and usually not the family) of the host from which the virus was originally isolated. For example, CpGV strain CMGv4 is expected to have an arthropod host range limited to the codling moth.

As such, minimum adverse effects following environmental exposure are expected for non-target and beneficial terrestrial arthropod species. As well, CpGV strain CMGv4 is not expected to adversely affect aquatic invertebrates, fish, birds, mammals, non-arthropod invertebrates, and both terrestrial and aquatic plants.

Considering the current conditions of use and low toxicity and infectivity profile of CpGV strain CMGv4, the potential risk of CpGV strain CMGv4 is not expected to be of concern to the environment when used according to label directions. For more details, refer to REG2000-10.

No additional risk mitigation measures are proposed. Updates to standard labels statements are proposed to meet the current labelling standard for run-off and spray drift (Appendix II).

## 5.0 Value

CpGV strain CMGv4 has value in providing an additional solution to control codling moth on apple trees.

## 6.0 Pest Control Product Policy Considerations

### 6.1 Toxic Substances Management Policy Considerations

In accordance with the PMRA Regulatory Directive DIR99-03,[3] the assessment of CpGV strain CMGv4 against Track 1 criteria of the Toxic Substances Management Policy (TSMP) under the *Canadian Environmental Protection Act* was conducted. It determined that:

- CpGV strain CMGv4 is a biological organism and does not meet the TSMP track 1 criteria of chemical control products

### 6.2 Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical grade active ingredient and formulants and contaminants in the end-use product are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*.[4] The list is used as described in the PMRA Notice of Intent NOI2005-01[5] and is based

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

[4] *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

[5] NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act*.

on existing policies and regulations including DIR99-03 and DIR2006-02,[6] 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:

- CpGV strain CMGv4 does not contain any contaminants of health or environmental concern identified in the *Canada Gazette.*

## 7.0 Incident Reports

Since 26 April 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. As of 9 February 2018, no human, domestic animal or environment incident reports involving baculoviruses were submitted to the PMRA.

## 8.0 Conclusion

CpGV strain CMGv4 has value in providing an additional solution for insect control.

CpGVs are naturally occurring and widespread in the environment, and there is a long history of human exposure to natural populations of CpGVs with no attributed adverse effects. With respect to human health, CpGV strain CMGv4 has a low toxicity and infectivity profile, and when used according to the proposed updated label directions, human health risks are not expected to be of concern for all populations.

Under current conditions of use the potential risk of CpGV strain CMGv4 to the environment is not expected to be of concern. Updates to label directions are being proposed to meet the current labelling standards.

On this basis, Health Canada's Pest Management Regulatory Agency, under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration of products containing *Cydia pomonella* granulovirus strain CMGv4 for sale and use in Canada.

[6] DIR2006-02, *Formulants Policy and Implementation Guidance Document.*

# Appendix I Registered Products Containing *Cydia pomonella* granulovirus strain CMGv4 as of 2 January, 2018

| Registration Number | Marketing Class | Registrant | Product Name | Formulation Type | Guarantee |
|---|---|---|---|---|---|
| 26532 | T | BIOTEPP INC. | CYDIA POMONELLA GRANULOVIRUS | suspension | $4 \times 10^{13}$ Occlusion bodies (Obs) per liter |
| 26533 | C | BIOTEPP INC. | VIROSOFT CP4 | suspension | $4 \times 10^{13}$ Occlusion bodies (Obs) per liter |

# Appendix II Proposed Label Amendments for Products Containing *Cydia pomonella* granulovirus strain CMGv4

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Information on labels of currently registered products should not be removed unless it contradicts the label statements provided below.

The following label statements are proposed to be included on the TGAI label (PCP Reg. no. 26532):

I) The following statement must be included under the **PRINCIPAL DISPLAY** panel:

"CAUTION – EYE AND SKIN IRRITANT"

II) Under **PRECAUTIONS:**

Replace

"Wear a long-sleeved shirt, long pants, waterproof gloves, shoes, socks and eye goggles when handling or mixing/loading the product and during all clean-up/repair activities"

With

"Wear a long-sleeved shirt, long pants, water-proof gloves, shoes, socks, eye goggles and a NIOSH approved mist filtering mask or NIOSH approved mist filtering respirator when handling."

The following label statements are proposed to be included on the end-use product label (PCP Reg. no. 26533):

I) The following statement must be included under the **PRINCIPAL DISPLAY** panel:

"CAUTION – EYE AND SKIN IRRITANT"

II) Under **RESTRICTED ENTRY INTERVAL** section, the following statements must be added **on all end-use product label**:

"DO NOT enter or allow re-entry into treated areas for 4 hours or until sprays have dried, unless wearing appropriate personal protective equipment including mist filtering NIOSH-approved respirator/mask, long-sleeved shirt, long pants, shoes plus socks, and waterproof gloves."

III) Under **PRECAUTIONS**, the following statements must be added **on end-use product label**:

Replace

"Wear a long-sleeved shirt, long pants, waterproof gloves, shoes, socks and eye goggles when handling or mixing/loading the product and during all clean-up/repair activities"

With

"Wear a long-sleeved shirt, long pants, water-proof gloves, shoes, socks, eye goggles and a NIOSH approved mist filtering mask or NIOSH approved mist filtering respirator when handling, mixing/loading, or applying the product and during all clean-up/repair activities."

Add

"May irritate the skin and eyes. Avoid breathing spray mist."

"Apply only when the potential for drift to areas of human habitation or areas of human activity such as houses, cottages, schools and recreational areas is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings."

"Can be applied up to and including the day of harvest. The pre-harvest interval (PHI) is 0 days."

IV) The following statements must be included in a section entitled **ENVIRONMENTAL PRECAUTIONS on end-use product label**:

"To reduce runoff from treated areas into aquatic habitats, avoid application to areas with a moderate to steep slope, compacted soil, or clay."

"Avoid application when heavy rain is forecast."

"Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body."

V) The following statements must be included under the **DIRECTIONS FOR USE SECTION for end-use product:**

"DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes."

# References

## A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

Unpublished information

| PMRA Document Number | Reference |
|---|---|
| 2821369 | Product characterization |

## B. ADDITIONAL INFORMATION CONSIDERED

Published information


| PMRA Document Number | Reference |
|---|---|
| 649338 | Regulatory Note REG2000-10, Virosoft CP4 *Cydia pomonella* granulosis virus. Pest Management Regulatory Agency. September 25, 2000. |
| 1871428 | Evaluation Report for Application Number 2009-2093 |
| 1871467 | Evaluation Report for Application Number 2009-2095 |