Evaluation Report ERC2011-08

Fluopicolide

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Overview

Registration Decision for Fluopicolide

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, has granted conditional registration for the sale and use of Fluopicolide Technical, Fluopicolide 4 SC Fungicide and Presidio™ Fungicide, containing the technical grade active ingredient fluopicolide, to control important fungal diseases on vegetable crops and outdoor ornamentals (bedding plants and cut flowers).

Fluopicolide Technical and V-10161 4 SC Fungicide, an end-use product similar to Fluopicolide 4 SC Fungicide and Presidio™ Fungicide, were previously reviewed by the PMRA in support of a request to establish import maximum residue limits (MRLs) for the active ingredient fluopicolide. The detailed review for fluopicolide can be found in the Evaluation Report for the original import MRL application (Application Number 2007-4677), located within the PMRA Public Registry on the Health Canada website.

An evaluation of available scientific information found that, under the approved conditions of use, the products has value and do not present an unacceptable risk to human health or the environment.

Although the risks and value have been found acceptable when all risk reduction measures are followed, the applicant must submit additional scientific information as a condition of registration.

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 Fluopicolide Technical, Fluopicolide 4 SC Fungicide and Presidio™ Fungicide.

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 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. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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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."

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 (for example, those most sensitive to environmental contaminants). 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 PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What Is Fluopicolide?

Fluopicolide is the active ingredient present in the end-use products Presidio™ Fungicide and Fluopicolide 4 SC Fungicide which belongs to a new chemical class (Group 43). Fluopicolide causes rapid destabilization of fungal cell structures. It is a systemic and protectant fungicide applied as a foliar or a drench treatment that is used to control some important diseases on plants.

Health Considerations

Can Approved Uses of Fluopicolide Affect Human Health?

Fluopicolide is unlikely to affect your health when used according to label directions.

Potential exposure to fluopicolide may occur through the diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when fluopicolide products are used according to label directions.

The toxicity of fluopicolide and its associated end-use product, V-10161 4 SC Fungicide, were evaluated previously for the purpose of setting the import maximum residue levels (MRL). The present document discusses the data submitted in support of the domestic registration, namely the non-oral acute toxicity studies and short-term dermal exposure study, and sets the toxicological endpoints for occupational exposure risk assessment. For an evaluation of acute, short term, chronic/oncogenicity, reproductive, developmental, metabolism, and genotoxicity studies for fluopicolide, please refer to the Evaluation Report for the original import MRL application (Application Number 2007-4677) found within the PMRA Public Registry on the Health Canada website.

The end-use products Fluopicolide 4 SC Fungicide and Presidio™ Fungicide are toxicologically equivalent to V-10161 4 SC Fungicide.

Fluopicolide is of low acute toxicity by oral, dermal and inhalation routes in the rat. It is non-irritating to the skin and minimally irritating to the eyes of rabbits and it is not a dermal sensitizer in guinea pigs. Consequently, no signal words are required on the label. The end-use product V-10161 4 SC Fungicide is of low acute toxicity by the oral and dermal routes of exposure and is slightly toxic by the inhalation route in the rat. It is minimally irritating to the skin and mildly irritating to the eyes of rabbits. V-10161 4 SC Fungicide is not a dermal sensitizer in guinea pigs. The signal words "CAUTION POISON - EYE IRRITANT" are required on the label for the end-use products.

No treatment-related toxicity was observed in rats after repeated exposure with high dose levels of fluopicolide via the dermal route.

Fluopicolide is not genotoxic and is not likely to pose a carcinogenic risk to humans. There was no indication that fluopicolide caused damage to the nervous system and there were no effects on reproduction. The first signs of toxicity in animals given daily doses of fluopicolide over long periods of time were decreases in body weight and body weight gain and changes to the kidney, liver and adrenal glands. When fluopicolide was given to pregnant animals, malformations (rats) and abortions (rabbits) were observed at doses that were also toxic to the dams. Due to the nature of these endpoints and their potential implications on the health of the foetus, extra protective factors were applied during the risk assessment to further reduce the allowable level of human exposure to fluopicolide.

The risk assessment was conducted to ensure that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests. The dose levels used to assess risks are established to protect the most sensitive human population (e.g., children, nursing mothers and women of child bearing age). Only those uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Residues in Water and Food

Dietary risks from food and water are not of concern

Aggregate dietary intake estimates (food plus water) revealed that the general population and infants, the subpopulation which would ingest the most fluopicolide relative to body weight, are expected to be exposed to less than 36.1% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from fluopicolide is not of concern for all population sub-groups.

The acute aggregate (food and water) dietary intake estimate for women aged 13-49 years was 15.44% of the reference dose, which is not a health concern.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act* (PCPA). Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted primarily in the United States using fluopicolide on root vegetables (Crop Subgroup 1A), leaves of root and tuber vegetables (Crop Group 2), bulb vegetables (Crop Group 3-07), leafy vegetables (Crop Group 4), brassica head and stem vegetables (Crop Subgroup 5A), cucurbit vegetables (Crop Group 9), fruiting vegetables (Crop Group 8-09), grapes, and potatoes were acceptable. The MRLs for this active ingredient can be found in the Science Evaluation of this Evaluation Report and in the Evaluation Report for Application Number 2007-4677.

Risks in Residential Environments

Postapplication risks for adults and youth contacting ornamental plants treated with Fluopicolide 4 SC Fungicide or Presidio™ Fungicide are not of concern.

There is potential for dermal exposure to adults and youth through contact with transferable residues following commercial application of fluopicolide on treated ornamentals in residential areas. Residential postapplication exposure to ornamental plants is not expected to be significant for children and toddlers.

Postapplication risk estimates for adults and youth contacting treated ornamental plants are acceptable. Therefore, contact with the foliage of treated ornamentals is acceptable once residues have dried.

Occupational Risks From Handling Fluopicolide 4 SC Fungicide or Presidio™ Fungicide

Occupational risks are not of concern when Fluopicolide 4 SC Fungicide or Presidio™ Fungicide is used according to the proposed label directions, which include protective measures.

Farmers, custom applicators, or ornamental nursery operators who mix, load or apply Fluopicolide 4 SC Fungicide or Presidio™ Fungicide as well as field workers re-entering treated fields and nurseries can come in direct contact with fluopicolide residues on the skin. Therefore, the label specifies that anyone mixing/loading and applying Fluopicolide 4 SC Fungicide or Presidio™ Fungicide must wear a long-sleeved shirt and long pants, chemical-resistant gloves, socks and shoes. The label also requires that workers do not enter treated fields or other treated sites for one to 16 days after application for specific activities in some crops. For all other uses, a restricted-entry interval (REI) of 12 hours is specified. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the risk to workers handling Fluopicolide 4 SC Fungicide or Presidio™ Fungicide is not a concern.

For bystanders, exposure is expected to be much less than that for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Fluopicolide Is Introduced Into the Environment?

Fluopicolide poses a potential risk to aquatic organisms, therefore additional risk reduction measures need to be observed.

When fluopicolide is released into the environment some of it can be found in soil and surface water. In the terrestrial environment, fluopicolide is expected to be persistent and residues may carryover into the following growing season. Fluopicolide is shown to bind weakly to soils, however, there is evidence that adsorption to soil may increase over time as the product is used. The major transformation product, 2,6-dichlorobenzamide (BAM), is expected to be mobile in soils. Both fluopicolide and BAM are expected to leach through soil and have the potential to reach groundwater.

In aquatic environments, fluopicolide is expected to be persistent and to partition from the water phase to the sediment; the major transformation product BAM has been shown to partition mainly into the water phase. Fluopicolide residues are not expected in the air because of its low volatility and it has a low potential for bioaccumulation in biota. The transformation product BAM is not expected to be a concern to terrestrial and aquatic life.

Fluopicolide may pose a risk to aquatic organisms. In order to minimize the potential exposure of aquatic organisms to fluopicolide, an unsprayed area (spray buffer zone) is needed between the sprayer and downwind sensitive habitats. The width of these spray buffer zones is specified on the product label.

Value Considerations

What Is the Value of Fluopicolide 4 SC Fungicide and Presidio™ Fungicide?

Fluopicolide, the active ingredient in Fluopicolide 4 SC Fungicide and Presidio™ Fungicide, controls or suppresses economically important diseases on vegetable crops and outdoor ornamentals (bedding plants and cut flowers).

Presidio™ Fungicide and Fluopicolide 4 SC Fungicide are products formulated as a foliar or a drench treatment against important diseases on vegetable crops and outdoor ornamentals (bedding plants and cut flowers). Presidio™ Fungicide and Fluopicolide 4 SC Fungicide are active against selective pathogens affecting the reproduction cycle with systemic and curative properties, and offers an additional tool for disease and resistance management, particularly for the control of downy mildew on various vegetable crops as well as late blight on potato and tomato. Presidio™ Fungicide and Fluopicolide 4 SC Fungicide are most effective when applied in a regularly scheduled spray program and are to be used as a tank-mix with other registered fungicides with a different mode of action.

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 label of Fluopicolide 4 SC Fungicide or Presidio™ Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with fluopicolide on the skin, anyone mixing, loading, applying, and involved in clean-up or repair activities with Fluopicolide 4 SC Fungicide or Presidio™ Fungicide must wear the recommended personal protective equipment (PPE). In addition, standard label statements to protect against drift during application are included on the label. The label also requires REIs of 8 days for hand pruning, thinning, tying and leaf pulling in grapes, 16 days for cane turning and girdling in table grapes, and 1 day for hand pruning and irrigation in Brassica vegetables. A 12-hour REI is required for all other re-entry activities.

Environment

Precautionary statements and spray buffer zones for non-target aquatic habitats are required as a result of the environmental risk assessment. To reduce the potential for runoff of fluopicolide to adjacent aquatic habitats precautionary statements for sites with characteristics that may be conducive to runoff and when heavy rain is forecasted are required. Fluopicolide residues could have a high leaching potential, therefore, a label statement is required advising that use may result in contamination of groundwater, particularly in areas where soils are permeable and/or the depth to the water table is shallow. Fluopicolide is persistent and may carryover into the following growing season, therefore a label statement is required advising that products containing fluopicolide should not be used in areas treated during the previous season.

What Additional Scientific Information Is Being Requested?

Although the risks and value have been found acceptable when all risk-reduction measures are followed, the applicant must submit additional scientific information as a condition of registration. More details are presented in the Science Evaluation section of this Evaluation Report or in the Section 12 Notice associated with these conditional registrations. The applicant must submit the following information within the time frames indicated.

All required trials should be submitted within three years from the time of conditional registration being granted.

Chemistry

Analytical data from at least five batches of technical grade active ingredient representing full-scale production.

Human Health

Data are required demonstrating the stability of fluopiciolide derived residues during the maximum storage intervals used during some of the crops field trials (35 months for broccoli, 40 months for cabbage, 38 months for celery and spinach, 41 months for bulb onions, 38 months for green onions, 47 months for carrots, 45 months for radish roots and tops, and 40 months for sugar beet roots and tops) and field crop rotation trial study (fluopicolide, BAM and PCA residues in/on wheat forage and PCA residues in/on wheat straw for 24 months).

Value

The following small-scale field or greenhouse trials are required for the disease claims within the conditional registration:

- Three trials on downy mildew of brassica (head and stem) vegetables and brassica root vegetables (cabbage, radish and/or turnip);
- Two trials on phytophthora blight/crown rot of cucurbit vegetables (pumpkin or/and eggplant);
- Two trials infected by *Phytophthora ramorum* and *P. parasitica* on outdoor ornamentals.

Other Information

As these conditional registrations relate to a decision on which the public must be consulted.[3] the PMRA will publish a consultation document when there is a proposed decision on applications to convert the conditional registrations to full registrations or on applications to renew the conditional registrations, whichever occurs first.

The test data cited in this Evaluation Report (i.e. the test data relevant in supporting the registration decision) will be made available for public inspection when the decision is made to convert the conditional registrations to full registrations or to renew the conditional registrations (following public consultation). If more information is required, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

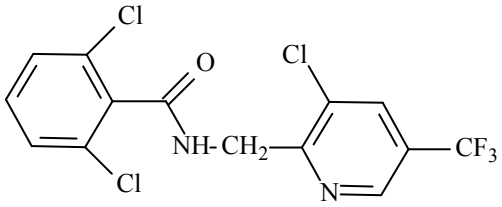
[3] As per subsection 28(1) of the *Pest Control Products Act.*

Science Evaluation

Fluopicolide

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Fluopicolide
Function	Fungicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	2,6-Dichloro-N-{[3-chloro-5-(trifluoromethyl)pyridin-2-yl]methyl}benzamide
2. Chemical Abstracts Service (CAS)	2,6-Dichloro-N-{[3-chloro-5-(trifluoromethyl)-2-pyridinyl]methyl}benzamide
CAS number	239110-15-7
Molecular formula	$C_{14}H_8Cl_3F_3N_2O$
Molecular weight	383.58
Structural formula	
Purity of the active ingredient	98.8%

1.2 Physical and Chemical Properties of the Active Ingredients and End-use Product

Table 1.2.1 Technical Product—Fluopicolide Technical Fungicide

Property	Result
Colour and physical state	Beige solid
Odour	Odourless
Melting range	149°C (135-165°C)
Boiling point or range	Not available
Specific gravity at 4°C	1.65
Vapour pressure at 20°C	3.03×10^{-7} Pa (extrapolated)
Ultraviolet (UV)-visible spectrum	Solvent — λ (nm) — λ_{max} (nm) Methanol — 203, 271, 291 — 203 Methanol/HCl — 202, 270, 291 — 202 Methanol/NaOH — 219, 271, 291 — 219
Solubility in water at 20°C	3.02 mg/L
Solubility in organic solvents at 20°C	Solvent — Solubility (g/L) ethanol — 19.2 n-hexane — 0.20 toluene — 20.5 dichloromethane — 126 acetone — 74.7 ethylacetate — 37.7 dimethyl sulfoxide — 183
n-Octanol-water partition coefficient (K_{ow})	pH — log K_{ow} 4.0 — 2.9 7.3 — 2.9 9.1 — 2.9
Dissociation constant (pK_a)	Not available
Stability (temperature, metal)	Stable at 54°C for 14 days in presence of aluminum or aluminum acetate.

Table 1.2.2 End-use Product—Fluopicolide 4 SC Fungicide/Presidio™ Fungicide

Property	Result
Colour	Beige
Odour	Not available
Physical state	Liquid
Formulation type	SU (suspension)
Guarantee	Formulation 1: 478 g/L Formulation 2: 480 g/L
Container material and description	20 to 1000 kg, bulk, plastic, polyethylene totes
Density	1.21 g/mL at 20°C
pH of 1% dispersion in water	Formulation 1: 6.6 Formulation 2: 8.1
Oxidizing or reducing action	No chemical incompatibility if the test item comes in contact with reducing (zinc powder) or oxidizing (ammonium nitrate) agents.
Storage stability	Stable in HDPE white opaque can for at least three years at ambient temperature
Corrosion characteristics	The HDPE white opaque can shows no negative interactions with the formulation for at least three years at ambient temperature.
Explodability	The product does not present a danger of explosion under the thermal sensitivity and shock tests.

1.3 Directions for Use

Presidio™ Fungicide and Fluopicolide 4 SC Fungicide, a systemic and protectant fungicide, is proposed for use as a foliar or drench treatment against important oomycete diseases on vegetable crops and outdoor ornamentals (bedding plants and cut flowers) (refer to Table 1.3.1). No more than two (2) sequential applications can be applied before alternating with another registered fungicide with a different mode of action. The higher rate and shorter interval should be applied under conditions of high disease pressures. Presidio™ Fungicide and Fluopicolide 4 SC Fungicide must be tank mixed with other effective fungicides with a different mode of action when there is an alternative available.

Table 1.3.1 Crop and Disease Claims Proposed for Presidio™ Fungicide and Fluopicolide 4 SC Fungicide

Crop & Crop Group	Disease Controlled	Rates (mL/ha)
Brassica (head and stem) vegetables and brassica root vegetables	Downy mildew (*Peronospora parasitica*)	220-292
Cucurbit vegetables	Downy mildew (*Pseudoperonospora cubensis*) and phytophthora blight/crown rot (*Phytophthora capsici*)	220-292
Fruiting vegetables	Late blight (*Phytophthora infestans*) and phytophthora blight (*Phytophthora capsici*)	220-292
Grapes	Downy mildew (*Plasmopara viticola*)	220-292
Leafy vegetables (except brassica vegetables)	Downy mildews (*Bremia lactucae* and *Peronospora farinosa*)	220-292
Potato	Late blight (*Phytophthora infestans*)	220-292
Outdoor ornamentals (field and container grown)*	Downy mildew (*Peronospora* spp.), phytophthora crown and root rot (*Phytophthora* spp.) and pythium root rot (*Pythium* spp.)	60-119 mL in 380 L water

* Both foliar and drench applications are proposed for use on outdoor ornamentals.

1.4 Mode of Action

Fluopicolide belongs to a new chemical class, the acyl picolides. Fluopicolide has an effect on spectrin-like proteins that play a role in maintaining the membrane stability in fungi. The process causes rapid redistribution of these proteins from the membrane to the cytoplasm in both hyphae and zoospores. Fluopicolide is a systemic and protectant fungicide.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and the impurities in Fluopicolide Technical have been validated and assessed to be acceptable for the determinations.

2.2 Method for Formulation Analysis

The method provided for the analysis of the active ingredient in the formulation has been validated and assessed to be acceptable for use as an enforcement analytical method.

2.3 Methods for Residue Analysis

With respect to analytical methods for environmental media, high-performance liquid chromatography methods with tandem mass spectrometry (HPLC-MS/MS) were developed and proposed for data generation and enforcement purposes. These methods fulfilled the requirements with regards to selectivity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70–120%) were obtained in plant and animal matrices and environmental media. Methods for residue analysis are summarized in Appendix I, Table 1.

With respect to analytical methods for residues in/on crop commodities, the LC/MS/MS Methods 00782 and the modifications M001, M002 and M003, and 1611-00.02 and 1629-00.00 are considered acceptable data gathering methods for residues of fluopicolide and metabolites in/on crop commodities. RM-43C-1 and RM-43C-2 are based on method 00782 and its modifications. Since there is no major variation in extraction or clean-up schemes, or differences in the chromatographic system used (LC/MS/MS), the extraction efficiency and independent laboratory validation data submitted for 00782-M002 and M003 can be extended to method RM-43C-2. Therefore, method RM-43C-2 is acceptable as the enforcement method for crop commodities.

Method AR 303-02 (LC/MS/MS) is suitable as a data gathering method for the determination of fluopicolide residues in livestock matrices (milk, meat and meat by-products) based on acceptable validation data. An interference study or confirmatory conditions have not been submitted. However, given that finite residues of fluopicolide are not anticipated in/on meat, milk and eggs based on the approved uses in Canada, an enforcement method is not required at this time.

Fluopicolide and the metabolites 2,6-dichlorobenzamide (BAM), 3-chloro-5-(trifluoromethyl)-2-pyridinecarboxylic acid (PCA), 3-methylsulfinyl-5-trifluoromethylpyridine-2-carboxylic acid (P1X), and 2,6-dichloro-3-hydroxybenzamide (3-OH-BAM) were subjected to the U.S. Food and Drug Administration multiresidue method protocols (PAM I), and the methods were deemed inadequate to determine residues of fluopicolide and all the metabolites.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

Only the data submitted in support of the domestic registration are discussed in this document. A detailed review of the toxicological database for fluopicolide was previously conducted. Please refer to the Evaluation Report for the original import MRL application (Application Number 2007-4677) which can be found in the PMRA Public Registry on the Health Canada website.

Following acute exposure, fluopicolide was of low toxicity by the oral, dermal and inhalation routes of exposure in rats. It was non-irritating to the skin and minimally irritating to the eyes of rabbits. Fluopicolide was not a dermal sensitizer in guinea pigs.

The end-use-product V-10161 4 SC Fungicide, which is toxicologically equivalent to the end-use products Fluopicolide 4 SC Fungicide and Presidio™ Fungicide, was of low acute toxicity by the oral and dermal routes of exposure in rats and slightly acutely toxic by the inhalation route in the same species. V-10161 4 SC Fungicide was mildly irritating to the eyes and minimally irritating to the skin of rabbits. It was not a dermal sensitizer in guinea pigs.

No treatment-related toxicity was observed in rats following repeat dosing with a limit dose of fluopicolide via the dermal route.

Results of the acute and dermal toxicity tests conducted on laboratory animals with fluopicolide and its associated end-use product, along with the toxicology endpoints for use in the human health risk assessment, are summarized in Appendix I , Tables 2, 3, and 4.

Incident Reports
Since April 26, 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. Information on the reporting of incidents can be found on the PMRA website. Incidents from Canada and the United States were searched and reviewed for the active ingredient fluopicolide. As of December 2010, the PMRA had received no incident reports for products containing fluopicolide. Detailed information for any reported incident in the future would be found on the PMRA Public Registry.

3.1.1 PCPA Hazard Characterization

For a detailed assessment of the toxicological database for fluopicolide, please refer to the Evaluation Report for the original import MRL application (Application Number 2007-4677) which can be found in the PMRA Public Registry on the Health Canada web site..

3.2 Determination of Acute Reference Dose

For a detailed assessment of the toxicological database for fluopicolide, please refer to the Evaluation Report for the original import MRL application (Application Number 2007-4677) which can be found in the PMRA Public Registry on the Health Canada web site.

3.3 Determination of Acceptable Daily Intake

For a detailed assessment of the toxicological database for fluopicolide, please refer to the Evaluation Report for the original import MRL application (Application Number 2007-4677) which can be found in the PMRA Public Registry on the Health Canada web site.

3.4 Occupational and Residential Risk Assessment

Occupational exposure to fluopicolide is characterized as short- to intermediate-term and is predominately by the dermal and inhalation routes for chemical handlers and by the dermal route for workers re-entering treated areas.

3.4.1 Toxicological Endpoints

For all exposure scenarios, a developmental toxicity study in rabbits for fluopicolide was considered to be the most appropriate endpoint for short-term dermal/inhalation and intermediate-term dermal/inhalation exposure risk assessment. The NOAEL in this study was 20 mg/kg bw/day. The standard uncertainty factors (10-fold for interspecies extrapolation and 10-fold for intraspecies variability) were applied and an additional factor of 3-fold was applied on the basis of the concerns in the PCPA Hazard Characterization Section (seriousness of endpoint; please refer to the Evaluation Report for the original import MRL, Application Number 2007-4677). Therefore, the target margin of exposure (MOE) is 300. Use of this endpoint is considered to be protective of all sub-populations, including nursing infants and unborn children of exposed female workers.

3.4.1.1 Dermal Absorption

An acceptable *in vivo* rat dermal absorption study was provided. Dermal administration of [14C-phenyl] fluopicolide in a soluble concentrate formulation to five male Sprague-Dawley rats at a dose of either 1.43 or 659 µg a.i./cm2 skin resulted in a mean recovery of 41-69% of the low dose and 87-91% of the high dose from skin wash (the swabs used to remove the test compound from the skin) after 8 hours of treatment. A total of 56-81% (low dose) or 92-95% (high dose) was considered not absorbed.

Estimates of dermal absorption were based on the sum of urine + feces + cage wash + tissues + treated skin + stratum corneum. Mean dermal absorption values (n=5) from the high dose groups were 4.5% (8h), 9.0% (24h), 3.9% (72h) and 3.1% (144h); and from the low dose groups were 36.1% (8h), 41.8% (24h), 34.8% (72h) and 24.5% (144h). The overall recoveries of radioactivity were found to be acceptable in the range of 91% to 109% of the total radioactivity administered.

An acceptable *in vitro* dermal absorption study was provided. [14C-phenyl] fluopicolide was applied to excised human and rat skin at two dose concentrations, 1.89 and 744 µg/cm2 skin. Receptor fluid samples were collected each hour after treatment for 24 hours. At 8 hours after application, the skin was swabbed with a mild detergent solution. After 24 hours, the experiment was terminated, and the skin membranes were tape stripped. All tape strips, the remaining skin and the receptor fluid remaining in the cell and outlet tubing at the end of the experiment were assayed. Total recovery was considered acceptable at 92.3-96.5%. The total amounts of applied radioactivity absorbed within 24 hours at the high dose level were 0.96% in humans and 2.62% in rats, while at low dose levels the amounts absorbed were 7.28% in humans and 33.25% in rats.

While the results of the *in vitro* study indicate that the percutaneous absorption of radiolabeled fluopicolide was greater through rat skin membrane than through human skin membrane, a quantitative comparison of dermal absorption values was not possible given the differences in application rates and the high variability of the results from the *in vitro* study.

Given the uncertainty regarding actual deposition under field conditions, it is considered appropriate to derive an estimate of dermal absorption based on the *in vivo* low dose group as dermal absorption was highest in this group. As no clear trend in absorption over time was noted in this group, the average estimate of 34% was considered most appropriate to adopt for risk assessment purposes.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/Loader/Applicator Exposure and Risk Assessment

Exposure to workers mixing, loading and applying Fluopicolide 4 SC Fungicide or Presidio™ Fungicide to crops and field-grown ornamentals for postemergence control and/or suppression of certain diseases is expected to be short- to intermediate-term in duration and to occur primarily by the dermal and inhalation routes.

As chemical-specific exposure data for assessing human exposures during pesticide handling activities were not submitted, exposure estimates for mixers, loaders and applicators (M/L/A) were based on data from the Pesticide Handlers Exposure Database (PHED). PHED version 1.1 is a compilation of generic mixer/loader and applicator passive dosimetry data which facilitates the generation of scenario-specific exposure estimates. To estimate exposure for each use scenario, appropriate subsets of A and B grade data (and C for low pressure hand-wand) were created from the liquid mixer/loader; aerial, airblast and groundboom applicator; and low pressure hand-wand and backpack mixer/loader/applicator database files of PHED. All data were normalized for kilogram (kg) active ingredient handled. Exposure estimates are presented on the basis of the best-fit measure of central tendency, i.e., summing of the measure of central tendency for each body part which is most appropriate to the distribution of data for that body part.

Dermal exposure was estimated by coupling the unit exposure values with the amount of product handled per day and the dermal absorption factor of 34%. Inhalation exposure was estimated by coupling the unit exposure values with the amount of product handled per day with 100% inhalation absorption. Exposure was normalized to mg/kg bw/day by using 70 kg adult body weight. Exposure estimates were compared to the toxicological endpoint (NOAEL of 20 mg/kg bw/day) to obtain the margin of exposure (MOE). The target MOE is 300.

A crop grouping approach was used to derive handler exposure estimates using the maximum area treated per day for each crop group. The clothing scenario used to estimate mixer/loader, applicator exposure is a single layer of clothing and gloves for mixing and loading and for low pressure hand-wand and backpack mixing/loading and applying. For airblast, groundboom and aerial application, non-gloved data were used.

Exposure and risk estimates for worker mixing/loading and applying Fluopicolide 4 SC Fungicide or Presidio™ Fungicide to the proposed crop groups and outdoor ornamentals (field and container grown) are summarized in Table 3.4.1. Based on a dermal absorption value of 34%, the target MOE of 300 is achieved for all proposed scenarios.

Table 3.4.1 Mixer/Loader/Applicator Exposure estimates and MOE

Scenario	Crops	Application Rate (kg a.i./ha)	PHED unit exposure (µg/kg a.i.)	Amount Handled (kg a.i./day) 1	Exposure (mg/kg bw/day) 2	MOE 3
Farmer (open M/L; groundboom, open cab)	Potatoes	0.14	31.16	14.98	0.0067	2 999
Custom applicator (open M/L; groundboom, open cab)	Potatoes	0.14		50.40	0.0224	891
Open M/L; Groundboom, open cab	All crops except potatoes	0.14		3.64	0.0016	12 343
Open M/L; Airblast, open cab	Grapes	0.14	306.39	2.80	0.0123	1 632
Open M/L; Groundboom, open cab	Outdoor ornamentals	0.15 (119 mL in 380 L water)	31.16	3.90	0.0017	11 520
LPHW			382.85	0.0225	0.0001	162 525
Backpack			1 913.69	0.0225	0.0006	32 514
Aerial M/L	Potatoes only	0.14	18.99	56.0	0.0152	1 316
Aerial applicator			3.35		0.0027	7 463
Aerial M/L/A (closed M/L)			9.90		0.0079	2 525

M/L = mixing/loading; LPHW = low pressure hand-wand; M/L/A = mixing, loading and applying

1 Amount of a.i. handled per day calculated using the application rate × Area Treated Per Day (ATPD)

2 Daily exposure was calculated using amount of a.i. handled per day × PHED unit exposure value/body weight (70 kg); a 34% dermal absorption value was used.

3 Exposure estimates were compared to a NOAEL of 20 mg/kg bw/day established in the developmental toxicity study in rabbits, target MOE = 300.

3.4.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

There is potential for exposure to workers re-entering treated areas to perform various activities including hand harvesting, pruning, thinning, irrigating, weeding, tying, staking, pinching, scouting and moving container-grown plants. Given the nature of activities performed, dermal contact with residues on leaves is expected.

Dermal exposure to workers contacting treated foliage is estimated by coupling dislodgeable foliar residue (DFR) values with activity-specific transfer coefficients and the dermal absorption factor for fluopicolide.

A chemical-specific DFR study in lettuce was submitted to estimate dislodgeable foliar residues and their dissipation on foliage after the application of a soluble concentrate formulation containing 40% fluopicolide at two test sites in Pennsylvania (PA) and California (CA). Three applications were made at a rate of 133 g a.i./ha/application, at four to six day retreatment intervals for a seasonal application rate of 400 g a.i./ha. Triplicate leaf punch samples were collected before and after each application, and at 1, 3, 5, 7, 10, 14, 21, 28 and 35 days after the final application for both sites. Dissipation rates were modeled using pseudo-first-order kinetics, resulting in R2 values of 0.967 for the PA site and 0.826 for the CA site. At the PA site, the maximum average residues were detected eight hours after the last treatment (0.4157 µg/cm2) and declined to 0.0123 µg/cm2 after 14 days, with all residues <LOQ by 21 days after the last treatment. At the CA site, the maximum average residues were detected one day after the last

treatment (0.4464 µg/cm2) and declined to 0.0034 µg/cm2 after 35 days, with residues in two of three samples <LOQ by 21 and 35 days after the last treatment. The estimated half-life values were 2.1 days and 5.0 days for leaf lettuce at the PA and CA sites, respectively. The data derived for residue dissipation at the PA site were considered more scientifically robust due to the high R2. The daily dissipation rate was calculated to be 28%.

The application method, frequency, monitoring times and use pattern of the study were relevant to the Canadian use pattern. Although the geographical and climatic conditions of the tested sites were not fully representative of Canadian growing regions, the peak DFR value (0.4157 µg/cm2) and the daily dissipation rate from the PA site were used to estimate postapplication exposure to leafy vegetables. Given the similarities in use pattern, application equipment and foliage type, these values were also used to estimate postapplication exposure to potatoes, root vegetables and brassica vegetables.

To estimate the postapplication exposure from all other crops and outdoor ornamental re-entry activities, the default dislodgeable foliar residue value of 20% of the application rate on the day of application and 10% daily dissipation rate was used in the exposure assessment. For all crops, a dermal absorption value of 34% was used and workers were assumed to be exposed for eight hours per day.

Exposure estimates were compared to the NOAEL of 20 mg/kg bw/day to obtain the MOE. The target MOE is 300. A crop grouping approach was used to derive exposure estimates. With the proposed 12-hour REI, the target MOE is achieved for all scenarios except the following: for hand pruning, thinning, tying and leaf pulling in grapes an REI of eight (8) days is required; for cane turning and girdling in table grapes an REI of 16 days is required; and for hand pruning and irrigation in brassica vegetables an REI of one (1) day is required. Exposure and risk estimates for postapplication re-entry activities are summarized in Tables 3.4.2, 3.4.3 and 3.4.4.

Table 3.4.2: Postapplication Exposure and Risk Estimates for Workers Entering Treated Fields Using Chemical-Specific DFR Data.

Crop	Re-entry activity	Peak DFR* (µg/cm^2)	Transfer Coefficient† (cm^2/h)	Dermal Exposure‡ (mg/kg bw/day)	MOE ¶	REI
Potatoes	Hand weeding	0.4157	300	0.0048	4 127	12 hours
	Scouting, irrigation	0.4157	1500	0.0242	825	12 hours
Root Vegetables	Hand harvesting	0.4157	2500	0.0404	495	12 hours
	Irrigation; scouting; hand weeding; thinning	0.4157	300	0.0048	4 127	12 hours
Leafy Vegetables	Scouting, irrigation, hand weeding	0.4157	1500	0.0242	825	12 hours
	Hand harvesting, pruning, hand thinning	0.4157	2500	0.0404	495	12 hours
Brassica Vegetables	Hand weeding, thinning	0.4157	2000	0.0323	619	12 hours
	Scouting	0.4157	4000	0.0646	310	12 hours
	Hand harvesting, hand pruning, irrigation	0.2993**	5000	0.0581	344	1 day

* Peak DFR (from lettuce DFR study)
** Peak DFR at specified REI, using 28% daily dissipation rate (from lettuce DFR study)
† Highest transfer coefficient for each crop group and activity
‡ Exposure = Peak DFR (µg/cm^2) * TC (cm^2/h) * 8 hours * 34% DA / 70 kg bw x 1000 µg/kg
¶ Based on a NOAEL of 20 mg/kg bw/day, the target MOE is 300
Shaded box denotes that the MOE is below the target of 300 on the day of the last application

Table 3.4.3 Postapplication Exposure and Risk Estimates for Workers Entering Treated Fields Using Default Values

Crop	Re-entry activity	Peak DFR* (µg/cm^2)	Transfer Coefficient† (cm^2/h)	Dermal Exposure‡ (mg/kg bw/day)	MOE ¶	REI
Cucurbit Vegetables	Scouting, irrigation, hand weeding	0.4780	1500	0.0279	718	12 hours
	Hand harvesting, pruning, hand thinning	0.4780	2500	0.0464	431	12 hours
Fruiting Vegetables	Hand weeding, thinning	0.4780	500	0.0093	2 153	12 hours
	Scouting, irrigation	0.4780	700	0.0130	1 538	12 hours
	Hand harvesting, staking, tying, hand pruning	0.4780	1000	0.0186	1 077	12 hours
Grapes	Hand weeding, scouting	0.4780	700	0.0130	1 538	12 hours
	Hand harvesting, hand pruning, thinning, tying, leaf pulling	0.2058**	8500	0.0680	294	8 days
	Cane turning and girdling in table grapes	0.0886**	19300	0.0664	301	16 days

* Peak DFR determined using the default 20% retained on foliage, 10% dissipation per day based on 3 applications at 1.4 µg/cm^2 made 7 days apart
** Peak DFR at the specified REI.
† Highest transfer coefficient for each crop group and activity
‡ Exposure = Peak DFR (µg/cm^2) * TC (cm^2/h) * 8 hours * 34% DA / 70 kg bw x 1000 µg/kg
¶ Based on a NOAEL of 20 mg/kg bw/day, the target MOE is 300
Shaded box denote that the MOE is below the target of 300 on the day of the last application.

Table 3.4.4 Postapplication Exposure and Risk Estimates for Workers Entering Treated Fields (Outdoor Ornamentals) Using Default Values

Crop	Re-entry activity	Peak DFR* ($\mu g/cm^2$)	Transfer Coefficient† (cm^2/h)	Dermal Exposure‡ (mg/kg bw/day)	MOE ¶	REI
Outdoor ornamentals (field and containers)	All	0.3686	400	0.0057	3 491	12 hours
Cut flowers	All	0.3686	4000	0.0573	349	12 hours

* Peak DFR determined using the default 20% retained on foliage, 10% dissipation per day based on 2 applications at 1.5 $\mu g/cm^2$ made 14 days apart

† Highest transfer coefficient for each crop group and activity

‡ Exposure = Peak DFR ($\mu g/cm^2$) * TC (cm^2/h) * 8 hours * 34% DA / 70 kg bw x 1000 µg/kg

¶ Based on a NOAEL of 20 mg/kg bw/day, the target MOE is 300

3.4.3. Residential Exposure and Risk Assessment

3.4.3.1 Handler Exposure and Risk

There are no domestic class products; therefore, a residential handler assessment was not required.

3.4.3.2 Postapplication Exposure and Risk

There is potential for acute/short-term and intermediate-term dermal exposure to adults and youth through contact with transferable residues following commercial application of fluopicolide on treated ornamentals. Residential postapplication exposure to ornamental plants is not expected to be significant for children and toddlers.

Postapplication risk estimates for adults and youth contacting foliage from treated ornamental plants are acceptable. Therefore, contact with the foliage of treated ornamentals is acceptable once residues have dried.

Table 3.4.5 Adult and Youth Postapplication Exposure on Residential Ornamentals

Formulation/ Rate	Treated Plants	Peak DFR [a] ($\mu g/cm^2$)	Transfer Coefficient (cm^2/h)	Dermal Exposure [b] (mg/kg/d)	MOE [c]
Adults (70 kg)					
liquid 1.5 $\mu g/cm^2$	Ornamental Flowers	0.3686	4000	0.0048	4 168
Youths (39 kg)					
liquid 1.5 $\mu g/cm^2$	Ornamental Flowers	0.3686	2756	0.0059	3 371

[a] Peak DFR calculated based on default 20% retained on foliage, 10% dissipation per day based on 2 applications at 1.5 $\mu g/cm^2$ made 14 days apart

[a] Dermal exposure = %DFR x rate x TC x 34% x duration / bw (70 kg for adults, 39 kg for youth) x 1000 µg/kg. Exposure duration is 0.67 hours. Transfer coefficients are scaled for the surface area of a 39 kg body weight

[b] Based on a NOAEL of 20 mg/kg bw/day, the target MOE is 300

3.4.3.3 Bystander Exposure and Risk

Bystander exposure is expected to be negligible since the potential for drift is expected to be minimal. Application is limited to agricultural crops only when there is low risk of drift to areas of human habitation or activity such as houses, cottages, schools and recreational areas, taking into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings.

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

The residue definition for enforcement in all crops (primary and rotational) is fluopicolide. The residue definition for risk assessment is fluopicolide and BAM in all primary crops, except tuberous and corm vegetables, and is fluopicolide, BAM and PCA in tuberous and corm vegetables. The residue definition for risk assessment is fluopicolide, BAM, 3-OH-BAM, PCA and P1X in all rotational crops. The LC/MS/MS Methods 00782 and the modifications M001, M002 and M003, and 1611-00.02 and 1629-00.00 are considered acceptable data gathering methods for residues of fluopicolide and metabolites in/on crop commodities. Method RM-43C-2 is acceptable as the enforcement method for residues of fluopicolide in/on crop commodities. The freezer storage stability data indicate that residues of fluopicolide, BAM and PCA are stable for 30 months in the processed commodities of wheat (flour, bran, shorts), tomato (paste, puree), sugar beet (refined sugar, molasses, dried pulp) and potato (dried flakes, chips, wet peel); residues of fluopicolide, BAM and PCA are stable for 30 months in grapes, wheat grain, potato tubers and cabbage leaves; residues of fluopicolide and BAM are stable in wheat straw for 41 months; and residues of P1X and 3-OH BAM are stable in wheat grain, straw and forage for 25 months. Additional freezer storage stability data will be required to support the maximum storage intervals of samples during some of the magnitude of the residues studies and during the field crop rotation trials study. In the processed commodities, residues of fluopicolide and PCA concentrated in pomace and yeast, and residues of fluopicolide, BAM and PCA concentrated in raisins from treated grapes; residues of fluopicolide concentrated in wet peel from potatoes; residues of fluopicolide concentrated in puree and paste of tomatoes; and residues of fluopicolide and BAM concentrated in the bran, middlings, shorts and germ, residues of PCA concentrated in the bran, middlings and shorts, residues of 3-OH-BAM concentrated in the bran, shorts and germ and residues of P1X concentrated in the bran and shorts of rotational wheat. Supervised residue trials conducted throughout the United States and Canada using end-use products containing fluopicolide at GAP or at exaggerated rates in or on root vegetables (Crop Subgroup 1A), leaves of root and tuber vegetables (Crop Group 2), bulb vegetables (Crop Group 3-07), leafy vegetables (Crop Group 4), brassica head and stem vegetables (Crop Subgroup 5A), potatoes, cucurbit vegetables (Crop Group 9), fruiting vegetables (Crop Group 8-09) and grapes are sufficient to support the proposed MRLs.

The residue definition in livestock is fluopicolide for enforcement, and fluopicolide and BAM for risk assessment. Method AR 303-02 (LC/MS/MS) is suitable as a data gathering method for the determination of fluopicolide residues in livestock matrices (milk meat and meat by-products) based on acceptable validation data. An enforcement method for residues of fluopicolide in livestock matrices is not required since finite residues of fluopicolide are not anticipated in feed commodities associated with the proposed uses. The freezer storage stability data indicate that residues of fluopicolide, BAM and PCA were stable in milk for 83 days; in muscle and fat for 4 months; and in liver and kidney for 9 months.

3.5.2 Dietary Risk Assessment

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.14), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

3.5.2.1 Chronic Dietary Exposure Results and Characterization

The refined chronic analysis assumed 100% crop treated, experimental processing factors (where available), and median values (STMdRs) for all plant commodities. The refined chronic dietary exposure from all supported fluopicolide food uses (alone) for the total population, including infants and children, and all representative population subgroups is ≤ 4.3% of the acceptable daily intake (ADI). Aggregate exposure from food and water is considered acceptable. The PMRA estimates that chronic dietary exposure to fluopicolide from food and water is 12.6% (0.008460 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for all infants (< 1 year) at 36.1% (0.024163 mg/kg bw/day) of the ADI.

3.5.2.2 Acute Dietary Exposure Results and Characterization

The refined acute analysis assumed 100% crop treated, experimental processing factors (where available), and maximum residue values for all plant commodities. The refined acute dietary exposure (food alone) for all supported fluopicolide registered commodities is estimated to be 10.46% (0.020915 mg/kg bw) of the acute reference dose (ARfD) for females 13–49 years old (95^{th} percentile, deterministic). Aggregate exposure from food and water is considered acceptable: 15.44% of the ARfD (0.03087 mg/kg bw) for females 13–49 years old.

3.5.3 Aggregate Exposure and Risk

The aggregate risk for fluopicolide consists of exposure from food and drinking water sources only.

3.5.4 Maximum Residue Limits

Table 3.5.1 Proposed Maximum Residue Limits

Commodity	Recommended MRL (ppm)
Leafy vegetables, except Brassica (Crop Group 4)*	25
Leaves of root and tuber vegetables (Crop Group 2)	15
Bulb vegetables (Crop Group 3-07)	7.0
Brassica head and stem vegetables (Crop Subgroup 5A)	5.0
Root vegetables (except sugar beet and carrot; Crop Subgroup 1A)	0.15
Potato**	0.02

*The proposed MRL of 16 ppm for head lettuce and leaf lettuce (PMRL2010-69) will be revised to accommodate an MRL on all commodities within Croup Group 4 (Leafy vegetables, except brassica).

**The proposed MRL for Tuberous and corm vegetables (except potatoes) (PMRL2010-69) will be extended to potato.

See Appendix III for a list of crop group commodities.

For additional information on MRLs in terms of the international situation and trade implications, refer to Appendix II.

The nature of the residues in animal and plant matrices, analytical methodology, field trial data, and the acute and chronic dietary risk estimates are summarized in Appendix I, Tables 1, 5 and 6.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Fluopicolide enters the terrestrial environment when it is used as a fungicide on a variety of crops and outdoor ornamentals. Based on its physical properties, fluopicolide has low solubility in water and has a low potential to volatilize from moist soil or water surfaces (Henry's Law Constant = 3.8×10^{-10} atm. m^3/mole). Hydrolysis and photolysis are not considered to be important routes of transformation for fluopicolide in the environment. Laboratory soil biotransformation studies conducted under aerobic conditions show that fluopicolide is persistent in soil (DT_{50} = 376 - 446 days). Only one major transformation product was identified in aerobic soil, BAM; in sandy clay loam soil BAM increased in sandy soil to a maximum of 40% AR after 369 days. PCA was identified as a minor transformation product in aerobic soil. Terrestrial field dissipation studies confirm that fluopicolide is persistent under field conditions and has the potential for carryover into the following growing season.

Adsorption data indicate that fluopicolide has medium to high mobility in soils (K_{oc} = 84–409); the potential mobility of fluopicolide is shown to decrease over time when soil is exposed to fluopicolide. Currently there are no available groundwater or surface water monitoring data for fluopicolide. The results of lysimeter studies conducted in Germany show that fluopicolide residues are capable of leaching through soil. The leaching assessment using groundwater ubiquity score (GUS[4]) also indicates that fluopicolide will leach in soil and satisfies most of the criteria of Cohen *et al*. 1984[5]. With its relatively low K_{oc} range (18–304), the transformation product BAM is expected to leach through soil and may reach groundwater under favourable conditions. This has been confirmed from water supply wells sampled in Europe, however, the BAM originated from the use of the herbicide dichlobenil and not fluopicolide. Groundwater modelling for the combined residues of fluopicolide and the major transformation product BAM, which utilized a scenario that would result in the conservative estimation of leaching, indicates that residues may reach groundwater. Based on Canadian and ecoregion relevant U.S. terrestrial field studies, however, fluopicolide residues were not detected beyond 30 cm soil depth.

Fluopicolide can enter aquatic environments through spray drift and run-off from the application site. Under aerobic and anaerobic conditions, fluopicolide is shown to dissipate slowly (DT50 = 848–1400 days and 2130 days, respectively), with significant partitioning of parent from the water phase to the sediment. BAM was identified as a major transformation product under aerobic aquatic conditions, reaching a maximum of 20% after 365 days in one test system, and is shown to partition mainly into the water phase. Under anaerobic conditions, BAM was < 3% over the 365 study period. PCA was identified as a minor transformation product under both aerobic and anaerobic conditions.

The log octanol/water partitioning coefficient for fluopicolide (K_{ow} = 2.9–3.2) suggests the potential for bioaccumulation in the food chain. However, the mean steady-state BCFs for edible tissue, nonedible tissue, and whole fish (40X, 175X, and 104X, respectively) indicate a low potential for bioconcentration in fish and living organisms. The short depuration half-lives of 0.51 days (low-dose) and 0.47 days (high dose) for total 14C-fluopicolide residues in whole fish also indicate that bioaccumulation is unlikely. Environmental fate data for fluopicolide and its transformation products, in the terrestrial and aquatic environment, are summarized in Appendix 1, Table 7 and 8, respectively.

[4] Gustafson, D.I. 1989. Groundwater ubiquity score: a simple method for assessing pesticide leachability. Environmental Toxicology and Chemistry, 8: 339–357.

[5] Cohen, S.Z., Creeger, S.M., Carsel, R.F., Enfield, C.G. 1984. Potential for pesticide contamination of groundwater resulting from agricultural uses. (PMRA 1573066).

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e. protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (e.g. direct application at a maximum cumulative 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 = 1). 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 (such as drift to non-target habitats) and might consider different toxicity endpoints. 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 Risks to Terrestrial Organisms

A risk assessment of fluopicolide to terrestrial organisms was based upon an evaluation of toxicity data for the following:

- one earthworm species, (acute and chronic exposure)
- one bee and three beneficial arthropod species (acute exposure)
- two bird species (acute, reproduction exposure)
- one mammal species (acute, reproduction exposure)
- ten plant species (seedling emergence and vegetative vigor)

A summary of terrestrial toxicity data for fluopicolide is presented in Appendix 1, Table 9. For the assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with fluopicolide.

Terrestrial Invertebrates

The screening level risk assessment for terrestrial invertebrates is summarized in Appendix 1, Table 10. Earthworms are at negligible risk of ecological effects from exposure to fluopicolide as the risk quotients are several orders of magnitude lower than the level of concern (RQ = < 0.0004 and 0.003 for acute and chronic effects, respectively). For acute contact and oral toxicity to bees the LD_{50} is > 100 and >241 µg a.i./bee, equivalent to 112 and 270 kg a.i./ha, respectively. These values are approximately 800 and 1900 times the maximum single application rate for fluopicolide (140.2 g a.i./ha), therefore, there is a negligible risk of acute adverse effects to honey bees due to exposure to fluopicolide (RQ < 0.0012 and 0.0005, respectively).

Toxicity data for beneficial arthropods are not available for fluopicolide as a sole active ingredient but are available based on formulated products containing fluopicolide and additional active ingredients. The toxicity studies consisted of laboratory and extended laboratory studies conducted with the parasitic wasp *Aphidius rhopalosiphi*, the predatory mite *Typhlodromus pyri*, and a standard laboratory limit test conducted with the common green lacewing *Chrysoperla carnea*; the LR50 endpoints for the extended laboratory for *A. rhopalosiphi* and *T. pyri* were >500 and >260 g fluopicolide/ha, and the LR50 was >400 g fluopicolide/ha for *C. carnea* (limit test). Given that these endpoints exceed the maximum single application rate for fluopicolide, 140.16 g a.i/ha, fluopicolide is expected to pose a negligible risk to beneficial arthropods.

Terrestrial Plants

Non-target plants could be exposed to fluopicolide by overspray and spray drift. The risk to non-target plants was assessed based on an EC25 of > 133 g a.i./ha from seedling emergence and vegetative vigor limit tests for ten plant species (4 monocots and 6 dicots). This rate is representative of the proposed maximum single crop application rate (140.2 g a.i./ha). At the maximum seasonal rate of 420.5 g a.i/ha, the risk quotient (RQ < 3.2) may exceed the PMRA's level of concern.

An off-field assessment of the risk to terrestrial plants was conducted taking into consideration the concentrations of fluopicolide that could be deposited in a terrestrial habitat directly adjacent to and downwind of the treated field as a result of spray drift. The percent drift expected from the use of ground-boom sprayer equipment and aerial application using a medium ASAE (American Society of Agricultural Engineers) droplet size, is 6 and 23%. At the maximum seasonal crop application rate of 420.5 g a.i./ha, the risk quotients for spray drift are < 0.2 and <0.7 for ground and aerial application, respectively. Fluopicolide is not expected to pose a risk to non-target terrestrial from spray drift.

Terrestrial vertebrates

Wild birds and mammals may be exposed to residues of fluopicolide as a result of sprayed vegetation and/or contaminated prey. Standard exposure scenarios on vegetation and other food sources based on correlations in Hoerger and Kenaga (1972)[6] and Kenaga (1973)[7] and modified according to Fletcher *et al.* (1994)[8] were used to determine the concentration of pesticide in the diet of small wild birds and mammals. Exposure is dependent on the body weight of the organism and the amount and type of food consumed. In the screening level assessment a set of generic body weights was used for birds and mammals (20, 100 and 1000 g, and 15, 35, 1000 g, respectively) to represent a range of small wild bird and small mammal species. It is noted that diets of animals can be highly variable from season to season as well as day to day. Furthermore, animals are often opportunists and if they encounter an abundant and/or desirable food source, they may consume large quantities of that food. For these reasons, the screening level assessment uses relevant food categories or feeding guilds for each size group consisting of 100% of a particular dietary item. At the screening level, only one feeding guild for each category of bird and mammal weights is selected. The selected feeding guilds are relevant to each specific size of bird or mammal and based on the most conservative residue values (maximum residues determined in the Hoeger and Kenega nomogram). A diet consisting of 100% plant material is not considered realistic for small and medium sized birds (20 and 100 g) and small mammals (15 g) and, therefore, was not included in the determination of estimated daily exposures (EDEs). The most conservative exposure estimate for these categories of bird and mammal weights is associated with a diet comprised of 100% small insects.

The 'leaves and leafy crops' category of the nomogram is associated with the highest exposure estimate in the assessment (i.e. 300 mg a.i./kg dw diet). This category of vegetation is defined by plants with very high moisture content (comparable to lettuce and cabbage). It is very unlikely that the diets of birds and mammals would be made up of an important proportion of this food item as these do not contain sufficient nutrients to meet their daily energy requirements. However, it is thought to be possible that small herbivorous mammals would feed on these crops in some situations; even though these crops may not meet all the energy requirements of a small mammal, these represent an abundant and easily accessible source of food. Both fluopicolide end-use products, Fluopicolide 4 SC Fungicide and Presidio Fungicide, are proposed for use on lettuce. Therefore, for the screening level assessment, a diet of 100% leaves and leafy crops is considered for 35 and 1000 g mammals.

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6 Hoerger F; Kenaga EE. 1972. Pesticide residues on plants: correlation of representative data as basis for estimation of their magnitude in the environment. *In*: Coulston F; Korte F. (eds). Global aspects of chemistry, toxicology and technology as applied to the environment, Vol. I. Thieme, Stuttgart, and Academic Press, New York. pp. 9-28. (PMRA 1918526)

7 Kenaga EE. 1973. Factors to be considered in the evaluation of the toxicity of pesticides to birds in their environment. In: Coulston F; Dote F. (eds). Global aspects of chemistry, toxicology and technology as applied to the environment, Vol. II. Thieme, Stuttgart, and Academic Press, New York. pp. 166-181. (PMRA 1918527)

8 Fletcher, J.S., Nellessen, J.E., and Pfleeger, T.G. 1994. Literature review and evaluation of the EPA food-chain (Kenaga) nomogram, an instrument for estimating pesticide residues on plants. Environmental Toxicology and Chemistry 13:1383-1391. (PMRA 1918522)

A similar assessment for birds is not necessary as birds are not known to purposely feed on lettuce-type crops (only some incidental ingestion has been noted when birds are feeding on insect pests on the crop; birds may also feed on young shoots of various types of crop, which would be more similar to grass-like vegetation or forage crops). For birds (1000 g), a diet of 100% short grass is considered for the screening level assessment.

The screening level EDEs were calculated based on the maximum residue values in food items at the highest cumulative fluopicolide application rate for vegetables. The maximum season application rate for vegetables is 420.5 g a.i./ha; single applications rates can be made at 105.6–140.2 g a.i./ha at seven day intervals. The proposed product labels state that no more than two sequential applications can be made before alternating with an effective fungicide from a different resistance management group. Therefore, EECs were calculated based on two applications of 140.2 g a.i./L with a seven day interval followed by a 14 day interval (during which an alternate fungicide would be used), then a final application at 140.2 g a.i./ha. A default foliar dissipation half-life of 10 days was used to estimate the number of days that residues remain on food items. This value is based on the foliar dissipation of a variety of active ingredients reported by Willis and McDowell (1987)[9], with 93% of the foliar dissipation half-life of 10 days is considered to be a reasonable estimate of typical foliar half-lives.

The calculated screening level risk quotients for birds and mammals are shown in Appendix 1, Table 11 and 12, respectively. For birds and mammals feeding on-field, the level of concern is not exceeded for acute and reproductive effects with the following exception: for reproductive effects, the LOC is slightly exceeded for 35 g mammals feeding on leafy foliage (RQ = 1.06).

The reproductive NOEL used for the mammalian screening level risk assessment (36.4 mg a.i./kg bw/day) is based on decrease body weights observed in rat offspring at a much higher dose concentration (LOEL = 145 mg a.i./kg bw/day); at this dose concentration, the decrease in body weights observed were very low (8 - 9% and 10 - 13% in F1 and F2 pups at 14, 21 and 28 days). The mammalian reproductive endpoint of 36.4 mg a.i./kg bw/day, therefore, is considered to be highly conservative for the risk assessment and may greatly overestimate the reproductive risk to mammals. In addition, the screening level assessment assumes a diet of 100% leafy foliage. Given that small herbivorous mammals are unlikely to feed exclusively on these crops and that other vegetative food items do not exceed the LOC, the screening assessment is representative of a highly conservative scenario. Although the screening level RQ value for reproductive effects in 35 g mammals feeding on leafy foliage is slightly exceeded, (RQ = 1.06), this risk is not likely to manifest itself in the field.

Fluopicolide is expected to pose negligible risk to birds or mammals feeding on or adjacent to treated fields.

[9] Willis, G.H. and L.L. McDowell, 1987. Pesticide Persistance on Foliage. Reviews of Environmental Contamination and Toxicology, Vol. 100. (PMRA 1930629)

4.2.2 Risks to Aquatic Organisms

A risk assessment for fluopicolide to aquatic organisms was based upon an evaluation of toxicity data for the following:

- one freshwater invertebrate species (acute and chronic exposure)
- five freshwater fish species (acute and chronic exposure)
- three freshwater algae species (acute exposure)
- one freshwater vascular plant species (acute exposure)
- two estuarine/marine invertebrate species (acute exposure)
- Two estuarine/marine fish species (acute exposure)
- one estuarine marine algae species (acute exposure)

Additional toxicity data were also available for the major transformation product BAM; the risk assessment for BAM to aquatic organisms was based upon an evaluation of toxicity data for one freshwater invertebrate species (acute), one freshwater fish species (acute and chronic exposure), one freshwater algal and diatom species (acute) and one vascular plant species (acute). A summary of aquatic toxicity data for fluopicolide and BAM is presented in Appendix 1, Table 9.

Screening Level Assessment
Aquatic organisms can be exposed to fluopicolide as a result of drift and run-off. To assess the potential for effects from exposure to fluopicolide, screening level EECs in the aquatic environment based on direct application to water were used as exposure estimates. The calculated EECs were those determined in 15 cm body of water for amphibians and 80 cm body of water for all other aquatic organisms. The highest cumulative fluopicolide application rate was chosen to calculate the screening level EECs; dissipation between applications was determined by using the most conservative whole system DT50 available from aerobic water sediment studies (SFO DT50 = 1400 d).

Detailed screening level assessments of the risk from fluopicolide and the transformation product BAM to aquatic organisms are summarized in Appendix 1, Table 13. For fluopicolide, the risk quotients indicate that the LOC for acute effects is exceeded for freshwater fish and for marine and estuarine fish and algae (RQ = 1.4, 1.3 and 2.4, respectively). Although no amphibian data were available, effects were estimated from fish toxicity data (1/10 LC50, acute; NOEC early life stage test, chronic); the LOC was exceeded in amphibians for both acute and chronic effects (RQ = 8.0 and 1.9, respectively).

For BAM, the risk quotients show that the LOC for effects are not exceeded for freshwater organisms.

Spray drift risk assessment

The risk to aquatic organisms was further characterized by taking into consideration the concentrations of fluopicolide that could be present in aquatic habitat directly adjacent to the site of application through drift of spray. The spray drift data of Wolfe and Caldwell (2001)[10] was used to determine that the maximum amount of spray deposited into a habitat adjacent to a field sprayed using ground boom equipment. The maximum amount of spray that is expected to deposit one metre downwind from the application site during spraying using ground boom equipment and a medium droplet size (ASAE) will not exceed 6%. Similarly, it was estimated from the data of Ganzelmeier et al. (1995)[11] that the maximum amount of spray deposited into a habitat adjacent to an orchard sprayed using airblast equipment will not exceed 74% of the applied application rate for early applications and 59% of the applied application rate for late applications. Aerial application spray drift was determined through model simulations using AGDISP v. 8.15; the maximum amount of spray that is expected to deposit one metre downwind from the application site during aerial spraying and a medium droplet size (ASAE) will not exceed 23%. This information was used to determine the risk to aquatic habitats adjacent to sites where fluopicolide is applied. The highest cumulative fluopicolide application rate was chosen to calculate the EECs; dissipation between applications was determined by using the most conservative whole system DT50 available from aerobic water sediment studies (SFO DT_{50} = 1400 d).

The risk assessment for non-target aquatic organisms exposed to fluopicolide from spray drift is summarized in Appendix 1, Table 14. Spray drift from ground applications of fluopicolide are expected to pose a negligible risk to aquatic organisms. The risk quotients for airblast use show that the LOC for acute effects is exceeded in amphibians (RQ = 4.0–5.3) and marine algae (1.5–1.8); the LOC for chronic effects is exceeded for amphibians (RQ = 1.0–1.4). For aerial use, the risk quotients show that the LOC for acute effects is exceeded in amphibians (RQ = 1.6). In order to reduce the potential risk of fluopicolide to aquatic species from airblast and aerial applications, spray buffer zones are required.

Run-off risk assessment

Aquatic organisms can also be exposed to fluopicolide from foliar applications as a result of runoff into a body of water. The linked models PRZM (Pesticide Root Zone Model) and EXAMS (Exposure Analysis Modeling System) were used to predict EECs resulting from runoff of fluopicolide following application.

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[10] Wolf, T and B.C. Caldwell, 2001. Development of a Canadian spray drift model for the determination of buffer zone distances. *In* Expert Committee on Weeds, Proceedings of the 2001 National Meeting, Quebec City, Sainte Anne de Bellevue, Quebec: ECW-CEM. D. Bernier, DRA Campbell, D. Cloutier, Eds

[11] Ganzelmeier, H; Rautmann, D; Spangenberg, R; Streloke, M; Herrmann, M; Wenzelburger, H-J; Walter, H-F 1995. Studies on the spray drift of plant protection protection products: Results of a test program carried out throughout the Federal Republic of Germany. Report Number 305 from the Biologischen Bundesanstalt fur Land-und Forstwirtschaft, Berlin-Dahlem. Blackwell Wissenschafts-Verlag GmbH, Berlin/Vienna.

The fluopicolide EECs in a 1-ha receiving water body and at two depths (80 and 15 cm deep) predicted by PRZM-EXAMS for crop applications are presented in Table 4.2.1 below. The values reported by PRZM/EXAMS are 90th percentile concentrations of the concentrations determined at a number of time-frames including the yearly peak, 96-hour, 21-day, 60-day, 90 -day and yearly average.

Table 4.2.1: Ecoscenario water modelling EECs (µg a.i./L) for fluopicolide in water bodies 80 and 15 cm deep, excluding spray drift

Region (Scenario)	EEC (µg a.i./L)					
	Peak	**96-hour**	**21-day**	**60-day**	**90-day**	**Yearly**
80 cm water body						
BC (Rasp-BC)	1.3	1.3	1.2	1.1	1.1	0.70
BC (Potato-MB)	22	21	21	20	19	15
Prairie (Potato-MB)	26	26	25	24	23	15
ON (Corn-ON)	18	17	16	15	15	11
QC (Corn-QC)	13	13	12	12	11	9.3
Atlantic (Potato-PEI)	21	20	18	17	17	12
15 cm water body						
BC (Rasp-BC)	6.6	5.7	4.2	3.4	3.2	2.4
BC (Potato-MB)	89	82	71	65	62	54
Prairie (Potato-MB)	115	106	90	78	73	58
ON (Corn-ON)	78	73	57	50	48	38
QC (Corn-QC)	61	55	46	41	40	25
Atlantic (Potato-PEI)	96	85	66	58	55	44

The EECs used for calculation of the RQs were the highest values at the appropriate depth and appropriate time-frame. The screening level risk assessment indicated that the registered application rates of fluopicolide formulations would pose an acute risk to some freshwater and marine organisms. The acute RQ values, based on the aquatic ecoscenario modelling EECs for these aquatic organisms are reported in Appendix 1, Table 15. The RQ for acute effects in amphibians exceeds the LOC (RQ = 2.7).

4.2.3 Incident Reports

As fluopicolide is a new active proposed for use in Canada, no incidents with fluopicolide exist in the Canadian pesticide incident reporting system. Fluopicolide is registered for crop use in the U.S. No environmental incident reports were found for fluopicolide in the USEPA Ecological Incident Information System (EIIS) database.

5.0 Value

5.1 Effectiveness Against Pests

5.1.1 Acceptable Efficacy Claims

5.1.1.1 Control of downy mildew (*Peronospora parasitica*) on brassica (head and stem) vegetables and brassica root vegetables

Results from three trials conducted on collard (two trials) and broccoli in the U.S. (CA and South Carolina) were reviewed. In one broccoli trial under moderate disease pressure, Presidio™ Fungicide reduced downy mildew severity by 73 and 87% on upper leaves or by 90 and 95% on lower leaves at the rates of 105 and 140 g a.i./ha, respectively, when combined with Bravo® 500 (Registration Number 15723). Bravo® 500 alone reduced disease severity by 35% on upper leaves and 26% on lower leaves. In one collard trial under low disease pressure, Presidio™ Fungicide reduced downy mildew severity by 81% at the rate of 105 g a.i./ha, compared to 56% disease reduction in the commercial standard Aliette® Wettable Powder Systemic Fungicide (Registration Number 24564). The tank-mix of Presidio™ Fungicide at 140 g a.i./ha with K-Phite 7LP (containing 56% phosphorous acid, not registered in Canada) demonstrated the same level of disease control as Presidio™ Fungicide at 105 g a.i./ha alone. K-Phite 7LP alone reduced disease severity by 69%. In another collard trial, Presidio™ Fungicide at 105 g a.i./ha reduced downy mildew AUDPC (area under the disease progress curve) by 30%, and the weight of diseased leaves were also significantly reduced compared to the non-treated check. The claim is conditionally supported, pending three additional trials on cabbage, radish and/or turnip to confirm the efficacy.

5.1.1.2 Control of downy mildew (*Pseudoperonospora cubensis*) on cucurbit vegetables

Results from six trials conducted on cucumber and two trials on squash in Ontario and the U.S. (OH, MI, NC and NY) were reviewed. All eight trials on cucumber and squash were conducted under moderate to high disease pressure. Presidio™ Fungicide reduced downy mildew severity by 64–99% at both proposed rates (105–140 g a.i./ha). In three out of five trials, Presidio™ Fungicide applied at the high proposed rate reduced downy mildew severity by 88–99% (average of 94%) compared to the non-treated control. Various commercial standards, such as Ranman™ 400 SC Agricultural Fungicide (Registration Number 27984), Bravo® 500 and Reason™ 500 SC Fungicide (Registration Number 27462), were applied in these trials; however, their efficacy varied from no effect to good control (91%). The performance of these commercial standards was generally low (between 61% and 65%). Presidio™ Fungicide was also tested at the rates below and above the proposed rates in four trials. The level of disease control was 69% when applied at the rate of 70 g a.i./ha in four trials, while it was only 54% at the rate of 35 g a.i./ha in one trial. The lowest effective rate (LER) was well established based on the cucumber trials. Presidio™ Fungicide at the rate of 210 g a.i./ha reduced disease severity by 81%, which was numerically better than the proposed high rate but was not statistically different. In two squash trials, Presidio™ Fungicide was only applied at the low proposed rate (105 g a.i./ha), which reduced downy mildew severity by 67% on average. Two commercial standards Cabrio™ EG Fungicide (Registration Number 27323) and Tanos® 50 DF Fungicide (Registration Number

27435) failed to control the disease, while Revus® Fungicide (Registration Number 29074) reduced disease severity by 82% in one trial. The claim is supported at the rates of 105–140 g a.i./ha.

5.1.1.3 Suppression of phytophthora blight/crown rot (*Phytophthora capsici*) on cucurbit vegetables

Results from two trials conducted on squash in the U.S. (MI) were reviewed. Both trials were conducted under high disease pressure. Presidio™ Fungicide reduced disease severity by 46% and 63% at both proposed rates (105 - 140 g a.i./ha). Several conventional fungicides were compared in the trials, however, only Revus® Fungicide is currently registered for suppression of phytophthora blight on pepper. Revus® Fungicide reduced disease severity by 62% and 66% in these trials. The treatment with Presidio™ Fungicide increased yield and decreased infected fruits at harvest in both trials. Presidio™ Fungicide also showed similar effect on phytophthora blight on pepper and tomato as reviewed under the claims of fruiting vegetables.

Phytophthora blight, caused by *Phytophthora capsici,* is a disease that is very difficult to control since the pathogen has a wide host range and survives for a long time in the soil. Moreover, the development of resistance to fungicides is also an issue for this disease. In Canada, Revus® Fungicide is the only product currently registered for suppression of this pathogen on pepper. The efficacy of fluopicolide on *P. capsici* has been reported recently in a research publication (Jackson *et al.* 2010), in which fluopicolide effectively suppressed *P. capsici* on squash in both laboratory and field evaluations. Under field conditions, fluopicolide applied at 86.6 or 115.4 g/ha consistently reduced disease incidence by 44 - 59% in field trials conducted in the U.S. (GA) in 2008 and 2009. Based on the information reviewed, the claim is conditionally supported, pending three additional trials on pumpkin and/or eggplant to confirm the efficacy. The tank-mix claim for phytophthora blight on cucurbit vegetables is not supported as there are no other products currently registered for control of this disease in Canada. Since there are no products currently registered, a maximum of two applications per season is accepted for phytophthora blight on cucurbit vegetables.

5.1.1.4 Control of late blight (*Phytophthora infestans*) on tomato

There were no efficacy data submitted, however, the applicant intended to extrapolate the data from potato to support this claim. Since the claim for control of late blight (*Phytophthora infestans*) on potato can be supported at the proposed rates (105–140 g a.i./ha), late blight occurs similarly on tomato, the extrapolation from potato to tomato is supported. However, other crops within the fruiting vegetable crop group are not hosts of *P. infestans;* extrapolation to the crop group is not supported. The claim is supported on tomato only at the rates of 105–140 g a.i./ha.

5.1.1.5 Suppression of phytophthora blight (*Phytophthora capsici*) on pepper

Results from three trials conducted on pepper and tomato in the U.S. (GA and NJ) were reviewed. All three trials were conducted under moderate to high disease pressure. Presidio™ Fungicide provided good control at all rates in one pepper trial, where the number of infected fruits was reduced by 93 - 96%. However, Presidio™ Fungicide only partially suppressed disease in the other two trials. Presidio™ Fungicide reduced disease infection by 41–60% at the high proposed rate, and reduced disease by 27 - 57% at the low proposed rate. The lowest rate (70 g a.i./ha) did not provide disease control in the trial. Similar levels of disease suppression were also observed in fungicide programs including Presidio™ Fungicide, however, the performance of Presidio™ Fungicide in the spraying programs could not be reviewed because other conventional fungicides were used in the programs as well. There was no commercial standard included in any of the three trials.

Presidio™ Fungicide showed suppression on phytophthora blight on squash as reviewed under the claims of cucurbit vegetables. *P. capsici* does not cause substantial crop damage on tomato and other fruiting vegetables. Revus® Fungicide is the only other registered product for this use on pepper. The claim is fully supported on pepper only.

5.1.1.6 Control of downy mildew (Plasmopara viticola) on grape

Results from four trials conducted in Ontario and the U.S. (NY) were reviewed. All four trials were conducted under moderate to high disease pressure. Presidio™ Fungicide significantly reduced downy mildew at all rates applied. In three trials, Presidio™ Fungicide provided 100% control at the rates between 101 and 140 g a.i./ha with two applications, compared to the commercial standard Supra Captan 80 WDG (Registration Number 24613) with 91% (82–100%) disease control in the same trials. The claim is fully supported on grape.

5.1.1.7 Control of downy mildew (*Bremia lactucae, Peronospora farinosa*) on leafy vegetables (except brassica vegetables)

Results from six trials conducted on lettuce (five trials) and spinach in the U.S. (AZ, CA and FL) were reviewed. All trials were conducted under moderate to high disease pressure. In three trials, Presidio™ Fungicide provided 92% (88–99% in severity) control at the proposed high rate (140 g a.i./ha), which was comparable to the commercial standard Aliette® Wettable Powder Systemic Fungicide with 88% (82–94%) disease control in the same trials. Presidio™ Fungicide suppressed downy mildew by 74% (67–80% in severity) at the proposed high rate in other three trials, and suppressed or controlled disease by 70% or 98% at the proposed low rate (105 g a.i./ha) in two trials. Presidio™ Fungicide only suppressed downy mildew by 74% when applied at the rate of 70 g a.i./ha in one trial. The pathogen *Bremia lactucae* was tested in all five trials on lettuce, while *Peronospora farinosa* was tested in the trial on spinach. The claim is supported on leafy vegetables.

5.1.1.8 Control of late blight (*Phytophthora infestans*) on potato

Results from four trials conducted in British Columbia and Prince Edward Island were reviewed. All trials were conducted under high disease pressure. The commercial standards Bravo® 500 and Polyram® 16 Dust Fungicide (Registration Number 22029) were applied, however, both failed to control late blight disease with only 6 - 41% control in most cases. Bravo® 500 only suppressed late blight by 75 - 83% in one trial when it was applied at 1.2 or 3.5 L/ha, respectively. Presidio™ Fungicide at a reduced rate (63 g a.i./ha) partially suppressed the disease by 57% (54–63%) in three trials and controlled the disease by 85% in one trial.

Low water spray volume of 50 L/ha was compared with the regular volumes of ground application using Presidio™ Fungicide at 105 g a.i./ha in these trials. Low volume provided 87% (73–95% in severity) control, which was comparable to the regular volume treatment. The tank mixing of Presidio™ Fungicide with Bravo® 500 also provided numerically slightly higher but comparable results to Presidio™ Fungicide alone. Increases in yield over the non-treated control were observed in all rates of Presidio™ Fungicide, and were statistically significant in three out of four trials. The claims for control of late blight (*Phytophthora infestans*) and aerial application on potato are fully supported.

5.1.1.9 Control of downy mildew (*Peronospora* spp.) on field and container grown outdoor ornamentals (bedding plants and cut flowers)

Results from ten trials conducted on coleus (two trials), snapdragon (three trials), rose (three trials) and lamium (two trials) in British Columbia and the U.S. (MI) were reviewed. Two trials on coleus were conducted under high disease pressure. The drench application was applied in both trials. Presidio™ Fungicide provided 83% (73 and 92% in severity) and 100% control at the proposed rates of 105 and 140 g a.i./ha, respectively. Presidio™ Fungicide, at a rate lower than proposed (79 g a.i./ha), provided 88% disease control in one trial and only 56% control in another trial. The species of *Peronospora* was not identified in both trials.

Three trials on snapdragon were conducted under disease pressure at 6% in severity (5–9%) in the non-treated control. Presidio™ Fungicide was applied as foliar applications. Presidio™ Fungicide provided 87% (73–98% in severity) and 96% (93–100% in severity) control at the proposed rates of 105 and 140 g a.i./ha, respectively. Presidio™ Fungicide at the low rate (79 g a.i./ha) provided 94% disease control in two trials and zero control in one trial. The reduced efficacy was also observed when Presidio™ Fungicide was only applied once. The commercial standard Acrobat 50WP Fungicide (Registration Number 27700) reduced disease severity by 83% (76–86%) in the same trials. *Peronospora antirrhini* was the causal pathogen in all three trials.

Three trials on rose were conducted under high disease pressure. In all three trials, Presidio™ Fungicide provided disease control for up to 14 or 21 days after the second foliar application, and reduced disease severity by 80–100% at the proposed rates (105–140 g a.i./ha) in two out of the three trials. Presidio™ Fungicide at the low rate (79 g a.i./ha) provided no control in two trials and suppression (71%) in one trial. The commercial standard Acrobat 50WP Fungicide only partially suppressed disease severity by 53% in one trial. *Peronospora sparsa* was identified as the causal pathogen in all three trials.

Two trials on lamium were conducted under moderate disease pressure. Presidio™ Fungicide was applied as foliar applications. Presidio™ Fungicide provided 71% and 95% control at the proposed rates of 105 and 140 g a.i./ha, respectively. Presidio™ Fungicide at the low rate (79 g a.i./ha) provided 83% disease control in two trials. The reduced efficacy was also observed when Presidio™ Fungicide was only applied once. The commercial standard Acrobat 50WP Fungicide reduced disease severity by 79% (72 and 86%) in the same trials. *Peronospora lamii* was the causal pathogen in both trials. The claim is supported on field and container grown outdoor ornamentals (bedding plants and cut flowers). In addition, both foliar and drench applications are supported.

5.1.1.10 Suppression of phytophthora crown and root rot (*Phytophthora* spp.) on field and container grown outdoor ornamentals (bedding plants and cut flowers)

Results from seven trials conducted on gerbera (four trials), snapdragon (two trials) and poinsettia (one trial) in the U.S. (MI and NC) were reviewed. Four trials on gerbera were conducted under high disease pressure. Presidio™ Fungicide provided 71% (55–90% in severity) and 75% disease suppression of foliar symptoms, 67% (60 - 70% in severity) and 80% disease suppression of root rot at the proposed rates of 60 and 118 mL in 380 L water, respectively. Presidio™ Fungicide at a very low rate (30 mL in 380 L water) provided partial disease suppression (63% disease reduction on leaves and 51% on root) in three trials. Presidio™ Fungicide partially suppressed disease (54%) in two trials, and did not control the disease in the other two trials. The efficacy was comparable to Subdue Maxx Fungicide (Registration Number 27055) which is currently registered for suppression of phytophthora crown and root rot on ornamental plants. *Phytophthora cryptogea* and *Phytophthora drechsleri* were the causal pathogens identified in these trials.

Two trials on snapdragon were conducted under moderate to high disease pressure. Presidio™ Fungicide at two rates (30 and 60 mL in 380 L water) provided the same level of disease control (89 and 90%) in both trials. The efficacy of Presidio™ Fungicide was the same as the commercial standard Subdue Maxx Fungicide. *Phytophthora nicotianae* was the pathogen identified in both trials.

One trial on poinsettia was conducted under high disease pressure. Presidio™ Fungicide at two rates (30 and 60 mL in 380 L water) provided the same level of disease suppression (78%) in both trials. The efficacy of Presidio™ Fungicide was the same as the commercial standard Subdue Maxx Fungicide. *Phytophthora drechsleri* was the pathogen identified in the trial.

Three species of *Phytophthora* were tested in these trials. However, two important *Phytophthora* species on ornamentals, including *P. ramorum* and *P. parasitica* should be tested in order to support the claim on field and container grown outdoor ornamentals (bedding plants and cut flowers). In addition, ornamental trees and shrubs were not tested in the trials. Ornamental trees and shrubs represent some high value outdoor ornamental plants, and the plant biology would be very different from the plants tested in the efficacy trials, as such, the claim on ornamental trees and shrubs can not be supported. The claim is conditionally supported on field and container grown outdoor ornamentals (bedding plants and cut flowers), pending two additional trials on ornamental plants infected by *P. ramorum* and *P. parasitica*. Both foliar and drench applications are supported.

5.1.1.11 Presidio™ Fungicide and Fluopicolide 4 SC Fungicide tank-mix with Aliette® Wettable Powder Systemic Fungicide, Bravo® 500 and Supra Captan 80 WDG fungicides

Presidio™ Fungicide and Fluopicolide 4 SC Fungicide is only to be used as a tank-mix with other registered fungicides with a different mode of action when there are registered alternatives available. The efficacy and compatibility of tank mixes of Presidio™ Fungicide with Aliette® Wettable Powder Systemic Fungicide, Bravo® 500 and Supra Captan 80 WDG were demonstrated in various trials on broccoli, cucumber, potato, spinach and squash. The label rates were proposed for all tank-mix recommendations. The use of Presidio™ Fungicide and Fluopicolide 4 SC Fungicide as a tank-mix partner is supported on all crops except phytophthora blight/crown rot on cucurbit vegetables, which does not have another product currently registered for control of this disease in Canada.

The tank-mix claim for downy mildew (*Peronospora* spp.) on field and container grown outdoor ornamentals (including bedding plants and cut flowers) is not supported as there are no other products currently registered for control of this disease in Canada.

5.2 Phytotoxicity to Host Plants

There were no reports of phytotoxicity to the crops tested in any of the trials submitted.

5.3 Economics

No market analysis was done for this application.

5.4 Sustainability

5.4.1 Survey of Alternatives

Refer to Appendix I, Table 17 for a summary of the active ingredients currently registered for the same uses as Presidio™ Fungicide and Fluopicolide 4 SC Fungicide.

5.4.2 Compatibility with Current Management Practices Including Integrated Pest Management

The use of Presidio™ Fungicide and Fluopicolide 4 SC Fungicide is compatible with current integrated pest management practices and production practices.

5.4.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

Presidio™ Fungicide and Fluopicolide 4 SC Fungicide contain fluopicolide, a Group 43 Fungicide (belonging to pyridinylmethyl benzamides chemical group). Risk of the development of pest resistance for fluopicolide is unknown at this time, as this represents a fairly new mode of action. Use pattern rates and maximum yearly applications have been chosen to minimize resistance development. There is currently no known/documented resistance to this active ingredient globally.

Proposed label statements, which will aid in resistance management, include applying no more than two sequential applications of Presidio™ Fungicide or Fluopicolide 4 SC Fungicide before alternating with an effective fungicide from a different resistance management group. Presidio™ Fungicide and Fluopicolide 4 SC Fungicide must be used as a part of an integrated pest management program. Presidio™ Fungicide and Fluopicolide 4 SC Fungicide is to be applied as a foliar spray or soil drench in a tank-mix with another labelled fungicide product with a different mode of action on the same target pathogen when there is an alternative available.

5.4.4 Contribution to Risk Reduction and Sustainability

Presidio™ Fungicide and Fluopicolide 4 SC Fungicide offer an additional tool to Canadian growers for disease and resistance management, particularly for the control of downy mildew on various vegetable crops as well as late blight on potato and tomato. Presidio™ Fungicide and Fluopicolide 4 SC Fungicide are most effective when applied in a regularly scheduled spray program and are to be used as a tank-mix partner with other registered fungicides with a different mode of action.

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 [those that meet all four criteria outlined in the policy, i.e., 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*].

During the review process, fluopicolide and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[12] and evaluated against the---- Track 1 criteria. The PMRA has reached the following conclusions:

- Fluopicolide does not meet all Track 1 criteria, and is not considered a Track 1 substance. See Appendix 1, Table 16 for comparison with Track 1 criteria.
- Fluopicolide does not form any transformation products that meet all Track 1 criteria.

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

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[13]. The list is used as described in the PMRA Notice of Intent NOI2005-01[14] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02[15], 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:

- Technical grade fluopicolide and its end-use products do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette.*

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for fluopicolide is adequate to define the majority of toxic effects that may result from exposure to fluopicolide. In subchronic and chronic studies on laboratory animals, the primary target was the liver in all tested species and also the kidneys in the rat. Most of the liver effects were considered to be adaptive and non-adverse. Typical liver effects were increased weights and centrilobular hepatocytic hypertrophy, while the kidney effects were cortical tubular basophilia and cortical tubules with hyaline droplets, hyaline tubular casts, hyperplasia of the papillary epithelium with mineralization of the latter. There was no evidence of carcinogenicity in rats after longer-term dosing. There was an increased incidence of hepatocellular adenomas seen at the high dose in mice, but this was not considered relevant for human risk assessment as the maximum tolerated dose was exceeded and fluopicolide was not considered genotoxic from the weight of evidence in genotoxicity and mechanistic studies. There was no evidence of increased susceptibility of the young in the reproduction study, but serious adverse effects were noted in the developmental toxicity studies in both species tested. Malformations were seen in the rat development toxicity study at the highest dose tested and in the presence of maternal toxicity and abortions occurred in the rabbit developmental toxicity study at maternally toxic levels. Fluopicolide is not considered to be a neurotoxicant.

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[13] *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.*

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

[15] DIR2006-02, PMRA Formulants Policy.

Mixers, loaders and applicators handling fluopicolide and workers re-entering treated fields and nurseries are not expected to be exposed to levels of fluopicolide that will result in unacceptable risk when Fluopicolide 4 SC Fungicide or Presidio™ Fungicide are used according to label directions. The personal protective equipment on the product labels is adequate to protect workers.

Risk to workers re-entering treated areas is not of concern as long as the specified restricted-entry intervals are observed. Risk for adults and youth entering treated ornamental gardens is not of concern on the day of application.

The nature of the residue in plants and animals is adequately understood. The residue definition for enforcement in all crops (primary and rotational) is fluopicolide. The residue definition for risk assessment is fluopicolide and BAM in all primary crops, except tuberous and corm vegetables and is fluopicolide, BAM and PCA in tuberous and corm vegetables. The residue definition for risk assessment is fluopicolide, BAM, 3-OH-BAM, PCA and P1X in all rotational crops. The residue definition in livestock is fluopicolide for enforcement, and fluopicolide and BAM for risk assessment. The use of fluopicolide on crops listed on the labels and the import--of fluopicolide-treated commodities does not constitute an unacceptable chronic or acute dietary risk (food and drinking water) to any segment of the population, including infants, children, adults and seniors. Sufficient crop residue data have been reviewed to recommend maximum residue limits to protect human health. The PMRA recommends that the following maximum residue limits be specified for fluopicolide:

Commodity	Recommended MRL (ppm)
Leafy vegetables, except Brassica (Crop Group 4)*	25
Leaves of root and tuber vegetables (Crop Group 2)	15
Bulb vegetables (Crop Group 3-07)	7.0
Brassica head and stem vegetables (Crop Subgroup 5A)	5.0
Root vegetables (except sugar beet and carrot; Crop Subgroup 1A)	0.15
Potato**	0.02

*The proposed MRL of 16 ppm for head lettuce and leaf lettuce (PMRL2010-69) will be revised to accommodate an MRL on all commodities within Croup Group 4 (Leafy vegetables, except Brassica).

**The proposed MRL for Tuberous and corm vegetables (except potatoes) (PMRL2010-69) wil be extended to potato.

7.2 Environmental Risk

Available environmental studies suggest that in the natural environment, fluopicolide will persist in both soil and water; fluopicolide residues are expected to carryover into the following growing season. Adsorption data show that fluopicolide adsorbs weakly to soil. Although initial soil adsorption is shown to be partially reversible, there is evidence that adsorption may increase slightly over time. The major transformation product BAM is shown to have high to very high mobility in soils.

In aquatic environments, fluopicolide is expected to partition from the water phase to the sediment; the major transformation product BAM is shown to partition mainly into the water phase. Both fluopicolide and BAM are expected to leach through soil and have the potential to reach groundwater.

At the proposed application rate and use patterns, run-off and drift of fluopicolide may pose risks to aquatic organisms. The observance of spray buffer zones can effectively mitigate the entry of spray drift into aquatic systems. Spray buffer zones will not mitigate runoff. To reduce the potential for runoff of fluopicolide to adjacent aquatic habitats precautionary statements for sites with characteristics that may be conducive to runoff and when heavy rain is forecasted are required. In addition, a vegetative strip between the area and the edge of a water body is recommended to reduce runoff of fluopicolide to aquatic areas.

7.3 Value

Sufficient evidence of efficacy was provided to support the use of Presidio™ Fungicide and Fluopicolide 4 SC Fungicide to control or suppress important oomycete diseases on brassica (head and stem) vegetables and brassica root vegetables, cucurbit vegetables, grape, leafy vegetables, tomato, potato, pepper and outdoor ornamentals (bedding plants and cut flowers). Presidio™ Fungicide and Fluopicolide 4 SC Fungicide offer an additional tool to Canadian growers for disease and resistance management, particularly for the control of downy mildew on various vegetable crops listed above as well as late blight on potato and tomato. Presidio™ Fungicide and Fluopicolide 4 SC Fungicide is most effective when applied in a regularly scheduled spray program and is to be used in a tank-mix with other registered fungicides with a different mode of action when there is an alternative available.

A summary of the proposed and accepted/conditionally accepted uses for Presidio™ Fungicide and Fluopicolide 4 SC Fungicide is presented in Appendix I, Table 18 and 19.

7.4 Unsupported Uses

All uses proposed by the applicant were supported and are presented in see Appendix 1, Tables 18 and 19.

8.0 Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, has granted conditional registration for the sale and use of Fluopicolide Technical, Fluopicolide 4 SC Fungicide and Presidio™ Fungicide, containing the technical grade active ingredient fluopicolide, to control important fungal diseases on vegetable crops and outdoor ornamentals (bedding plants and cut flowers)

An evaluation of available scientific information found that, under the approved conditions of use, the products have value and do not present an unacceptable risk to human health or the environment.

Although the risks and value have been found acceptable when all risk-reduction measures are followed, as a condition of these registrations, additional scientific information is being requested from the applicant. For more details, refer to the section 12 Notice associated with these conditional registrations. The applicant will be required to submit this information within the time frames indicated below.

NOTE: The PMRA will publish a consultation document at the time when there is a proposed decision on applications to convert these conditional registrations to full registrations or on applications to renew the conditional registrations, whichever occurs first.

All required trials should be submitted within three years from the time of conditional registration being granted.

Human Health

Data are required demonstrating the stability of fluopicolide derived residues during the maximum storage intervals used during some of the crops field trials (35 months for broccoli, 40 months for cabbage, 38 months for celery and spinach, 41 months for bulb onions, 38 months for green onions, 47 months for carrots, 45 months for radish roots and tops, and 40 months for sugar beet roots and tops) and field crop rotation trial study (fluopicolide, BAM and PCA residues in/on wheat forage and PCA residues in/on wheat straw for 24 months).

Value

The following small-scale field or greenhouse trials are required for the disease claims with the conditional registration:

- Three trials on downy mildew of brassica (head and stem) vegetables and brassica root vegetables (cabbage, radish and/or turnip);
- Two trials on phytophthora blight/crown rot of cucurbit vegetables (pumpkin or/and eggplant);
- Two trials infected by *Phytophthora ramorum* and *P. parasitica* on outdoor ornamentals.

List of Abbreviations

3-OH-BAM	2,6-dichloro-3-hydroxybenzamide
λ	wavelength
µg	microgram(s)
a.i.	active ingredient
AD	administered dose
ADI	acceptable daily intake
AGDISP	Agricultural Dispersal model
AR	applied radioactivity
ARfD	acute reference dose
ASAE	American Society of Agricultural Engineering
atm	atmosphere
ATPD	area treated per day
AUDPC	area under the disease progress curve
AZ	Arizona
BAF	bioaccumulation factor
BAM	2,6-dichlorobenzamide
BBCH	Biologische Bundesanstalt, Bundessortenamt and Chemical Industry Scale of growth stages for mono- and dicotyledonous plant species
BC	British Columbia
BCF	bioconcentration factor
bw	body weight
BW	mean body weight
CA	California
CAF	composite assessment factor
CAS	Chemical Abstracts Service
CEPA	*Canadian Environmental Protection Act*
cm	centimetre(s)
cm^2	centimetre(s) squared
cm^3	centimetre(s) cubed
d	day(s)
DA	dermal absorption
DALA	days after last application
DF	dry flowable
DFOP	double first order in parallel
DFR	dislodgeable foliar residue
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
DT_{90}	dissipation time 90% (the dose required to observe a 90% decline in concentration)
dw	dry weight
EC_{25}	effective concentration on 25% of the population
EC_{50}	effective concentration on 50% of the population
ECD	electron capture detector
EDE	expected dietary exposure
EEC	estimated environmental concentration
EG	emulsifiable granule(s)

ELS	early life stage
EXAMS	Exposure Analysis Modeling System
F0	parent generation
F1	first generation
F2	second generation
FDA	*Food and Drugs Act*
FIR	food ingestion rate
FL	Florida
FRAC	Fungicide Resistance Action Committee of the Specialist Technical Group of CropLife International
g	gram(s)
GA	Georgia
GAP	good agricultural practice
GC	gas chromatography
GUS	groundwater ubiquity score
h	hour(s)
ha	hectare(s)
HAFT	highest average field trial
HDPE	high density polyethylene (plastic)
HPLC	high performance liquid chromatography
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_d	soil-water partition coefficient
K_{oc}	organic-carbon partition coefficient
*K*ow	*n*–octanol-water partition coefficient
L	litre(s)
LC	liquid chromatography
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LER	lowest effective rate
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOEC	low observed effect concentration
LOEL	lowest observed effect level
LOQ	limit of quantitation
LPHW	low pressure hand-wand
LR_{50}	lethal rate 50%
m^3	metre(s) cubed
MAS	maximum average score
Max	maximum
MB	Manitoba
mg	milligram(s)
MI	Michigan
mL	millilitre(s)
Min	minimum
MIS	maximum irritation score
M/L/A	mixer, loader and applicator
MOE	margin of exposure

MRL	maximum residue limit
MS	mass spectrometry
MTD	maximum tolerated dose
n	sample size
N/A	not applicable
NAFTA	*North American Free Trade Agreement*
NC	North Carolina
NJ	New Jersey
nm	nanometre(s)
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NY	New York
OECD	*Organisation for Economic Co-operation and Development*
OC	organic carbon content
OH	Ohio
ON	Ontario
OPPTS	USEPA Office of Prevention, Pesticides and Toxic Substances
P1X	3-methylsulfinyl-5-trifluoromethylpyridine-2-carboxylic acid
Pa	pascal
PA	Pennsylvania
PAM	Pesticide Analytical Manual
PBI	plantback interval
PCA	3-Chloro-5-(trifluoromethyl)-2-pyridinecarboxylic acid
PCPA	*Pest Control Product Act*
PEI	Prince Edward Island
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	parts per million
PRZM	Pesticide Root Zone Model
QC	Quebec
RA	risk assessment
RAC	raw agricultural commodity
REI	restricted-entry interval
RQ	risk quotient
SC	soluable concentrate
SFO	single first order
Std. Dev.	standard deviation
STMdR	supervised trial median residue
STMR	supervised trial mean residue
$t_{1/2}$	half-life
TC	transfer coefficient
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
UF	uncertainty factor

USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution
WDG	water dispersible granule(s)
WP	wettable powder
w/w	weight per weight

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ	Reference
Plant	00782	Fluopicolide (AE C638206); BAM (AE 653711); PCA (AE 657188)	LC/MS/MS (data gathering)	0.010 ppm per analyte	1446434
	00782-M001	Fluopicolide; BAM; PCA	LC/MS/MS (data gathering)	0.010 ppm per analyte	1446435
	00782-M002	Fluopicolide; BAM; PCA; P1X (AE 1344122)	LC/MS/MS (data gathering)	0.010 ppm per analyte	1446436, 1446442
	00782-M003	3-OH-BAM (AE C657378)	LC/MS/MS (data gathering)	0.010 ppm per analyte	1446437, 1446442, 1446439
	1611-00.02	Fluopicolide; BAM; PCA	LC/MS/MS (data gathering)	0.010 ppm per analyte	1446450, 1446451, 1446472, 1446474, 1446475
	1629-00.00	Fluopicolide; BAM; PCA	LC/MS/MS (data gathering)	0.010 ppm per analyte	1446470, 1446471, 1446473
	RM-43C-2	Fluopicolide	LC/MS/MS (enforcement)	0.01 ppm	1446443
Livestock	AR 303-02	Fluopicolide; BAM; PCA	LC/MS/MS (data gathering)	0.01 ppm per analyte in milk; 0.02 ppm per analyte in meat; 0.05 ppm per analyte in fat, liver and kidney	1446420
Soil	AR 265-01	Fluopicolide	LC/MS/MS	0.005 mg/kg	1912015
	AR 265-01	AE C657188	LC/MS/MS	0.005 mg/kg	1912015
	AR 265-01	AE C653711	LC/MS/MS	0.005 mg/kg	1912015
	AR 265-01	RPA 427967	LC/MS/MS	0.005 mg/kg	1912015
	N/A	AE C657188	GC-ECD	0.02 mg/kg	1912223

Matrix	Method ID	Analyte	Method Type	LOQ	Reference
Surface/ drinking water	AR 307-03	Fluopicolide	LC/MS/MS	0.1 µg/L	1912017
	00924	Fluopicolide	HPLC/MS/MS	0.02 µg/L	1912089, 1912165
	AR 307-03	AE C657188	LC/MS/MS	0.1 µg/L	1912017
	00924	AE C657188	HPLC/MS/MS	0.02 µg/L	1912089, 1912165
	AR 307-03	AE C653711	LC/MS/MS	0.1 µg/L	1912017
	00924	AE C653711	HPLC/MS/MS	0.02 µg/L	1912089, 1912165

Table 2 Acute Toxicity of Fluopicolide and Its Associated End-use Product (V-10161 4 SC Fungicide)

Study Type	Species	Result	Comment	Reference
Acute Toxicity of Fluopicolide (Technical)				
Oral	Rat	LD_{50} >5000 mg/kg bw	Low Toxicity	1446247
Dermal	Rat	LD_{50} >5000 mg/kg bw	Low Toxicity	1446252
Inhalation	Rat	LC_{50} >5.16 mg/L	Low Toxicity	1446253, 1446254
Skin irritation	Rabbit	MIS = 0/8 MAS= 0/8	Non-irritating	1446257, 1446258
Eye irritation	Rabbit	MIS= 2/110 (1h) MAS= 0.44/110	Minimally irritating	1446255, 1446256
Skin sensitization (Maximization)	Guinea pig	Not a skin sensitizer	Not a skin sensitizer	1446259, 1446260
Acute Toxicity of End-Use Product - V-10161 4 SC Fungicide				
Oral	Rat	LD_{50} >5000 mg/kg bw	Low Toxicity	1446378, 1446379
Dermal	Rat	LD_{50} >4000 mg/kg bw	Low Toxicity	1446380, 1446382
Inhalation	Rat	LC_{50} > 0.93 mg/L	Slightly Toxic "CAUTION POISON"	1446387, 1446388
Skin irritation	Rabbit	MIS=0.33/8 (24h) MAS=0.11/8	Minimally irritating	1446381, 1446384
Eye irritation	Rabbit	MIS=16/110 (24h) MAS=12.22/110 with scores >0 at 72 h	Mildly irritating "CAUTION EYE IRRITANT"	1446389
Skin sensitization (Buehler)	Guinea pig	Not a skin sensitizer	Not a skin sensitizer	1446390, 1446391

a MAS = maximum average score for 24, 48 and 72 hours

b MIS = maximum irritation score

Table 3 Toxicity Profile of Technical Fluopicolide

Study Type	Species	Results[a] / Comments	Reference
28-day dermal	Rat	Dermal irritation: No treatment related effects were observed at any dose. NOAEL: 1000 mg/kg bw/day LOAEL was not determined.	1446286

a Effects observed in males as well as females unless otherwise reported

Table 4 Toxicology Endpoints for Use in Health Risk Assessment for Fluopicolide

Exposure Scenario	Dose (mg/kg bw/day)	Study	Endpoint	UF/CAF[1] or Target MOE[2]
Acute dietary, females aged 13+	NOAEL = 60	Rat developmental toxicity study	Skeletal malformations at maternally toxic dose	300
	ARfD = 0.2 mg/kg bw			
Chronic Dietary	NOAEL = 20	Rabbit developmental toxicity study	Deaths, abortions, and decreased body weight gains in the dams	300
	ADI = 0.067 mg/kg bw/day			
Short-term Dermal/inhalation	NOAEL = 20	Rabbit developmental toxicity study	Deaths, abortions, and decreased body weight gains in the dams	300
Intermediate-term Dermal/inhalation	NOAEL = 20	Rabbit developmental toxicity study	Deaths, abortions, and decreased body weight gains in the dams	300

[1] Dietary scenarios
[2] Exposure scenarios

Table 5 Integrated Food Residue Chemistry Summary

NATURE OF THE RESIDUE IN GRAPE				**PMRA 1446416**	
Radiolabel Position	[U-^{14}C-phenyl-fluopicolide] and [2,6-^{14}C-pyridinyl-fluopicolide]				
Test Site	Grape vines grown in pots filled with loamy sand were moved into a greenhouse 10-16 days prior to treatment.				
Treatment	Fluopicolide was applied as a foliar spray to grape vines using a hand sprayer. An adjuvant (0.05% v/v) was included in all spray applications. The first, second and third applications were made at BBCH growth stages 55-57, BBCH growth stages 71-73 and 21days prior to normal harvest, respectively.				
Rate	Three sequential applications were made at 0.116-0.169 kg a.i./ha/application (low treatment rate) or at 1.12-1.69 kg a.i./ha/application (high treatment rate), for seasonal application rates of 0.399-0.401 kg a.i./ha and 3.99-4.03 kg a.i./ha, respectively.				
End-use product	Suspension concentrate.				
Pre-harvest Interval	Immature foliage were harvested just after the first application and 26-28 days later prior to the second application. Mature fruit and foliage were harvested 21 days after the third application.				
		[U-^{14}C-phenyl-fluopicolide]		**[2,6-^{14}Cpyridinyl-fluopicolide]**	
Matrix	**PHI (days)**	**Mean TRR (ppm)**		**Mean TRR (ppm)**	
		Low Rate	**High Rate**	**Low Rate**	**High Rate**
Grape, Immature Foliage	0*	32.3	338.8	32.6	382.4
Grape, Immature Foliage	26-28*	23.6	269.5	19.2	270.2
Grape, Mature Foliage	21**	15.5	154.5	23.9	181.0
Grape, Mature Fruit	21**	1.27	9.96	1.04	10.9
*Immature foliage was harvested immediately after the first application (Day 0) and 26-28 days later prior to the second application.					

NATURE OF THE RESIDUE IN GRAPE					PMRA 1446416
**Mature foliage and fruit were harvested 21 days after the third application.					
Metabolites Identified	**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**		
Radiolabel Position	**[U-^{14}C-phenyl-fluopicolide]**	**[2,6-^{14}C-pyridinyl - fluopicolide]**	**[U-^{14}C-phenyl-fluopicolide]**	**[2,6-^{14}C-pyridinyl - fluopicolide]**	
	Low and High Rate	**Low and High Rate**	**Low and High Rate**	**Low and High Rate**	
Grape, Fruit	Fluopicolide	Fluopicolide	BAM	PCA	

NATURE OF THE RESIDUE IN LETTUCE	PMRA 1446418
Radiolabel Position	[U-^{14}C-phenyl-fluopicolide] and [2,6-^{14}C-pyridinyl-fluopicolide]
Test Site	Lettuce plants were grown in stainless steel tanks filled with sandy loam soil to a depth of 30 cm and located in field cages.
Treatment	Fluopicolide was applied either as a foliar treatment or as a soil drench treatment. An adjuvant (0.05%) was included in all applications. Foliar Treatment: Two applications were made, the first at 41 days after planting and the second 21 days later. Both applications were made using a hand sprayer. Soil Drench Treatment: A single application was made at 41 days after planting by pipetting the test substance directly onto the soil between the lettuce rows.
Rate	Foliar Treatment: Two applications at 202.0-202.8 g a.i./ha, for a seasonal rate of 405.3 g a.i./ha (phenyl label) and 404.1 g a.i./ha (pyridinyl label). Soil Drench Treatment: One application at 202.8 g a.i./ha (phenyl label)
End-use product	Suspension concentrate.
Pre-harvest Interval	Foliar Treatment: Immature plants were harvested zero and 21 days after the first application. Mature plants were harvested 14 days after the last application (DALA). Soil Drench Treatment: Immature and mature plants were harvested 21 days and 35 days after application, respectively.

		Foliar Treatment		Soil Drench Treatment
Matrix	**PHI (days)**	**[U-^{14}C-phenyl-fluopicolide]**	**[2,6-^{14}C-pyridinyl – fluopicolide]**	**[U-^{14}C-phenyl-fluopicolide]**
		Mean TRR (ppm)	**Mean TRR (ppm)**	**Mean TRR (ppm)**
Lettuce, Immature	0	10.8	13.4	Not applicable
	21	1.33	1.31	0.076
Lettuce, Mature	35	13.4	14.5	0.175

Metabolites Identified	**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**	
Radiolabel Position	**[U-^{14}C-phenyl-fluopicolide]**	**[2,6-^{14}C-pyridinyl – fluopicolide]**	**[U-^{14}C-phenyl-fluopicolide]**	**[2,6-^{14}Cpyridinyl – fluopicolide]**

NATURE OF THE RESIDUE IN GRAPE			PMRA 1446416	
Lettuce, Immature (Day 0; Foliar Treatment)	Fluopicolide	Fluopicolide	BAM	-
Lettuce, Immature (Day 21; Foliar Treatment)	Fluopicolide	Fluopicolide	BAM; AE C643890	PCA; AE C643890
Lettuce, Mature (Day 35; Foliar Treatment)	Fluopicolide	Fluopicolide	BAM	PCA
Lettuce, Immature (Day 21; Soil Drench Treatment)	Fluopicolide; BAM	Not applicable	-	Not applicable
Lettuce, Mature (Day 35; Soil Drench Treatment)	Fluopicolide; BAM	Not applicable	AE C643890	Not applicable

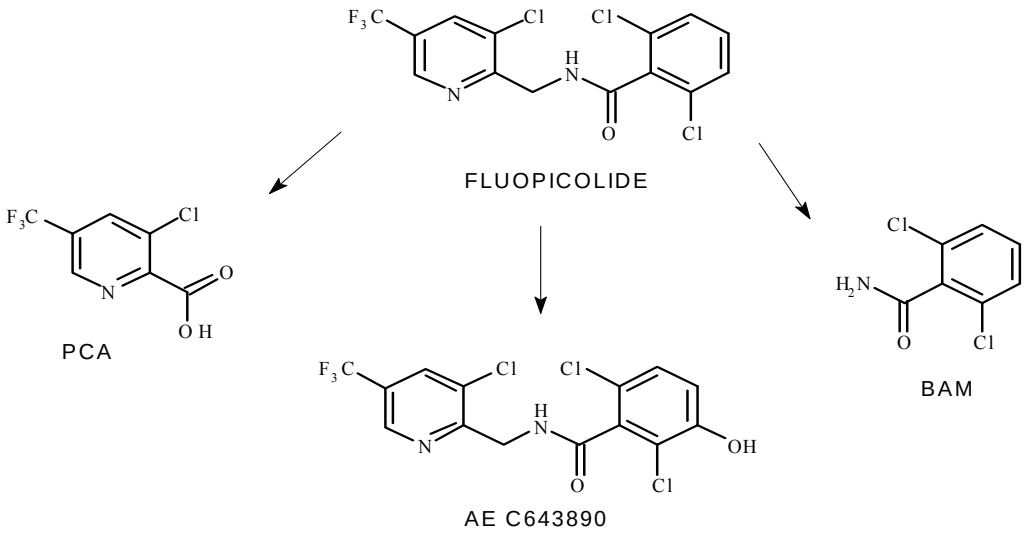
NATURE OF THE RESIDUE IN POTATO	PMRA 1446417
Radiolabel Position	[U-^{14}C-phenyl-fluopicolide] and [2,6-^{14}C-pyridinyl-fluopicolide]
Test Site	Potato plants were grown in stainless steel tanks filled with field soil (sandy loam) and located in field cages.
Treatment	Fluopicolide was applied as a foliar treatment. The first application was made 69 days before harvest, at BBCH growth stages 31-35. A second application was made 49 days later, at 20 days before harvest. An adjuvant (0.05 %) was included in all spray applications.
Rate	Low Treatment Rate: Two applications at 0.200-0.204 kg a.i./ha/application, for a seasonal rate of 0.403-0.407 kg a.i./ha High Treatment Rate: Two applications at 1.91-2.03 kg a.i./ha/application, for a seasonal rate of 3.93-4.04 kg a.i./ha.
End-use product	Suspension concentrate.
Pre-harvest Interval	Immature plants were harvested zero and 40-41 days after the first application. Mature plants were harvested 20 days after the second application.

Matrix	**Low Treatment Rate**		**High Treatment Rate**	
	[U-^{14}C-phenyl-fluopicolide]	**[2,6-^{14}C-pyridinyl –fluopicolide]**	**[U-^{14}C-phenyl-fluopicolide]**	**[2,6-^{14}Cpyridinyl – fluopicolide]**
	Mean TRR (ppm)	**Mean TRR (ppm)**	**Mean TRR (ppm)**	**Mean TRR (ppm)**
Potato, Immature Foliage (PHI = 0 days)	47.2	54.3	418.3	472.1

NATURE OF THE RESIDUE IN GRAPE			PMRA 1446416	
Potato, Immature Foliage (PHI = 40-41 days)	10.2	7.62	38.9	121.7
Mature Foliage	12.3	9.63	201.6	221.7
Mature Tubers	0.081	0.053	0.502	0.771
Metabolites Identified	**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**	
Radiolabel Position	**[U-^{14}C-phenyl-fluopicolide]**	**[2,6-^{14}C-pyridinyl –fluopicolide]**	**[U-^{14}C-phenyl-fluopicolide]**	**[2,6-^{14}Cpyridinyl – fluopicolide]**
Low Treatment Rate				
Potato, Immature Foliage (PHI = 41 days)	Fluopicolide	Fluopicolide	-	-
Potato, Mature Foliage	Fluopicolide	Fluopicolide	BAM; AE C643890	PCA; AE C643890
Potato, Mature Tuber	Fluopicolide; BAM	Fluopicolide; PCA	AE C643890	AE C643890
High Treatment Rate				
Potato, Immature Foliage (PHI = 41 days)	Fluopicolide	Fluopicolide	-	-
Potato, Mature Tuber	Fluopicolide; BAM	Fluopicolide; PCA	-	-

NATURE OF THE RESIDUE IN GRAPE	PMRA 1446416

Proposed metabolic scheme in Primary Crops (Grape, Lettuce and Potato)



CONFINED ACCUMULATION IN ROTATIONAL CROPS – lettuce, radish and wheat				PMRA 1912085	
Radiolabel Position		[U-^{14}C-phenyl-fluopicolide]		[2,6-^{14}C-pyridinyl-fluopicolide]	
Test site		Under outdoor conditions, three stainless steel tanks were filled with sandy loam soil. One tank was used for each label and the remaining tank for the control. The tanks were covered with fibreglass panes to control irrigation and prevent flooding.			
Formulation used for trial		Each radiolabel test substance was combined with non-labeled fluopicolide, formulated as a suspension concentrate and mixed with adjuvant.			
Application rate and timing		Fluopicolide (AE C638206) was applied once to bare sandy loam soil at ~400 g a.i./ha using a hand-held sprayer. The single broadcast application was made 29, 133 and 365 days prior to planting of rotational lettuce, wheat and radish. PBI = plantback interval			
Metabolites Identified		**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**	
Matrix	**PBI (days)**	[U-^{14}C-phenyl-fluopicolide]	[2,6-^{14}C-pyridinyl-fluopicolide]	[U-^{14}C-phenyl-fluopicolide]	[2,6-^{14}C-pyridinyl-fluopicolide]

NATURE OF THE RESIDUE IN GRAPE				PMRA 1446416	
Lettuce, leaves	29	Fluopicolide; BAM	Fluopicolide; P1X; PCA	-	pyridinol (AE B102859)
	133	Fluopicolide; BAM	Fluopicolide	-	-
	365	BAM	Fluopicolide; PCA	Fluopicolide	AE C653598; P1X; pyridinol
Radish, tops	29	Fluopicolide; BAM	Fluopicolide; PCA	-	P1X; pyridinol
	133	Fluopicolide; BAM	Fluopicolide	-	-
	365	BAM	Fluopicolide; PCA	Fluopicolide	P1X; pyridinol
Radish, roots	29	Fluopicolide; BAM	Fluopicolide; PCA	-	P1X
	133	Fluopicolide; BAM	Fluopicolide; pyridinol	-	P1X; PCA
	365	Fluopicolide; BAM	Fluopicolide	-	AE C653598; P1X; PCA
Wheat, forage	29	Fluopicolide; 3-OH-BAM; P2ab; P4a; P4b; P5; P10	Fluopicolide; PCA; P4a; P4b; P5	BAM; AE C643890; P2c	P1X; AE C643890; P4c; P10; P11
	133	Fluopicolide; 3-OH-BAM	Fluopicolide; P1X; pyridinol	BAM	PCA
	365	3-OH-BAM; BAM	Fluopicolide; P1X	Fluopicolide	AE C653598; PCA; pyridinol
Wheat, grain	29	Fluopicolide; AE C643890	P1X; PCA	BAM	Fluopicolide
	133	3-OH-BAM; BAM	P1X; PCA	Fluopicolide	Fluopicolide
	365	3-OH-BAM; BAM	P1X; PCA	Fluopicolide	Fluopicolide

NATURE OF THE RESIDUE IN GRAPE				PMRA 1446416	
Wheat, straw	29	Fluopicolide; 3-OH-BAM; P4a/P4b; P5; P8a; P8b; P10; P11	Fluopicolide; P1X; P4a/P4b/P4c; P5; P8a/P8b; P10; P11	BAM	P1X; PCA
	133	Fluopicolide; 3-OH-BAM; BAM	Fluopicolide; pyridinol	-	AE C653598; P1X; PCA
	365	3-OH-BAM	Fluopicolide; P1X	Fluopicolide; BAM	AE C653598; PCA

The metabolism of fluopicolide in rotational crops is more extensive than that observed in the primary crops (grapes, lettuce and potato). The major metabolites identified in rotational crops were BAM, PCA, P1X and 3-OH-BAM. PIX, 3-OH-BAM and two other rotational crop metabolites (AE C65398 and pyridinol) were not identified in the primary crop metabolism studies.

NATURE OF THE RESIDUE IN LAYING HEN	PMRA 1446412, 1446414, 1912086, 1911911, 1911940

Laying hens were dosed orally daily with either [U-^{14}C-phenyl]-fluopicolide or [2,6-^{14}C-pyridinyl]-fluopicolide for 14 consecutive days, one group (n = 5) at 1.0-1.2 ppm and a second group (n = 5) at 10.0-10.7 ppm in the diet. Eggs were collected daily throughout the study, and tissues (fat, liver, skin with fat and muscle) were collected at sacrifice, 23-24 hours after the final dose. Excreta and cage wash were collected at 24-hour intervals during the dosing period.

In the case of the phenyl label study, metabolic profiling was conducted on egg white (composite of day 8, day 9 and day 10), egg yolk (composite of day 7 and day 8), liver, skin (with fat), fat (peritoneal and perirenal) and muscle (composite of breast and thigh) from the high-dose hens. No metabolites were identified in muscle.

In the case of the pyridinyl label study, single samples of muscle (breast and thigh) and fat (abdominal fat pad) were collected. Metabolic profiling was conducted on egg yolk (day 13) and liver from the low-dose hens, and on egg white (day 4 and day 13), egg yolk (day 4 and day 13), liver, fat and skin (with fat) from the high-dose hens. No metabolites were identified in egg yolk and liver from the low-dose hens. The extracts of egg white (day 13), breast muscle and thigh muscle from the high-dose hens were not analyzed due to low radioactivity levels.

* (indicates % AD not reported)

Matrices	% of Administered Dose			
	[U-^{14}C-Phenyl]		[2,6-^{14}C-Pyridinyl]	
	1.2 ppm dose	10.7 ppm dose	1.0 ppm dose	10.0 ppm dose
Excreta (cumulative)	69.7-87.6	90.2-97.6	89.4-94.8	88.0-95.3
Cage wage (cumulative)	0.123-1.09	0.317-0.676	2.11-4.81	1.93-3.10
Cage wash (sacrifice)	0.042-0.662	0.144-0.279	Not collected	Not collected
Muscle	0.012-0.020	0.016-0.052	*	*
Skin with Fat	0.001-0.006	0.002-0.004	*	*
Fat	<0.001-0.001	0.001-0.004	*	*
Liver	0.133-0.329	0.129-0.270	0.07-0.11	0.04-0.08
Egg Pre-Lay (sacrifice)	Not collected	Not collected	<0.01-0.04	0.01-0.02

NATURE OF THE RESIDUE IN GRAPE			PMRA 1446416		
Egg white (cumulative)		0.017-0.081	0.019-0.049	0.03-0.05	0.02-0.03
Egg yolk (cumulative)		0.009-0.095	0.021-0.092	0.07-0.10	0.04-0.06
Blood		<0.001	<0.001	*	*
Plasma		<0.001	<0.001	*	*
High Dose Hens					
Metabolites identified	**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**		
Radiolabel Position	**[U-^{14}C-Phenyl]**	**[2,6-^{14}C-Pyridinyl]**	**[U-^{14}C-Phenyl]**	**[2,6-^{14}C-Pyridinyl]**	
Egg White	Metabolite 1	Dihydroxy sulphate of fluopicolide (Day 4); AE 0712556 (Day 4)	Fluopicolide	-	
Egg Yolk	Fluopicolide	Fluopicolide (Day 4); Dihydroxy sulphate of fluopicolide (Day 4 + 13); AE 0712556 (Day 13)	-	Fluopicoliode (Day 13); Hydroxy sulphate of fluopicolide (Day 4 + 13); AE 0712556 (Day 4)	
Liver	BAM	-	AE C643890/ AE 0608000	Hydroxy sulphate of fluopicolide; Dihydroxy sulphate of fluopicolide; AE 0712556	
Skin with Fat	AE C643890	AE 0712556	Metabolite 1	-	
Fat	Metabolite 1	AE 0712556	Fluopicolide	-	

NATURE OF THE RESIDUE IN LACTATING COW	PMRA 1712582, 1446415, 1911938, 1911910, 1912084

Lactating cows were dosed orally twice daily with either [U-^{14}C-phenyl]-fluopicolide (AE C638206) or [2,6-^{14}C-pyridinyl]-fluopicolide for seven consecutive days. One animal was dosed at 1.0-1.1 ppm and a second animal was dosed at 10.0-10.6 ppm in the diet. Urine, feces and cage wash were collected at 24 hour intervals during the dosing period, and the cage wash was collected after sacrifice. Milk was collected twice daily prior to dosing throughout the study. Samples of muscle, fat, kidney and liver were collected at sacrifice, ~23-24 hours after the final dose.

In the case of the phenyl label, metabolic profiling was conducted on milk (day 6), fat (composite of omental and renal), muscle (composite of fore and hindquarter), liver and kidney from the high-dose cow.

In the case of the pyridinyl label, metabolic profiling was conducted on liver, kidney and renal fat from the low-dose cow, and on milk (day 2 and day 8), fat (renal and omental), muscle (skeletal; mixture of forequarter, hindquarter and loin), kidney and liver from the high-dose cow. In renal fat from the low-dose cow, fluopicolide was the only identified metabolite (64.4%). No metabolites were identified in liver from the low-dose cow. The extracts of milk, omental fat and muscle from the high-dose cow, and the extracts of kidney from the low-dose cow were not analyzed due to low radioactivity levels.

* (indicates % AD not reported)

NATURE OF THE RESIDUE IN GRAPE	PMRA 1446416

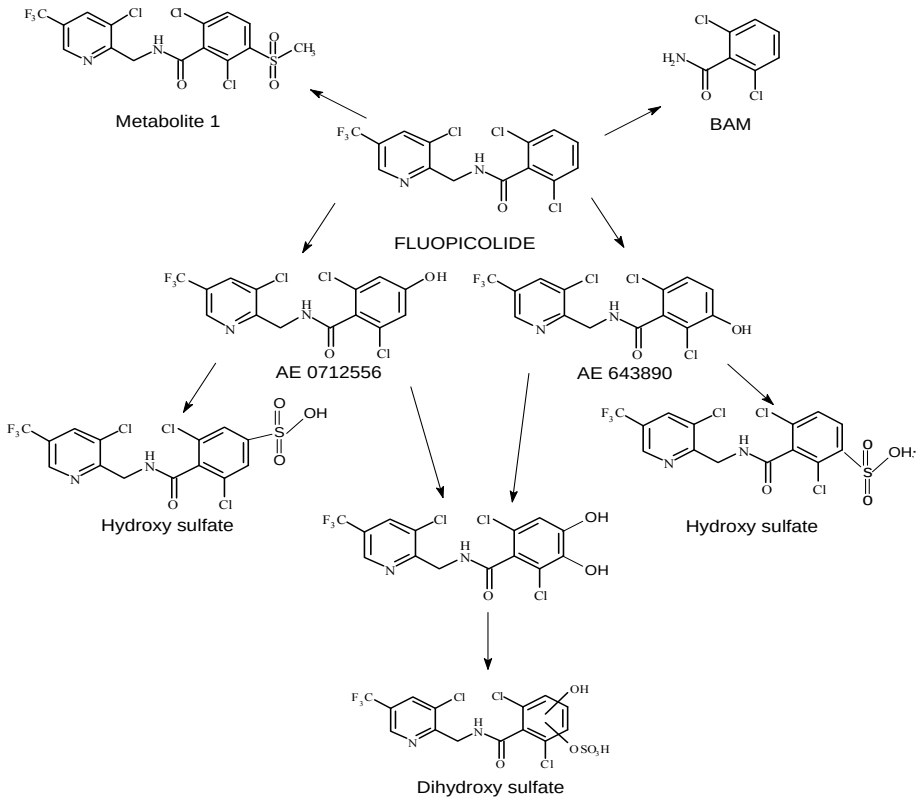
Matrices	% of Administered Dose			
	[U-^{14}C-Phenyl]		[2,6-^{14}C-Pyridinyl]	
	1.1 ppm dose	10.6 ppm dose	1.0 ppm dose	10.0 ppm dose
Urine (Cumulative)	16.8	19.3	13.50	10.71
Feces (Cumulative)	57.2	54.9	69.10	67.00
Cage Wash (Cumulative)	0.868	1.02	Not collected	Not collected
Cage Wash (Sacrifice)	0.050	0.056	1.15	2.09
Muscle	*	*	*	*
Fat, Renal	0.004	0.002	*	*
Fat, Omental	0.004	0.003	*	*
Kidney	0.039	0.040	0.03	0.02
Liver	0.736	0.493	0.36	0.27
Milk (Cumulative)	0.141	0.133	0.09	0.08
Blood	*	*	*	*
Plasma	*	*	*	*

High-Dose Cow

Metabolites identified	Major Metabolites (> 10% TRR)		Minor Metabolites (< 10% TRR)	
Radiolabel Position	[U-^{14}C-Phenyl]	[2,6-^{14}C-Pyridinyl]	[U-^{14}C-Phenyl]	[2,6-^{14}C-Pyridinyl]
Milk	Fluopicolide	-	BAM	-
Fat	Fluopicolide	Fluopicolide	-	-
Muscle	-	-	Fluopicolide	-
Liver	-	-	Fluopicolide; AE C643890; AE 0712556	Fluopicolide; Hydroxy glucuronide of fluopicolide; hydroxy sulphate of fluopicolide; AE C643890/ AE 0712556
Kidney	-	-	Fluopicolide; AE C643890; AE 0712556	Fluopicolide; Hydroxy glucuronide of fluopicolide; Dihydroxy glucuronide of fluopicolide; Hydroxy sulphate of fluopicolide/ Dihydroxy sulphate of fluopicolide; AE C643890/AE 0712556

NATURE OF THE RESIDUE IN GRAPE	PMRA 1446416

Proposed Metabolic Scheme in Livestock



STORAGE STABILITY- CROP AND PROCESSED COMMODITIES	PMRA 1446446; 1446447; 1446448; 1446449

The freezer storage stability data indicate that residues of fluopicolide, BAM and PCA are stable for 30 months in the processed commodities of wheat (flour, bran, shorts), tomato (paste, puree), sugar beet (refined sugar, molasses, dried pulp) and potato (dried flakes, chips, wet peel); residues of fluopicolide, BAM and PCA are stable for 30 months in grapes, wheat grain, potato tubers and cabbage leaves; residues of fluopicolide and BAM are stable in wheat straw for 41 months; and residues of P1X and 3-OH BAM are stable in wheat grain, straw and forage for 25 months.

STORAGE STABILITY- LIVESTOCK COMMODITIES	PMRA 1446421

The freezer storage stability data indicate that residues of fluopicolide, BAM and PCA were stable in milk for 83 days; in muscle and fat for 4 months; and in liver and kidney for 9 months.

CROP FIELD TRIALS ON BRASSICA HEAD AND STEM VEGETABLES (BROCCOLI AND CABBAGE)	PMRA 1446474; 1446475

NATURE OF THE RESIDUE IN GRAPE	PMRA 1446416

During the 2002 growing season a sufficient number of trials were conducted in representative NAFTA growing regions to evaluate the magnitude of fluopicolide in/on head and stem Brassica.

At each trial site, three broadcast foliar applications of a suspension concentrate formulation of fluopicolide were made at four to six day retreatment intervals to broccoli and cabbage at 0.130-0.138 kg a.i./ha/application, for a total seasonal rate of 0.394-0.408 kg a.i./ha. An adjuvant was added to the spray mixture for all applications. Samples were harvested two days after the last application. Additional samples were collected from two trials (one broccoli and one cabbage) at 1, 3, 5, and 7 days following the last application to generate residue decline data.

Residues of fluopicolide and the metabolites BAM and PCA were determined using the method 1611-00.02 (LC/MS/MS). Residues of fluopicolide, BAM, and PCA are reported as the analyte *per se*. The limit of quantitation (LOQ) for each analyte is 0.010 ppm.

In the residue decline trials, residues of fluopicolide generally decreased with increasing sampling interval in/on broccoli, and cabbage. Given that residues of BAM and PCA were non-quantifable in/on broccoli samples, and were variable or non-quantifiable in/on cabbage samples, the potential for residue decline could not be assessed.

Commodity	Total Application Rate (kg a.i./ha)	PHI (days)	n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Fluopicolide									
Broccoli	0.395-0.408	2	12	0.122	0.690	0.601	0.373	0.360	0.176
Cabbage, with Wrapper Leaves	0.394-0.402	2	14	0.056	3.93	3.77	0.71	1.24	1.24
Cabbage without Wrapper Leaves	0.394-0.402	2	14	<0.01	2.63	2.36	0.104	0.532	0.852
BAM									
Broccoli	0.395-0.408	2	12	<0.01	<0.01	<0.01	<0.01	<0.01	-
Cabbage, with Wrapper Leaves	0.394-0.402	2	14	<0.01	0.017	0.016	0.010	0.011	0.002
Cabbage without Wrapper Leaves	0.394-0.402	2	14	<0.01	0.011	0.011	0.010	0.010	0.000
PCA									
Broccoli	0.395-0.408	2	12	<0.01	0.017	0.016	0.010	0.011	0.002
Cabbage, with Wrapper Leaves	0.394-0.402	2	14	<0.01	0.020	0.018	0.010	0.011	0.003
Cabbage without Wrapper Leaves	0.394-0.402	2	14	<0.01	0.015	0.013	0.010	0.010	0.001

NATURE OF THE RESIDUE IN GRAPE	PMRA 1446416

CROP FIELD TRIALS ON ROOT VEGETABLES (CARROT, SUGAR BEET AND RADISH)	PMRA 1446470; 1446471; 1446473

During the 2002-2003 growing seasons a sufficient number of trials were conducted in representative NAFTA growing regions to evaluate the magnitude of fluopicolide in/on carrot, sugar beet and radish.

At each trial site, three broadcast foliar applications of a suspension concentrate formulation of fluopicolide were made at four to seven day retreatment intervals to carrot, radish, or sugar beet plants at 0.129-0.139 kg a.i./ha/application for a total seasonal rate of 0.395-0.411 kg a.i./ha. An adjuvant was added to the spray mixture for all applications. Mature carrot roots, radish roots and tops, and sugar beet roots and tops were harvested seven days after the last application. Additional samples were collected from one trial for each crop at 2, 4/5, 10, and 14 days following the last application to generate residue decline data.

Residues of fluopicolide and the metabolites BAM and PCA were determined using method 1629-00.00 (LC/MS/MS). Residues of fluopicolide, BAM, and PCA are reported as the analyte *per se*. The limit of quantitation (LOQ) for each analyte is 0.010 ppm.

Based on the residue decline data, fluopicolide residues in/on samples of carrot, radish root and tops, and sugar beet tops peaked at the 7-day PHI, and decreased at the longer PHIs. Residues of fluopicolide in/on sugar beet roots remained relatively constant over time. Residues of BAM and PCA were both non-quantifiable in/on carrots, radish roots and sugar beet roots, and residues of PCA were non-quantifable in/on sugar beet tops from all sampling intervals. Residues of BAM and PCA generally decreased from the 2-day to 14-day sampling interval in/on radish tops, and residues of BAM appeared to increase slightly from the 2-day to the 14-day sampling interval in/on sugar beet tops.

Commodity	Total Application Rate (kg a.i./ha)	PHI (days)	n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Fluopicolide									
Carrot	0.395-0.405	7	14	<0.01	0.144	0.125	0.030	0.050	0.043
Radish, Root	0.395-0.407	7	12	0.017	0.103	0.086	0.028	0.039	0.026
Radish, Top	0.395-0.407	7	12	2.32	10.2	8.76	4.73	4.95	2.45
Sugar Beet, Root	0.398 - 0.411	7	20	<0.01	0.061	0.054	0.029	0.031	0.017
Sugar Beet Tops	0.398 - 0.411	7	20	3.61	11.20	10.51	5.47	6.21	2.27
BAM									
Carrot	0.395-0.405	7	14	<0.01	<0.01	<0.01	<0.01	<0.01	0
Radish, Root	0.395-0.407	7	12	<0.01	<0.01	<0.01	<0.01	<0.01	0
Radish, Top	0.395-0.407	7	12	0.012	0.163	0.156	0.045	0.063	0.051
Sugar Beet, Root	0.398 - 0.411	7	20	<0.01	0.016	0.0131	0.010	0.0105	0.001
Sugar Beet Tops	0.398 - 0.411	7	20	0.014	0.121	0.107	0.021	0.033	0.029
PCA									
Carrot	0.395-0.405	7	14	<0.01	<0.01	<0.01	<0.01	<0.01	0
Radish, Root	0.395-0.407	7	12	<0.01	0.011	0.011	<0.01	<0.01	<0.01
Radish, Top	0.395-0.407	7	12	<0.01	0.028	0.023	0.014	0.015	0.005
Sugar Beet, Root	0.398 - 0.411	7	20	<0.01	<0.01	<0.01	<0.01	<0.01	0

NATURE OF THE RESIDUE IN GRAPE							PMRA 1446416		
Sugar Beet Tops	0.398 - 0.411	7	20	<0.01	0.027	0.022	0.010	0.012	0.004

CROP FIELD TRIALS ON CUCURBIT VEGETABLES (CANTALOUPE, CUCUMBER AND SQUASH) — **PMRA 1446459, 1446460, 1446462**

During the 2002 growing season a sufficient number of trials were conducted in representative NAFTA growing regions to evaluate the magnitude of fluopicolide in/on cucurbit vegetables.

At each trial site, three broadcast foliar applications of a suspension concentrate formulation of fluopicolide were made at three to six day retreatment intervals to cantaloupe, cucumber and summer squash plants at 0.127-0.139 kg a.i./ha/application for a total seasonal rate of 0.391-0.411 kg a.i./ha. An adjuvant was added to the spray mixture for all applications. Samples of cantaloupe, cucumber and summer squash fruit were harvested two days after the last application. Additional samples were collected from one cantaloupe, cucumber and summer squash at 1, 3, 5 and 7 days following the last application to generate residue decline data.

Residues of fluopicolide and the metabolites BAM and PCA were determined using method 00782/M001 (LC/MS/MS). Residues of fluopicolide, BAM, and PCA are reported as the analyte *per se*. The limit of quantitation (LOQ) for each analyte is 0.010 ppm.

Residue decline data in *cantaloupe* show that fluopicolide residues were variable over the 7-day sampling period. At the end of the decline period (day seven), the mean residues were only slightly less than the mean residues on day one. Residue decline could not be assessed for BAM and PCA as each analyte in/on cantaloupe were non-quantifiable at each of the sampling intervals.

Residue decline data in *cucumber* show that fluopicolide residues generally decrease with increasing pre-harvest intervals. Residue decline could not be assessed for BAM and PCA as each analyte in/on cucumber were non-quantifiable at each of the sampling intervals.

Residue decline data *in summer squash* indicate that fluopicolide and PCA residues increased up to three days after the last application, then decreased rapidly with increasing pre-harvest intervals. Residue decline could not be assessed for BAM in/on summer squash as residues were non-quantifiable at each of the sampling intervals.

Commodity	Total Application Rate (kg a.i./ha)	PHI (days)	n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Fluopicolide									
Cantaloupe	0.394-0.405	2	18	<0.01	0.258	0.181	0.055	0.068	0.061
Cucumber	0.391-0.404	2	12	<0.01	0.057	0.050	0.020	0.024	0.0147
Summer Squash	0.396-0.411	2	12	0.0135	0.0506	0.0448	0.0322	0.0301	0.0120
BAM									
Cantaloupe	0.394-0.405	2	18	<0.01	<0.01	<0.01	<0.01	<0.01	0
Cucumber	0.391-0.404	2	12	<0.01	<0.01	<0.01	<0.01	<0.01	0
Summer Squash	0.396-0.411	2	12	<0.01	<0.01	<0.01	<0.01	<0.01	0
PCA									
Cantaloupe	0.394-0.405	2	18	<0.01	<0.01	<0.01	<0.01	<0.01	0
Cucumber	0.391-0.404	2	12	<0.01	<0.01	<0.01	<0.01	<0.01	0
Summer Squash	0.396-0.411	2	12	<0.01	0.0207	0.0173	<0.01	<0.01	0.006

NATURE OF THE RESIDUE IN GRAPE	PMRA 1446416

CROP FIELD TRIAL ON FRUITING VEGETABLES (BELL PEPPER, CHILI PEPPER AND TOMATO)	PMRA 1446458, 1446463, 1446465

During the 2001-2002 growing seasons a sufficient number of trials were conducted in representative NAFTA growing regions to evaluate the magnitude of fluopicolide in/on fruiting vegetables.

At each trial site, three broadcast foliar applications of a suspension concentrate formulation of fluopicolide were made at four to six day retreatment intervals to bell pepper, chili pepper and tomato at 0.128 - 0.140 g a.i./ha/application for a total seasonal rate of 0.391 - 0.412 kg a.i./ha. An adjuvant was added to the spray mixture for all applications. Samples of bell pepper, chili pepper and tomato fruit were harvested two days after the last application. Additional samples were collected from two tomato trials and one bell pepper trial at 1, 3, 5 and 7 days following the last application to generate residue decline data.

Residues of fluopicolide and the metabolites BAM and PCA were determined using method 00782/M001 (LC/MS/MS). Residues of fluopicolide, BAM, and PCA are reported as the analyte *per se*. The limit of quantitation (LOQ) for each analyte is 0.010 ppm.

Residue decline data in *bell pepper* data indicate a general decline in fluopicolide residues with increasing pre-harvest intervals. Residue decline could not be determined for BAM and PCA as residues were non-quantifiable at each of the sampling intervals.

Residue decline data in *tomato* indicate that fluopicolide residues generally decrease with increasing pre-harvest intervals. Residue decline could not be assessed for BAM or PCA as residues were largely non-quantifiable at each of the sampling intervals.

Commodity	Total Application Rate (kg a.i./ha)	PHI (days)	n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Fluopicolide									
Bell Pepper	0.391-0.401	2	14	0.0411	0.557	0.523	0.099	0.156	0.163
Chili Pepper	0.398-0.407	2	6	0.0837	0.576	0.516	0.300	0.302	0.198
Tomato	0.399-0.412	2	24	0.015	0.420	0.375	0.145	0.150	0.094
BAM									
Bell Pepper	0.391-0.401	2	14	<0.01	<0.01	<0.01	<0.01	<0.01	0
Chili Pepper	0.398-0.407	2	6	<0.01	<0.01	<0.01	<0.01	<0.01	0
Tomato	0.399-0.412	2	24	<0.01	<0.01	<0.01	<0.01	<0.01	0
PCA									
Bell Pepper	0.391-0.401	2	14	<0.01	<0.01	<0.01	<0.01	<0.01	0
Chili Pepper	0.398-0.407	2	6	<0.01	<0.01	<0.01	<0.01	<0.01	0
Tomato	0.399-0.412	2	24	<0.01	0.013	0.012	0.01	0.01	0.0006

NATURE OF THE RESIDUE IN GRAPE	PMRA 1446416

CROP FIELD TRIALS ON GRAPES — **PMRA 1446468**

During the 2002 growing season a sufficient number of trials were conducted in representative NAFTA growing regions to evaluate the magnitude of fluopicolide in/on grapes.

At each trial site, three broadcast foliar applications of a suspension concentrate formulation of fluopicolide were made at four to six day retreatment intervals to grapes at 0.126-0.171 kg a.i./ha/application for a total seasonal rate of 0.387-0.449 kg a.i./ha. Samples of grapes were harvested 20-21 days after the last application.

Residues of fluopicolide and the metabolites BAM and PCA were determined using method 00782 (LC/MS/MS). Residues of fluopicolide, BAM, and PCA are reported as the analyte *per se*. The limit of quantitation (LOQ) for each analyte is 0.010 ppm

Commodity	Total Application Rate (kg a.i./ha)	PHI (days)	n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Fluopicolide									
Wine Grapes	0.387-0.449	20-21	32	0.065	1.10	0.985	0.210	0.312	0.289
BAM									
Wine Grapes	0.387-0.449	20-21	32	<0.01	<0.01	<0.01	<0.01	<0.01	0
PCA									
Wine Grapes	0.387-0.449	20-21	32	<0.01	0.013	0.012	0.010	0.010	0.001

CROP FIELD TRIALS ON LEAFY VEGETABLES (CELERY, HEAD LETTUCE, LEAF LETTUCE AND SPINACH) — **PMRA 1446450; 1446451; 1446466; 1446467**

During the 2002 growing season a sufficient number of trials were conducted in representative NAFTA growing regions to evaluate the magnitude of fluopicolide in/on leafy vegetables.

At each trial site, three broadcast foliar applications of a suspension concentrate formulation of fluopicolide were made at three to seven day retreatment intervals to celery, head lettuce, leaf lettuce and spinach plants at 0.126-0.141 kg a.i./ha/application for a total seasonal rate of 0.391-0.412 kg a.i./ha. Samples of leafy vegetables were harvested two days after the last application. Additional samples were collected from one trial each for celery, head lettuce, leaf lettuce and spinach at 1, 3, 5 and 7 days following the last application to generate residue decline data.

Residues of fluopicolide and the metabolites BAM and PCA were determined using method 00782/M001 (LC/MS/MS) for analysis of lettuce and method 1611-00.02 (LC/MS/MS) for analysis of spinach and celery. Residues of fluopicolide, BAM, and PCA are reported as the analyte *per se*. The limit of quantitation (LOQ) for each analyte is 0.010 ppm.

The residue decline data on *celery* indicate that residues of fluopicolide peaked at day 5 and decreased slightly by day 7. Residue decline of BAM and PCA could not be evaluated as residues were each non-quantifiable.

The residues decline data on *head lettuce* showed no trend with increasing pre-harvest intervals for fluopicolide residues. Residue decline of BAM and PCA could not be evaluated as residues were each non-quantifiable.

The residue decline data on *leaf lettuce* indicate that fluopicolide residues decrease with increasing pre-harvest intervals. Residues of BAM increased by the end of the sampling period. Residue decline could not be evaluated for PCA as residues were non-quantifiable (<0.01 ppm) at each of the sampling intervals.

The residue decline data on *spinach* indicate that with increasing pre-harvest intervals residues of fluopicolide decreased, residues of BAM remained relatively constant and residues of PCA increased.

NATURE OF THE RESIDUE IN GRAPE							PMRA 1446416		
Commodity	Total Application Rate (kg a.i./ha)	PHI (days)	n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Fluopicolide									
Celery	0.397-0.410	2	14	0.037	13.6	9.85	1.23	3.47	3.89
Head Lettuce with Wrapper Leaves	0.392-0.412	2	14	0.455	7.15	6.34	2.39	2.68	2.06
Head Lettuce Without Wrapper Leaves	0.392-0.412	2	14	<0.01	0.324	0.309	0.038	0.103	0.126
Leaf Lettuce	0.391-0.408	2	14	0.444	11.7	9.78	6.43	6.37	2.96
Spinach	0.400-0.410	2	14	5.43	16.8	16.2	8.53	9.71	3.87
BAM									
Celery	0.397-0.410	2	14	<0.01	0.041	0.039	0.01	0.017	0.011
Head Lettuce with Wrapper Leaves	0.392-0.412	2	14	<0.01	0.013	0.012	0.010	0.010	0.001
Head Lettuce Without Wrapper Leaves	0.392-0.412	2	14	<0.01	<0.01	<0.01	<0.01	<0.01	0
Leaf Lettuce	0.391-0.408	2	14	<0.01	0.038	0.031	0.010	0.014	0.008
Spinach	0.400-0.410	2	14	0.022	0.188	0.170	0.065	0.072	0.047
PCA									
Celery	0.397-0.410	2	14	<0.01	0.024	0.021	0.01	0.012	0.004
Head Lettuce with Wrapper Leaves	0.392-0.412	2	14	<0.01	<0.01	<0.01	<0.01	<0.01	0
Head Lettuce Without Wrapper Leaves	0.392-0.412	2	14	<0.01	<0.01	<0.01	<0.01	<0.01	0
Leaf Lettuce	0.391-0.408	2	14	<0.01	<0.01	<0.01	<0.01	<0.01	0
Spinach	0.400-0.410	2	14	<0.01	0.090	0.076	0.013	0.024	0.024

NATURE OF THE RESIDUE IN GRAPE	PMRA 1446416

CROP FIELD TRIALS ON ONION (BULB AND GREEN) — **PMRA 1446472**

During the 2002-2003 growing seasons a sufficient number of trials were conducted in representative NAFTA growing regions to evaluate the magnitude of fluopicolide in/on bulb vegetables.

At each trial site, three broadcast foliar applications of a suspension concentrate formulation of fluopicolide were made at four to six day retreatment intervals to bulb onion and green onion plants at 0.147-0.156 kg a.i./ha/application for a total seasonal rate of 0.392-0.410 kg a.i./ha. An adjuvant was added to the spray mixture for all applications. Bulb and green onions were harvested two days after the last application. Additional samples were collected from two trials (one bulb onion and one green onion) at 1, 3, 5 and 7 days following the last application to generate residue decline data.

Residues of fluopicolide and the metabolites BAM and PCA were determined using method 1611-00.02 (LC/MS/MS). Residues of fluopicolide, BAM, and PCA are reported as the analyte *per se*. The limit of quantitation (LOQ) for each analyte is 0.010 ppm.

In the residue decline trials, residues of fluopicolide generally decreased with increasing sampling intervals in/on bulb and green onions. Residues of BAM and PCA were non-quantifiable in/on bulb onions from all sampling intervals. Residues of BAM in/on green onions increased slightly from the 1-day sampling interval to the 7-day sampling interval. Residues of PCA in/on green onions were non-quantifiable.

Commodity	Total Application Rate (kg a.i./ha)	PHI (days)	n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Fluopicolide									
Bulb, Onion	0.398-0.410	2	14	0.013	2.52	1.57	0.052	0.328	0.664
Green Onion	0.398-0.404	2	6	1.49	4.50	4.49	1.90	2.64	1.44
BAM									
Bulb, Onion	0.398-0.410	2	14	<0.01	<0.01	<0.01	<0.01	<0.01	0
Green Onion	0.398-0.404	2	6	<0.01	0.014	0.014	0.011	0.012	0.002
PCA									
Bulb, Onion	0.398-0.410	2	14	<0.01	<0.01	<0.01	<0.01	<0.01	0
Green Onion	0.398-0.404	2	6	<0.01	<0.01	<0.01	<0.01	<0.01	0

NATURE OF THE RESIDUE IN GRAPE	PMRA 1446416

CROP FIELD TRIALS ON POTATO — **PMRA 1446457**

During the 2001 growing season a sufficient number of trials were conducted in representative NAFTA growing regions to evaluate the magnitude of fluopicolide in/on potato.

At each trial site, three broadcast foliar applications of a suspension concentrate formulation of fluopicolide were made at four to six day retreatment intervals to potato plants at 0.128-0.149 kg a.i./ha/application for a total seasonal rate of 0.392-0.417 kg a.i./ha. An adjuvant was added to the spray mixture for all applications. Mature potato tubers were harvested 6-8 days after the last application. Additional samples were collected from two trials at 2, 5, 10, and 14 days following the last application to generate residue decline data.

Residues of fluopicolide and the metabolites BAM and PCA were determined using method 00782/M001 (LC/MS/MS). Residues of fluopicolide, BAM, and PCA are reported as the analyte *per se*. The limit of quantitation (LOQ) for each analyte is 0.010 ppm.

Fluopicolide-derived residues were not detected above the LOQ (0.01 ppm) in either of the two residue decline studies. Therefore, residue decline could not be assessed.

Commodity	Total Application Rate (kg a.i./ha)	PHI (days)	n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Fluopicolide									
Potato, tuber	0.392-0.417	6-8	38	<0.01	0.0126	0.0113	0.01	0.01	0
BAM									
Potato, tuber	0.392-0.417	6-8	38	<0.01	<0.01	<0.01	<0.01	<0.01	0
PCA									
Potato, tuber	0.392-0.417	6-8	38	<0.01	0.0447	0.0438	0.01	0.012	0.008

FIELD ACCUMULATION IN ROTATIONAL CROPS- WHEAT — **PMRA 1912088**

The field rotational study was conducted was conducted in NAFTA growing Regions during the 2001-2002 growing season.

At each trial site, three broadcast foliar applications of a suspension concentrate formulation of fluopicolide were made at four to six day retreatment intervals to a primary crop of potatoes or to bare ground at 0.127-0.140 kg a.i./ha, for total application rates 0.388-0.417 kg a.i./ha. A spreader/sticker adjuvant was added to the spray mixtures for all applications. Potatoes were harvested ~7 days after the last application. The rotational wheat crop was planted 29-37 days after the last application (22-30 days after potato harvest). Wheat forage, hay, grain, and straw were collected at normal commercial harvest. The LOQ (limit of quantitation) was 0.01 ppm for each analyte.

Summary of Residue Data in Rotational Crops Following Primary Treatment with Fluopicolide

Commodity	Total Application Rate (kg a.i./ha)	PBI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Fluopicolide									
Wheat, forage	0.388-0.417	29-37	42	<0.01	0.213	0.160	0.027	0.044	0.047
Wheat, hay			42	0.014	0.501	0.364	0.051	0.100	0.119
Wheat, grain			42	<0.01	0.014	0.014	0.010	0.010	0.001
Wheat, straw			42	<0.01	0.350	0.338	0.034	0.055	0.075

NATURE OF THE RESIDUE IN GRAPE							PMRA 1446416		
BAM									
Wheat, forage	0.388-0.417	29-37	42	<0.01	0.123	0.106	0.019	0.028	0.027
Wheat, hay			42	<0.01	0.102	0.095	0.010	0.022	0.024
Wheat, grain			42	<0.01	<0.01	<0.01	<0.010	<0.010	0.000
Wheat, straw			42	<0.01	0.050	0.050	0.010	0.015	0.011
3-OH-BAM									
Wheat, forage	0.388-0.417	29-37	42	<0.01	0.050	0.045	0.013	0.019	0.012
Wheat, hay			42	<0.01	0.160	0.133	0.032	0.048	0.044
Wheat, grain			42	<0.01	<0.01	<0.01	<0.010	<0.010	0.000
Wheat, straw			42	<0.01	0.081	0.078	0.026	0.031	0.019
PCA (AE C657188)									
Wheat, forage	0.388-0.417	29-37	42	<0.01	0.043	0.027	0.010	0.013	0.007
Wheat, hay			42	<0.01	0.064	0.055	0.010	0.018	0.013
Wheat, grain			42	<0.01	0.062	0.060	0.011	0.016	0.011
Wheat, straw			42	<0.01	0.043	0.040	0.010	0.012	0.007
P1X (AE 1344122)									
Wheat, forage	0.388-0.417	29-37	42	<0.01	0.064	0.057	0.012	0.018	0.013
Wheat, hay			42	<0.01	0.073	0.070	0.025	0.028	0.017
Wheat, grain			42	<0.01	0.075	0.075	0.019	0.025	0.020
Wheat, straw			42	<0.01	0.055	0.049	0.020	0.021	0.011

PROCESSED FOOD AND FEED- WHITE GRAPES	PMRA 1446478 and 1446579
Test Site	Maine-et Loire, France; and Hesse and Rhineland-Palatinate, Germany
Treatment	Three foliar spray applications
Rate	121-137 g a.i./ha/application for a seasonal rate of 506-538 g a.i./ha
End-use product	SE10 Suspo-Emulsion
Pre-harvest interval	21 days

	Processing Factor (Mean)		
	Fluopicolide	BAM	PCA
Pomace	1.9	0.80	2.0
Must, Pasteurized	0.33	0.40	0.50
Yeast, Pasteurized	4.5	0.70	0.90
Young Wine, Pasteurized	0.24	0.40	0.50
Mature Wine, Pasteurized	0.30	0.50	0.50
Must, Non-Pasteurized	0.52	0.40	0.60
Yeast, Non-Pasteurized	7.4	1.0	3.0
Young Wine, Non-Pasteurized	0.5	0.50	0.40
Mature Wine, Non-Pasteurized	0.48	0.40	0.40

PROCESSED FOOD AND FEED- RED TABLE GRAPES	PMRA 1446455
Test Site	Thessaloniki, Greece and Andalusia, Spain
Treatment	Three foliar spray applications

NATURE OF THE RESIDUE IN GRAPE				PMRA 1446416
Rate	127-131 g a.i./ha/application for a seasonal rate of 386-387 g a.i./ha			
End-use product	Emulsifiable Concentrate (EC) formulation; 95 g fluopicolide/L			
Pre-harvest interval	21 days			
	Processing Factor (Mean)			
	Fluopicolide	BAM	PCA	
Raisins	3.4	4	4	

PROCESSED FOOD AND FEED- POTATO	PMRA 1446482
Test Site	Ephrata, Washington (NAFTA Zone 11)
Treatment	Three foliar applications at the BBCH 47-48 growth stages
Rate	651-656 g a.i./ha/application for a seasonal rate of 1.96 kg a.i./ha
End-use product	EXP 11067B; suspension concentrate containing 480 g fluopicolide/L
Pre-harvest interval	7 days

Residues of fluopicolide and its metabolites BAM and PCA were non-quantifiable (<LOQ; <0.01 ppm) in/on potato tubers and the potato processed commodities flakes and chips. As such no conclusion could be made regarding the potential concentration of residues upon processing into flakes and chips. In potato wet peel, only residues of fluopicolide were quantifiable. Fluopicolide residues concentrated into wet peels with an estimated concentration factor of ~4.9x.

PROCESSED FOOD AND FEED- TOMATO			PMRA 1446480
Test Site	Kerman, California (NAFTA Zone 12)		
Treatment	Three foliar applications.		
Rate	0.663-0.680 kg a.i./ha/application for a seasonal rate of 2.01 kg a.i./ha		
End-use product	Suspension concentrate		
Pre-harvest interval	2 days		
	Processing Factor (Mean)		
Processed Commodity	Fluopicolide	BAM	PCA
Puree	1.7	-	-
Paste	2.4	-	-

Residues of BAM were non-quantifiable (<LOQ; <0.01 ppm) in/on tomato RAC and the processed commodities puree and paste. Residues of PCA were found at 0.0111 ppm in one tomato paste sample at slightly above the LOQ of 0.01 ppm. Residues of PCA were below the LOQ in all other tomato RAC and processed commodities.

PROCESSED FOOD AND FEED- ROTATIONAL WHEAT					PMRA 1446481
Test Site	Carlyle, Illinois (NAFTA Zone 5)				
Treatment	Single spray application to bare ground; 36 days prior to the planting of winter wheat.				
Rate	1.98 kg a.i./ha				
End-use product	Suspension concentrate				
Pre-harvest interval	Wheat grain was collected at maturity, 250 days after planting.				
Processed Commodity	**Processing Factor (Mean)**				
	Fluopicolide	BAM	PCA	3-OH-BAM	P1X
Bran	3.0	~1.7	1.9	3.0	2.2

NATURE OF THE RESIDUE IN GRAPE			PMRA 1446416		
Flour	~0.4	~0.7	1.0	~0.3	0.60
Middlings	1.5	~1.1	1.3	1.0	1.0
Shorts	2.0	~1.2	1.8	1.5	1.4
Germ	4.7	~1.8	0.9	1.5	0.70
Estimated (~) processing factors were calculated when residues were reported below the LOQ in the RAC and/or the processed matrix.					

LIVESTOCK FEEDING – Dairy cattle — **PMRA 1446421**

A dairy cattle feeding study was conducted during which three treatment groups of three dairy cows each were dosed orally with fluopicolide in the feed at dose rates corresponding to 0.5, 1.7 and 5.7 ppm (dry feed weight) for 28 consecutive days. Cows were milked twice daily, and samples were composited daily for each cow. Cows were sacrificed within 17 hours of the final dose. Samples of liver, kidney, fat (composite of mesenterial, perirenal, and subcutaneous), and muscle (composite of round and loin) were collected from each cow. Samples of milk collected on study days 1, 4, 7, 10, 13, 16, 19, 22, 25 and 28 from all dose levels were reserved for analysis. Samples of cream and milk were generated from milk samples collected on study day 22 (high dose group only). Samples of cattle matrices wee analyzed for residues of fluopicolide, BAM and PCA using Method No. AR 303-02 (LC/MS/MS). The validated limits of quantitation (LOQs) were 0.010 ppm for each analyte in milk, 0.020 ppm for each analyte in muscle, and 0.050 ppm for each analyte in fat, liver and kidney.

Matrix	Feeding Level (ppm)	n	Min	Max	Median	Mean	Standard Deviation
Fluopicolide							
Milk	0.5	6	<0.010	<0.010	<0.010	0.010	0
	1.7	12	<0.010	<0.010	<0.010	0.010	0
	5.7	30	<0.010	0.024	0.010	0.011	0.003
Cream	5.7	3	0.012	0.018	0.017	0.016	0.003
Skim Milk	5.7	3	<0.010	< 0.010	<0.010	<0.010	0
Muscle	0.5	3	<0.020	<0.020	<0.020	<0.020	0
	1.7	3	<0.020	<0.020	<0.020	<0.020	0
	5.7	3	<0.020	<0.020	<0.020	<0.020	0
Fat	5.7	3	<0.050	<0.050	<0.050	<0.050	0
Liver	5.7	3	<0.050	<0.050	<0.050	<0.050	0
Kidney	5.7	3	<0.050	<0.050	<0.050	<0.050	0
AE C653711							
Milk	0.5	6	<0.010	<0.010	<0.010	0.010	0
	1.7	12	<0.010	<0.010	<0.010	0.010	0
	5.7	30	<0.010	<0.010	<0.010	0.010	0
Cream	5.7	3	<0.010	<0.010	<0.010	0.010	0
Skim Milk	5.7	3	<0.010	<0.010	<0.010	0.010	0
Muscle	0.5	3	<0.020	<0.020	<0.020	<0.020	0
	1.7	3	<0.020	<0.020	<0.020	<0.020	0
	5.7	3	<0.020	<0.020	<0.020	<0.020	0
Fat	5.7	3	<0.050	<0.050	<0.050	<0.050	0
Liver	5.7	3	<0.050	<0.050	<0.050	<0.050	0
Kidney	5.7	3	<0.050	<0.050	<0.050	<0.050	0

NATURE OF THE RESIDUE IN GRAPE					PMRA 1446416		
AE C657188							
Milk	0.5	6	<0.010	<0.010	<0.010	0.010	0
	1.7	12	<0.010	<0.010	<0.010	0.010	0
	5.7	30	<0.010	<0.010	<0.010	0.010	0
Cream	5.7	3	<0.010	<0.010	<0.010	0.010	0
Skim Milk	5.7	3	<0.010	<0.010	<0.010	0.010	0
Muscle	0.5	3	<0.020	<0.020	<0.020	<0.020	0
	1.7	3	<0.020	<0.020	<0.020	<0.020	0
	5.7	3	<0.020	<0.020	<0.020	<0.020	0
Fat	5.7	3	<0.050	<0.050	<0.050	<0.050	0
Liver	5.7	3	<0.050	<0.050	<0.050	<0.050	0
Kidney	5.7	3	<0.050	<0.050	<0.050	<0.050	0
The only feed commodities associated with the Canadian uses are potato culls and processed potato waste. Using the highest dietary burden estimate of 0.23 ppm for beef cattle, finite residues of fluopicolide are not anticipated in meat, milk and meat by-products given that residues were <LOQ in all commodities at the 0.5 ppm (2.2x) and 1.7 ppm (7.4x) dose levels.							
LIVESTOCK FEEDING – Laying hens							
Given that none of the registered crop commodities are fed to poultry, a poultry feeding study is not required at this time.							

Table 6 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

PLANT STUDIES	
RESIDUE DEFINITION FOR ENFORCEMENT **Primary crops** **Rotational crops**	Fluopicolide
RESIDUE DEFINITION FOR RISK ASSESSMENT **Primary crops** **Rotational crops**	Fluopicolide and BAM in all primary crops, except tuberous and corm vegetables. Fluopicolide, BAM and PCA in tuberous and corm vegetables. Fluopicolide, BAM, 3-OH-BAM, PCA and P1X in all rotational crops.
METABOLIC PROFILE IN DIVERSE CROPS	The metabolism of fluopicolide was similar in grape, lettuce and potato.
ANIMAL STUDIES	
ANIMALS	**Ruminant**
RESIDUE DEFINITION FOR ENFORCEMENT	Fluopicolide
RESIDUE DEFINITION FOR RISK ASSESSMENT	Fluopicolide and BAM
METABOLIC PROFILE IN ANIMALS (cow, hen, rat)	Yes
FAT SOLUBLE RESIDUE	Yes, based on log K_{ow} of 2.9.

PLANT STUDIES			
DIETARY RISK FROM FOOD AND WATER			
	POPULATION	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Only	**Food and Water**
Refined chronic non-cancer dietary risk **ADI = 0.067 mg/kg bw/day** **Estimated chronic drinking water concentration = 0.323 μg a.i./L**	**All infants < 1 year**	2.8	36.1
	Children 1–2 years	4.3	19.4
	Children 3 to 5 years	3.5	17.6
	Children 6–12 years	2.4	12.1
	Youth 13–19 years	1.8	9.2
	Adults 20–49 years	2.4	11.9
	Adults 50+ years	2.5	12.4
	Total population	2.5	12.6
Refined acute dietary exposure analysis, 95th percentile **Estimated acute drinking water concentration = 0.326 μg a.i./L**	**POPULATION**	**ESTIMATED RISK % of ACUTE REFERENCE DOSE (ARfD)**	
		Food Only	**Food and Water**
ARfD = 0.2 mg/kg bw	**Females 13–49 years**	10.46	15.44

Table 7 Fate and Behaviour in the Terrestrial Environment

Process	$t_{1/2}$ or DT_{50}	DT_{90}	Kinetics	Comments	Reference
Fluopicolide					
Abiotic transformation					
Hydrolysis	pH 5: 365 d pH 7: 330 d pH 9: 365	nr	SFO	not a major route of transformation	1912076
Phototransformation soil	80 d	nr	SFO	Based on a 12-hour light /12-hour day cycle; not a major route of transformation	1912018
	182 d	*nr*	*SFO*		***1912021***
Biotic transformation					
Aerobic sandy clay loam soil	415	1380	SFO	Persistent	1912040
Aerobic loamy sand soil	446	1760	DFOP	Persistent	
Sandy loam soil	376	1250	SFO	Persistent	1912038
Mobility					
Adsorption	Loam (EFS-54)	K_d = 8.46	K_{oc} = 409	Moderate	1912037
	Sand (EFS-65)	***K_d = 1.45***	***K_{oc} = 290***	Moderate	
	Sandy loam (EFS-86)	***K_d = 3.56***	***K_{oc} = 161***	Moderate	
	EFS-88	***K_d = 3.25***	***K_{oc} = 361***	Moderate	
	EFS-93	***K_d = 4.68***	***K_{oc} = 360***	Moderate	
	EFS-94	***K_d = 0.21***	***K_{oc} = 107***	High	
	EFS-95	***K_d = 0.17***	***K_{oc} = 84***	High	
Leaching	Not submitted				

Process	$t_{1/2}$ or DT_{50}	DT_{90}	Kinetics	Comments	Reference
Fluopicolide					
Abiotic transformation					
Field Studies					
Terrestrial Field Dissipation	St George, ON, Canada: 204 d	152 d	736 d	DFOP	Persistent; 42% carryover to following season	1911921
	Wisconsin U.S. (542 d) Washington U.S. (547 d)	38 d 314 d	2850 d 1040	DFOP SFO	Persistent; 42 and 38% carryover to following season at Wisconsin and Washington site, respectively	1911999
Transformation product – BAM					
Abiotic transformation					
Hydrolysis		Stable		Not a major route of transformation	1912153
Transformation product – PCA					
Biotic transformation					
Sandy loam soil		4.59	***15.2***	***SFO***	Non-persistent	1912097
Loamy sand soil		3.23	10.7	SFO		
Silt loam soil		4.45	14.8	SFO		

nr = not reported

Process	$t_{1/2}$ or DT_{50}	DT_{90}	Kinetics	Comments	Reference
Fluopicolide					
Abiotic transformation					
Hydrolysis	pH 5: 365 d pH 7: 330 d pH 9: 365	nr	SFO	not a major route of transformation	1912076
Aquatic Phototransformation	170 d	nr	SFO	Benzoyl-U-^{14}C label; environmental phototransformation half-life based on natural sunlight in summer at 40°N latitude; not a major route of transformation.	1912007
	Stable			Pyridyl-2, 6-^{14}C label; not a major route of transformation	1911944
Aerobic biotransformation					
Iron Hatch: water pH 7.2 0.5 % OC	Water phase: 235 Whole system: 849	Water phase: 1630 Whole system: 2820	DFOP SFO	Persistent	1912028
Mill Stream: Water pH 6.6 5.3 % OC	Water phase: 6 Whole system: 1400	Water phase: 226 Whole system: 4650	DFOP SFO		
Anaerobic biotransformation					
Pond water-sandy loam sediment (water pH 6.55)	23.9 d (water phase) 2130 d (whole system)	545 d (water phase) 7070 d (whole system)	DFOP SFO	Persistent	1912094

Table 8 Fate and Behaviour in the Aquatic Environment

nr = not reported

Table 9 Toxicity of Fluopicolide and BAM to Non-Target Species

Organism	Study type	Species	Test material	Endpoint	Value	Effect of concern	Reference
Terrestrial Organisms							
Earthworm	Acute	*Eisenia foetida*	Fluopicolide (97.1%)	14-d LC_{50} 14-d NOEC	>1000 mg a.i./kg soil < 62.5 mg a.i./kg soil	Mortality Reduced body weight	1912055
			BAM (97%)	14-d LC_{50} 14-d NOEC	750 mg a.i./kg soil 320 mg a.i./kg soil	Mortality Reduced body weight	1912082
	Chronic		Fluopicolide (96.1%)	28-d NOEC	62.5 mg a.i./kg soil	Reduced body weight	1911891
			BAM (97%)	28-d NOEC	250 mg a.i./kg soil	Reduced number of offspring	1912233
Bee	Contact	*Apis mellifera*	Fluopicolide (99.3%)	72-h LD_{50}	> 100 µg a.i./bee	Mortality	1911863
	Oral		nr	LD_{50}	> 241 µg a.i./bee	Mortality	2024179
Beneficial arthropods	Acute	*Typhlodromus pyri*	Formulated product EXT11074B: (44.4 g/kg fluopicolide and 666.7 g/kg fosetyl-Aluminum)	LR_{50}	Standard lab test: LR_{50} = 317 g fluopicolide/ha	Mortality	2024179
			Formulated product EXT1120A: (62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride)	LR_{50}	Standard lab test: LR_{50}= >500 g fluopicolide/ha Extended lab test: LR_{50} >260 g fluopicolide/ha		
		Aphidius rhopalosiphi	Formulated product EXT11074B: (44.4 g/kg fluopicolide and 666.7 g/kg fosetyl-Aluminum)	LR_{50}	Standard lab test: LR_{50} = 365 g fluopicolide/ha		
			Formulated product EXT1120A: (62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride)	LR_{50}	Standard lab test: LR_{50}= 155 g fluopicolide/ha Extended lab test: LR_{50} >500 g fluopicolide/ha		

Organism	Study type	Species	Test material	Endpoint	Value	Effect of concern	Reference
		Chrysoperla carnea	Formulated product EXT1120A: (62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride)	LR_{50}	Limit test: LR_{50} > 400 g fluopicolide/ha		
Birds	Acute	mallard duck (*Anas platyrhynchos*)	Fluopicolide (97.1%)	LD_{50}	>2250 mg a.i./kg bw	Mortality	1912201
		Bobwhite quail (*Colinus virginianus*)					1912199
	Reproduction	northern bobwhite quail (*Colinus virginuanus*)	Fluopicolide (96.1%)	NOEC / LOEC[1]	23.5 / 58.5 mg a.i./kg bw/day Endpoints affected: hatchling body weight, proportion of hatchling survivors to number hatched.		1911931
		mallard duck (*Anas platyrhynchos*)	Fluopicolide (95.9%)	NOEC / LOEC[1]	14 / 36 mg a.i./kg bw/day Endpoints affected: number viable embyos, live embryos, number hatched, ratio of number hatched to eggs laid and to eggs set, hatchling survival and proportion of survivors to eggs set.		1911934
Mammals	Acute	Rat	Fluopicolide (97.7%)	LD_{50}	> 5000 mg a.i./kg bw	Survival	1446247
			Formulation (AE C638206 SC 480, containing 489 g a.i./L)	LD_{50}	> 5000 mg a.i./kg bw	Survival	1446378, 1446379
	2 generation reproduction	Rat	Fluopicolide (95.9%)	NOEL	**Parental** NOAEL= 36.4/41.0 mg/kg bw/day ♂/♀ LOAEL= 145/160 mg/kg bw/day ♂/♀; (decreased body weight gain in F0 (10/14%) and F1 (11/10%) during pre-mating; decreased food consumption F0 pre-mating week one (8/9%) and week seven ♀ (10%) and F1 ♂ week one (7%); decreased body weight F0 ♀ at gestational day six and 13 (7%) and F1 ♀ at gestational day six and 13 (11 and 10%); decreased body weight gain F0 and F1 gestational days 0-13 (14-16%); decreased body weight gain F0 and F1 lactating ♀ (8 and 13%); decreased food consumption F0 and F1 ♀ (up to 12%) during first 13 days of lactation. **Reproductive** NOAEL= >180/193 mg/kg bw/day ♂/♀ LOAEL= not determined **Offspring** NOAEL= 36.4/41.0 mg/kg bw/day ♂/♀ LOAEL= 145/160 mg/kg bw/day ♂/♀; (based on decreased bodyweight in female F1 (8-9%) and F2 (10 – 13%) pups at 14, 21 and 28 days old).		1446296, 1449297

Organism	Study type	Species	Test material	Endpoint	Value	Effect of concern	Reference
Vascular plants	Seedling emergence	four monocot species: corn, wheat, onion, ryegrass six dicot species: buckwheat, cucumber, soybean, sunflower, tomato, turnip	AE C638206 SC40 (formulation: 485 g a.i./L) Tier I study : (133 g a.i./ha)	NOEC = 133 g a.i./ha EC_{25} >133 g a.i./ha (for all test species)			1912226
	Vegetative vigour			NOEC < 133 g a.i./ha (for ryegrass) EC_{25} >133 g a.i./ha (for all test species)			
Freshwater Organisms							
Invertebrates	Acute	*Daphnia magna*	fluopicolide (97.1%)	48-h LC_{50} NOEC (limit test)	>1.7 mg a.i./L 1.7 mg a.i./L	immobility	1911877
			BAM (99.5%)	48-h LC_{50} NOEC	184.1 mg a.i./L 101.0 mg a.i./L		1912156
	Chronic	*Daphnia magna*	fluopicolide (97.7%)	21-d LC_{50} (survival) NOEC (reproductive effects)	>0.75 mg a.i./L 0.19 mg a.i./L	mortality Reduced reproduction	1911873
Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	Fluopicolide (97.1%)	96-h LC_{50} NOEC	0.349 mg a.i./L 0.152 mg a.i./L	mortality	1912023
			BAM (99.5%)	96-h LC_{50} NOEC	246 mg a.i./L 103 mg a.i./L		1912158
			PCA (99.8%)	96-h LC_{50} NOEC	>102 mg a.i./L 102 mg a.i./L		1912073
		Carp (*Cyprinus carpio*)	Fluopicolide (99.4%)	96-h LC_{50} NOEC	1.3 mg a.i./L 0.25 mg a.i./L		1912212
		Rice fish (*Oryzial latipes*)	Fluopicolide (96.1%)	96-h LC_{50} NOEC	0.67 mg a.i./L 0.42 mg a.i./L		1911870
		Bluegill sunfish (*Lepomis macrochirus*)	Fluopicolide (97.1%)	96-h LC_{50} NOEC	0.75 mg a.i./L 0.56 mg a.i./L		1911874
	Chronic	Fathead minnow (*Pimephales promelas*)	Fluopicolide (97.7%)	33 day early life stage NOEC LOEC	0.15 mg a.i./L 0.29 mg a.i./L	Length of surviving fish	1912217

Organism	Study type	Species	Test material	Endpoint	Value	Effect of concern	Reference
Algae	Acute	Green algae (*Pseudokirchneriella subcapittata* –formerly known as *Selenastrum capricornutum*)	Fluopicolide (99.4%)	96-h EC_{50} NOEC	2.6 mg a.i./L 0.59 mg a.i./L	Cell density Cell density, biomass and growth rate	1911924
			Fluopicolide (97.1%)	96-h EC_{50} NOEC (limit test)	>1.8 mg a.i./L 1.8 mg a.i./L	Cell density, biomass and growth rate	1911876
			BAM (99.5%)	96-h EC_{50} NOEC	62 mg a.i./L 140 mg a.i./L 40 mg a.i./L	Biomass Growth rate Biomass and growth rate	1911888
		freshwater diatom *(Navicula pelliculosa)*	BAM (98%)	96-h EC_{50} NOEC	>10 mg a.i./L 10 mg a.i./L	Cell density, biomass and growth rate	1911926
		freshwater blue-green algae *(Anabaena flos-aquae)*	Fluopicolide (97.1%)	96-h EC_{50} NOEC (limit test)	>2.2 mg a.i./L 2.2 mg a.i./L		1911875
Vascular Plants	Acute	Duckweed (*L. gibba*)	Fluopicolide (97.7%)	7-d EC_{50} 7-d NOEC	>3.2 mg a.i./L 3.2 mg a.i./L	Frond count, growth rate and biomass	1912051
			BAM (98%)	7-d EC_{50} 7-d NOEC	80 mg a.i./L 25 mg a.i./L	Biomass	1911928
Marine and estuarine Organisms							
Invertebrates	Acute	Mysid shrimp (*Americamysis bahia*)	Fluopicolide 97.7%	96-h EC_{50} NOEC	3.2 mg a.i./L 1.6 mg a.i./L	Mortality	1912103
		Eastern oysters (*Crassostrea virginica*)	Fluopicolide 97.7%	96-h EC_{50} NOEC	>2.6 mg a.i./L 2.6 mg a.i./L	Shell deposition	1911994
Fish	Acute	Sheepshead minnow (*Cypronodon variegates*)	Fluopicolide 97.7%	96-h EC_{50} NOEC	0.41 mg a.i./L 0.20 mg a.i./L	Mortality	1912106
		Zebra fish (*Brachydanio rerio*)	Fluopicolide 96.1	96-h EC_{50} NOEC	1.7 mg a.i./L 0.96 mg a.i./L		1912215
Algae	Acute	Marine diatom *(Skeletonema costatum)*	Fluopicolide 97.7%	96-h EC_{50} NOEC	0.052 mg a.i./L cnd	Growth inhibition	1912049

1 - NOEL calculated using (concentration in diet x FIR)/BW; FIR = mean food ingestion rate reported in study, BW = mean body weight reported in study
cnd – could not determine
nr = not reported

Table 10 Screening Level Risk Assessment for Earthworms and Bees

Organisms	Exposure	Endpoint Value	Application Rate	EEC[1]	RQ[2]
Earthworm	Acute	14-d LC_{50} ÷ 2: >500 mg a.i./kg soil	140.16 g a.i./ha x 4	0.18 mg a.i./kg	<0.001
	Chronic	28-d NOEC: 62.5 mg a.i./kg soil	140.16 g a.i./ha x 4	0.18 mg a.i./kg	<0.01
Bee	Acute contact	48-h LD_{50}: > 100 µg a.i./bee[3]	140.16 g a.i./ha	140.16 g a.i./ha	<0.01
	Acute oral	LD_{50}: > 241 µg a.i./bee[3]			<0.001
Atkins EL; Kellum D; Atkins KW. 1981. Reducing pesticide hazards to honey bees: mortality prediction techniques and integrated management techniques. Univ Calif, Div Agric Sci, Leaflet 2883. 22 pp					

1 -The environmental exposure concentration (EEC) in soil was calculated based on a two applications of 140.16 g a.i./L with a 7 day interval followed by a 14 day interval (during which an alternate fungicide would be used), then a final application at 140.16 g a.i./ha. The screening level EEC in soil assumes an application is made to bare soil with a soil density of 1.5 g/cm^3 and even mixing through a 15 cm depth. Bee: maximum single application rate (application rate x no. of applications).

2 - Risk Quotient (RQ) = exposure/toxicity; Risk quotients shown in bold exceed the level of concern (RQ > 1)

3 - Toxicity in µg/bee converted to the equivalent kg a.i./ha using a conversion factor of 1.12 (Atkins et al., 1981)

Table 11 Screening level risk assessment for birds

	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ
Small Bird (0.02 kg)				
Acute	225.00	Insectivore (small insects)	11.39	0.05
Reproduction	14.00	Insectivore (small insects)	11.39	0.81
Medium Sized Bird (0.1 kg)				
Acute	225.00	Insectivore (small insects)	8.89	0.04
Reproduction	14.00	Insectivore (small insects)	8.89	0.63
Large Sized Bird (1 kg)				
Acute	225.00	Herbivore (short grass)	9.27	0.04
Reproduction	14.00	Herbivore (short grass)	9.27	0.66

Table 12 Screening level risk assessment for mammals

	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ[1]
Small Mammal (0.015 kg)				
Acute	500.00	Insectivore (small insects)	6.55	0.01
Reproduction	36.40	Insectivore (small insects)	6.55	0.18
Medium Sized Mammal (0.035 kg)				
Acute	500.00	Herbivore (leafy foliage)	38.67	0.08
Reproduction	36.40	Herbivore (leafy foliage)	38.67	**1.06**
Large Sized Mammal (1 kg)				
Acute	500.00	Herbivore (leafy foliage)	20.66	0.04
Reproduction	36.40	Herbivore (leafy foliage)	20.66	0.57

1 – Risk quotients shown in bold exceed the level of concern (RQ > 1).

Table 13 Summary of the risk of fluopicolide and the transformation product BAM to aquatic organisms: screening level

Organism	Exposure	Species	Endpoint value (mg a.i./L)	Endpoint for RA[1] (mg a.i./L)	EEC[2] (mg a.i./L)	RQ[3]
Fluopicolide - Freshwater organisms						
Invertebrate	Acute	*Daphnia magna*	48-h LC_{50} > 1.7	>0.85	0.05	<0.1
	Chronic	*Daphnia magna*	21-d NOEC = 0.19	0.19	0.05	0.3
Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	96-h LC_{50} = 0.35	0.04	0.05	**1.4**
	Chronic	Fathead minnow *(Pimephales promelas)*	34-d ELS NOEC = 0.15	0.15	0.05	0.3
Amphibians	Acute	Surrogate fish (*Oncorhynchus mykiss*))	96-h LC_{50} = 0.35	0.04	0.28	**8.0**
	Chronic	Surrogate fish *(Pimephales promelas)*	34-d ELS NOEC = 0.15	0.15	0.28	**1.9**
Freshwater alga	Acute	Blue-Green algae (*Anaebaena flos-aquae*)	120-h EC_{50} > 2.2	>0.22	0.05	0.2
Vascular plant	Acute	Duckweed *(Lemna gibba)*	7-d EC_{50} = >3.2	>0.16	0.05	0.3
Fluopicolide - Marine and estuarine organisms						
Invertebrate	Acute	Mysid shrimp *(Americamysis bahia)*	96-h LC_{50} = 3.2	1.6	0.05	<0.1
Mollusk	Acute	Eatern Oysters *(Crassostrea virginica)*	96-h LC_{50} = >2.6	>1.3	0.05	<0.1
Fish	Acute	Sheepshead minnow *(Cypronodon variegates)*	96-h LC_{50} = 0.41	0.04	0.05	**1.3**
Marine alga	Acute	Marine diatom *(Skeletonema costatum)*	120-h LC_{50} = 0.052	0.021	0.05	**2.4**
BAM – Freshwater organisms						
Invertebrate	Acute	*Daphnia magna*	48-h LC_{50} = 184	92	0.026	<0.1
Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	96-h LC_{50} = 246	25	0.026	<0.1
	Chronic	Rainbow trout (*Oncorhynchus mykiss*)	60-d (embryo-larvae) NOEC = 10	10	0.0.26	<0.1
Algae	Acute	Freshwater diatom *(Navicula pelliculosa)*	96-h LC_{50} =>10	>5	0.026	<0.1
Amphibian	Acute	Surrogate fish (*Oncorhynchus mykiss*))	96-h LC_{50} = 246	25	0.14	<0.1
	Chronic	Rainbow trout (*Oncorhynchus mykiss*)	60-d (embryo-larvae) NOEC = 10	10	0.14	<0.1
Vascular plants	Acute	Duckweed *(Lemna gibba)*	7-d EC_{50} = 80	40	0.026	<0.1

1 - Endpoints used in the acute exposure risk assessment (RA) are derived by dividing the EC_{50} or LC_{50} from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates and plants, and by a factor of ten (10) for fish and amphibians.
2 - EEC based on a 15 cm water body depth for amphibians and a 80 cm water depth for all other aquatic organisms (section 2..2, Table 2.9.2-1).
3 – Risk quotients shown in bold exceed the level of concern (RQ > 1).

Table 14 Refined Risk Assessment for non-target aquatic organisms using percent drift deposition.

Organism	Exposure	Species	Endpoint value (mg a.i./L)	Endpoint for RA[1] (mg a.i./L)	Use Scenario	EEC Exposure from drift[2] (mg a.i./L)	RQ[3]
Fluopicolide - Freshwater organisms							
Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	96-h LC_{50} = 0.35	0.04	Ground	0.003	<0.1
					Airblast (early/late)	0.038 / 0.031	<1.0
					Aerial	0.012	0.3
Amphibians	Acute	Surrogate fish (*Oncorhynchus mykiss*)	96-h LC_{50} = 0.35	0.04	Ground	0.016	<1.0
					Airblast (early/late)	0.21 / 0.16	**5.3 / 4.0**
					Aerial	0.064	**1.6**
	Chronic		34-d ELS NOEC = 0.15	0.15	Ground	0.016	0.1
					Airblast (early/late)	0.21 / 0.16	**1.4/1.0**
					Aerial	0.064	0.4
Fluopicolide - Marine and estuarine organisms							
Fish	Acute	Sheepshead minnow *(Cypronodon variegates)*	96-h LC_{50} = 0.41	0.04	Ground	0.003	<0.1
					Airblast (early/late)	0.038 / 0.031	<1.0
					Aerial	0.012	0.3
Marine alga	Acute	Marine diatom *(Skeletonema costatum)*	120-h LC_{50} = 0.052	0.021	Ground	0.003	<1.0
					Airblast (early/late)	0.038 / 0.031	**1.8 / 1.5**
					Aerial	0.012	0.6

1 - Endpoints used in the acute exposure risk assessment (RA) are derived by dividing the EC_{50} or LC_{50} from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates and plants, and by a factor of ten (10) for fish and amphibians.

2 - The assessment of potential risk from drift was assessed for the highest cumulative application rate. An assumption of medium sized spray droplets is made for fungicides applied using conventional methods: field sprayers (6%), airblast (74% and 59% for early and late season application and 23% for aerial application, respectively).

3 – Risk quotients shown in bold exceed the level of concern (RQ > 1).

Table 15 Refined risk assessment for fluopicolide on non target aquatic organisms using run-off values as predicted by PRZM-EXAMS Model

Organism	Exposure	Species	Endpoint reported (mg a.i./L)	Endpoint for RA[1] (mg a.i./L)	Use Scenario / EEC (mg a.i./L)	RQ[2]
Freshwater organisms						
Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	96-h LC_{50} = 0.35	0.04	Prairie (Potato-MB) 0.026	0.7
Amphibians	Acute	Surrogate fish (*Oncorhynchus mykiss*))	96-h LC_{50} = 0.35	0.04	Prairie (Potato-MB) 0.106	**2.7**
	Chronic		34-d ELS NOEC = 0.15	0.15	Prairie (Potato-MB) 0.090	0.6

Organism	Exposure	Species	Endpoint reported (mg a.i./L)	Endpoint for RA[1] (mg a.i./L)	Use Scenario / EEC (mg a.i./L)	RQ[2]
Marine/estuarine organisms						
Fish	Acute	Sheepshead minnow *(Cypronodon variegates)*	96-h LC_{50} = 0.41	0.04	Atlantic (Potato-PEI) 0.020	0.5
Marine alga	Acute	Marine diatom *(Skeletonema costatum)*	120-h LC_{50} = 0.052	0.021	Atlantic (Potato-PEI) 0.020	<1.0

1- Endpoints used in the acute exposure risk assessment (RA) are derived by dividing the EC_{50}, LC_{50} from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates and plants, and by a factor of ten (10) for fish and amphibians.
2 – Risk quotients shown in bold exceed the level of concern (RQ > 1).

Table 16 Toxic Substances Management Policy Considerations-Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Fluopicolide Are criteria met?
CEPA toxic or CEPA toxic equivalent[1]	Yes		Yes
Predominantly anthropogenic[2]	Yes		Yes
Persistence[3]:	Soil	Half-life ≥ 182 days	Yes: 376 – 446 days
	Water	Half-life ≥ 182 days	Yes: 6 - 235 days
	Sediment	Half-life ≥ 365 days	Not available
	Air	Half-life ≥ 2 days or evidence of long range transport	Half-life or volatilization is not an important route of dissipation and long-range atmospheric transport is unlikely to occur based on the vapour pressure (3.03 x 10^{-7} Pa) and Henry's Law Constant (3.82 x 10^{-10} atm m^3/mole).
Bioaccumulation[4]	Log K_{OW} ≥ 5		No: 2.9 – 3.26
	BCF ≥ 5000		No: 102 – 121x
	BAF ≥ 5000		Not available
Is the chemical a TSMP Track 1 substance? (all four criteria must be met)			**No, does not meet all TSMP Track 1 criteria.**

[1]All pesticides will be considered CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (i.e., all other TSMP criteria are met).
[2]The policy considers a substance "predominantly anthropogenic" if, based on expert judgment, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.
[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.
[4]The log K_{OW} and/or BCF and/or BAF are preferred over log K_{OW}.

Table 17 Summary of Alternatives for the Same Uses as Presidio™ Fungicide and Fluopicolide 4 SC Fungicide

Crop	Disease	Active ingredient and FRAC Fungicide Group
Brassica (head and stem) vegetables	Downy mildew (*Peronospora parasitica*)	*Bacillus subtilis* (44) Boscalid (7) (Suppression) Chlorothalonil (M5) (on broccoli, brussels sprouts, cabbage and cauliflower) Fosetyl AL (33) (on broccoli and bok choy) Mandipropamid (40) Zineb (M3) (on broccoli, brussels sprouts, cabbage and cauliflower)
Brassica root vegetables	Downy mildew (*Peronospora parasitica*)	Fosetyl AL (33) (for rutabaga)
Cucurbit vegetables	Downy mildew (*Pseudoperonospora cubensis*)	*Bacillus subtilis* (44) Chlorothalonil (M5) Copper oxychloride (M1) Cyazofamid (21) Fenamidone (11) Folpet (M4) Mancozeb (M3) Mandipropamid (40) (Suppression) Propamocarb (28) Pyraclostrobin (11) Zineb (M3)
	Phytophthora blight/crown rot (*Phytophthora capsici*)	N/A
Fruiting vegetables	Late blight (*Phytophthora infestans*)	Captan (M4) (on tomato) Chlorothalonil (M5) (on tomato) Copper hydroxide (M1) (on tomato) Copper oxychloride (M1) (on tomato) Cymoxanil (27) (on tomato) Famoxadone (11) (on tomato) Mancozeb (M3) (on tomato) Mandipropamid (40) (on tomato) Metiram (M3) (on tomato) Pyraclostrobin (11) Zineb (M3) (on tomato, eggplant and pepper)
	Phytophthora blight (*Phytophthora capsici*)	Mandipropamid (40) (Suppression on pepper)
Grapes	Downy mildew (*Plasmopara viticola*)	Azoxystrobin (11) Boscalid (7) Captan (M4) Copper oxychloride (M1) Folpet (M4) Kresoxim-methyl (11) Mancozeb (M3) Mandipropamid (40) Metalaxyl-M (4) Metiram (M3) Pyraclostrobin (11) Zoxamide (22)

Crop	Disease	Active ingredient and FRAC Fungicide Group
Leafy vegetables (except brassica vegetables)	Downy mildew (*Bremia lactucae, Peronospora farinosa*)	Azoxystrobin (11) (on spinach) *Bacillus subtilis* (44) (on lettuce) Boscalid (7) (Suppression on spinach) Fosetyl AL (33) (on greenhouse and field lettuce) Mandipropamid (40) (for *Bremia lactucae*) Metalaxyl-M (4) (on spinach) Zineb (M3) (on lettuce)
Potato	Late blight (*Phytophthora infestans*)	Azoxystrobin (11) Boscalid (7) Chlorothalonil (M5) Copper hydroxide (M1) Copper oxychloride (M1) Cyazofamid (21) Cymoxanil (27) Dimethomorph (40) Famoxadone (11) Fenamidone (11) Fluazinam (29) Mancozeb (M3) Mandipropamid (40) Metalaxyl-M (4) Metiram (M3) Propamocarb (28) Pyraclostrobin (11) Zineb (M3) Zoxamide (22)
Outdoor ornamentals	Downy mildew (*Peronospora* spp.)	Dimethomorph (40)
	Phytophthora crown and root rot (*Phytophthora* spp.)	Metalaxyl-M (4) (on foliage plants, bedding plants and flowers)

Table 18 Use (label) Claims Proposed by Applicant and Accepted

Proposed claim	Accepted claim
1) Control of downy mildew (*Pseudoperonospora cubensis*) on cucurbit vegetables at the rates of 220 - 292 mL/ha.	As proposed, excluding fruit chayote which is not growable in Canada.
2) Control of late blight (*Phytophthora infestans*) on fruiting vegetables at the rates of 220 - 292 mL/ha.	Accepted for tomato only since other crops within fruiting vegetable crop group are not hosts of *P. infestans.*
3) Control of phytophthora blight (*Phytophthora capsici*) on fruiting vegetables at the rates of 220 - 292 mL/ha.	Accepted for suppression, instead of control, for pepper only since *P. capsici* does not cause substantial crop damage on other fruiting vegetables. In addition, the efficacy on tomato could not be determined with confidence due to the low disease suppression expressed in the trial.
4) Control of downy mildew (*Plasmopara viticola*) on grape at the rates of 220 - 292 mL/ha.	As proposed.
5) Control of downy mildew (*Bremia lactucae, Peronospora farinosa*) on leafy vegetables (except brassica vegetables) at the rates of 220 - 292 mL/ha.	As proposed, excluding following crops which are non-host crops of both pathogens: roquette arugula, celery, celtuce, Chinese celery, chervil, corn salad, garden cress, upland cress, sorrel dock, fennel, florence, parsley, garden purslane, winter purslane and radicchio.

Proposed claim	Accepted claim
6) Control of late blight (*Phytophthora infestans*) on potato at the rates of 220 - 292 mL/ha.	As proposed.
7) Control of downy mildew (*Peronospora* spp.) on field and container grown outdoor ornamentals at the rates of 60 - 119 mL in 380 L water to runoff for foliar application or completely wet the root zone for drench application.	As proposed for bedding plants and cut flowers only since ornamental trees and shrubs were not tested in the trials which represent some high value outdoor ornamental plants, and the plant biology would be very different from the plants tested in the efficacy trials.
8) Aerial application for all crops except ornamental plants.	As proposed for potato only since other vegetable crops are mostly in small acreage and unlikely to require aerial application. The registrant has elected to withdraw aerial application from all vegetable crops and retained the option for potato.
9) Tank-mix for all crops except ornamental plants.	As proposed except where no alternative available (in the case for phytophthora disease on cucurbit vegetables).

Table 19 Use (label) Claims Proposed by Applicant and Conditionally Accepted

Proposed claim	Conditionally Accepted claim
1) Control of downy mildew (*Peronospora parasitica*) on brassica (head and stem) vegetables and brassica root vegetables at the rates of 220 - 292 mL/ha.	As proposed.
2) Control of phytophthora blight/crown rot (*Phytophthora capsici*) on cucurbit vegetables at the rates of 220 - 292 mL/ha.	Accepted for suppression, instead of control, excluding fruit chayote which is not growable in Canada.
3) Control of phytophthora crown and root rot (*Phytophthora* spp.) on field and container grown outdoor ornamentals at the rates of 60 - 119 mL in 380 L water to runoff for foliar application or completely wet the root zone for drench application.	Suppression, instead of control, on field and container grown outdoor ornamentals (including bedding plants and cut flowers).

Appendix II Supplemental Maximum Residue Limit Information—International Situation and Trade Implications

The proposed Canadian MRLs are the same as the corresponding tolerances established in the United States (tolerances listed in 40 CFR Part 180 by pesticide). Currently, Codex MRLs[16] (Codex MRLs searchable by pesticide or commodity) have not established for fluopicolide on any commodity.

As per Table 1, there is no corresponding tolerance (tolerances listed in 40 CFR Part 180 by pesticide) in the U.S. for potato. Currently, Codex MRLs1(Codex MRLs searchable by pesticide or commodity) have not been established for fluopicolide in/on any commodity.

Table 1 Comparison of Canadian MRLs, American Tolerances and Codex MRLs (where different)

Food Commodity	Canadian MRL (ppm)	American Tolerance (ppm)	Codex MRL (ppm)
Potato	0.02	*	-

*A tolerance of 0.02 ppm is established in the U.S. for Tuberous and corm vegetables (except potatoes; Crop Subgroup 1D).

[16] Codex is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.

Appendix III - Crop Groups: Numbers and Definitions

Crop Group Number and Name		Crop Subgroup Number and Name (if appropriate)		Food Commodities Included in the Crop Group or Subgroup
1	Root and tuber vegetables	1A	Root vegetable	Black salsify roots Carrot roots Celeriac roots Chicory roots Edible burdock roots Garden beet roots Ginseng roots Horseradish roots Oriental radish roots Parsnip roots Rutabaga roots Salsify roots Skirret roots Spanish salsify roots Sugar beet roots Turnip-rooted chervil roots Turnip-rooted parsley roots Turnip roots
2	Leaves of root and tuber vegetables			Black salsify tops Cassava leaves Celeriac tops Chicory tops Edible burdock tops Garden beet tops Oriental radish tops Radish tops Rutabaga tops Tanier leaves Taro leaves Turnip tops Turnip-rooted chervil tops
3-07	Bulb vegetables			Beltsville bunching onions Chinese onions Daylillies Dry bulb onions Elegans hosta Fresh Chinese chive leaves Fresh chive leaves Fresh onions

Crop Group Number and Name		Crop Subgroup Number and Name (if appropriate)		Food Commodities Included in the Crop Group or Subgroup
				Fritillaria bulbs Fritillaria leaves Garlic Great headed garlic Green onions Kurrats Lady's leeks Leeks Lillies Macrostem onions Pearl Onions Potato onions Serpent garlic Shallot bulbs Shallot leaves Tree onion tops Welsh onion tops Wild Leeks
4	Leafy vegetables (except Brassica vegetables)			Amaranth Argula Cardoon Celery Celtuce Chinese celery Corn salad Dandelion leaves Dock Edible leaved chrysanthemum

Crop Group Number and Name		Crop Subgroup Number and Name (if appropriate)		Food Commodities Included in the Crop Group or Subgroup
				Endives Fresh chervil leaves Fresh Florence fennel leaves and stalk Fresh parsley leaves Garden cress Garden Purslane Garland chrysanthemum Head lettuce and leaf lettuce New Zealand spinach Orach leaves Radicchio Rhubarb Spinach Swiss chard Vine spinach Winter Purslane
5	Brassica Leafy Vegetables	5A	Head and stem Brassica	Broccoli Brussels sprouts Cabbages Cauliflower Chinese Brocoli Chinese mustard cabbages Kohlrabi Napa Chinese cabbages

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A. List of Studies/Information Submitted by Registrant

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4.0 Value

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