Proposed Registration Decision PRD2019-13

Cyantraniliprole and Ference Insecticide

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Overview

Proposed Registration Decision for Cyantraniliprole

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act*, is proposing registration for the sale and use of Cyantraniliprole Technical and Ference Insecticide, containing the technical grade active ingredient cyantraniliprole, to control or supress a variety of insects on turf (golf courses and sod farms only), outdoor ornamentals and greenhouse ornamentals. The use of cyantraniliprole on turf (golf courses and sod farms only) is a new use for this active ingredient.

Cyantraniliprole is currently registered to control a variety of insect pests on fruits and vegetables, oilseeds, greenhouse ornamentals and outdoor ornamentals. For details, see Proposed Registration Decision PRD2013-09, *Cyantraniliprole*, and Registration Decision RD2013-25, *Cyantraniliprole*.

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

This Overview describes the key points of the evaluation, while the Science Evaluation section provides detailed technical information on the human health, environmental and value assessments of cyantraniliprole and Ference Insecticide.

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.

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

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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."

For more information on how the Health Canada regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides section of Canada.ca.

Before making a final registration decision on Cyantraniliprole Technical and Ference Insecticide, Health Canada's PMRA will consider any comments received from the public in response to this consultation document.[3] Health Canada will then publish a Registration Decision[4] on cyantraniliprole and Ference Insecticide, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and Health Canada's response to these comments.

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

What Is Cyantraniliprole?

Cyantraniliprole is a diamide insecticide, Mode of Action (MoA) Group 28 that is active by ingestion and contact. Diamides affect ryanodine receptors in insect muscle, causing paralysis and death of the insect. It is the active ingredient in the commercial class product Ference Insecticide.

Health Considerations

Can Approved Uses of Cyantraniliprole Affect Human Health?

Ference Insecticide, containing cyantraniliprole, is unlikely to affect your health when used according label directions.

Potential exposure to cyantraniliprole may occur through the diet (food and water), when handling and applying the end-use product, or during contact with treated surfaces. 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). As such, sex and gender are taken into account in the risk assessment. 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 pesticide products are used according to label directions.

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

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

In laboratory animals, cyantraniliprole was of low acute toxicity via the oral, dermal, and inhalation routes of exposure. It was non-irritating to the skin, non- to minimally irritating to the eye, and did not cause an allergic skin reaction.

The acute toxicity of Ference Insecticide, containing cyantraniliprole, was low via the oral, dermal, and inhalation routes of exposure. Ference Insecticide was not irritating to the skin or eye, and did not cause an allergic skin reaction.

Registrant-supplied short- and long-term (lifetime) animal toxicity tests, as well as information from the published scientific literature, were assessed for the potential of cyantraniliprole to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. The most sensitive endpoints for risk assessment were effects on the liver. There was no evidence to suggest that the young animal was more sensitive than the adult animal to cyantraniliprole. The risk assessment protects against the effects noted above and other potential effects by ensuring that the level of exposure to humans is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

An update to the dietary risk assessment was not required for this major new use on turf because the cumulative maximum application rate remains the same as that currently registered (PRD2013-09, *Cyantraniliprole* and RD2013-25, *Cyantraniliprole*).

Risks in Residential and Other Non-Occupational Environments

Residential and non-occupational risks are not of concern when cyantraniliprole is used according to the proposed label directions.

Ference Insecticide can be applied as a spray application to turf in golf courses. Therefore, there is the potential for adults and youth to be exposed via the dermal route to treated turf in golf courses.

The exposure assessments conducted for adults and youth when contacting turf treated with cyantraniliprole did not identify risks of concern when the label directions are followed.

Occupational Risks From Handling Cyantraniliprole

Occupational risks are not of concern when cyantraniliprole is used according to the proposed label directions.

Applicators who mix, load and apply Ference Insecticide to turf (golf courses and sod farms only), and workers entering treated turf can come in direct contact with cyantraniliprole residues on the skin and/or through inhalation. Therefore, the label specifies that anyone mixing/loading and applying cyantraniliprole must wear a long-sleeved shirt, long pants, chemical-resistant gloves, shoes and socks. The label prohibits workers from entering treated sod farms for 12 hours after application and from entering all other treated turf areas until sprays have dried.

Taking into consideration label directions and precautionary statements, it was determined that the risks to these individuals are not of concern.

For bystanders, exposure is considered negligible since the potential for drift is expected to be minimal. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Cyantraniliprole Is Introduced Into the Environment?

When cyantraniliprole is used according to the label directions, the risks to the environment have been determined to be acceptable.

Cyantraniliprole can enter the environment when it is used as an insecticide for control of a large number of pests in a variety of crops. Ference Insecticide will be used on turf (golf courses and sod farms only), greenhouse and outdoor ornamentals as a foliar, soil drench application, or by chemigation. Cyantraniliprole is systemic and, therefore, can reach pollen and nectar through movement inside the plant. In both soil and water cyantraniliprole transforms quickly. There is a total of eight major transformation products formed in soil and/or water. The degradation of the major transformation products ranges from not persistent to persistent. Cyantraniliprole and its transformation products have the potential to leach through the soil profile to enter ground water.

When used according to the label directions, cyantraniliprole and its transformation products do not present a risk of concern to soil dwelling organisms, birds and mammals, aquatic plants, algae, fish, and amphibians. Cyantraniliprole may pose risks of concern to aquatic invertebrates, terrestrial plants, beneficial arthropods, and bees; therefore, preventative measures and use restrictions are required on the product label.

Taking into consideration the preventative measures and use restrictions on the label, it was determined that the risks to these organisms are not of concern.

Value Considerations

What Is the Value of Ference Insecticide?

Ference Insecticide controls or suppresses numerous insect pests of turf on golf courses and sod farms.

Ference Insecticide is a new commercial class product that is applied to turf on golf courses and sod farms only for the control or suppression of chinch bugs, black cutworm, fall armyworm, European crane fly and various beetle pests. The product provides a new tool for use against the listed pests of golf course and sod farm turf.

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 Cyantraniliprole Technical and Ference Insecticide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

As direct contact with cyantraniliprole on the skin or through inhalation can occur, anyone mixing, loading and applying Ference Insecticide to turf using ground application equipment must wear a long-sleeved shirt, long pants, chemical-resistant gloves, shoes and socks. Chemical-resistant gloves are not required during application within a closed cab.

Environment

- Product specific buffer zones (up to 3 meters) to mitigate the risks identified for non-target terrestrial plants and aquatic organisms, resulting from a spray drift;
- Standard runoff statements; and
- Precautionary label statements indicating toxicity to non-target terrestrial plants, aquatic organisms, beneficial insects and bees.

Next Steps

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

Other Information

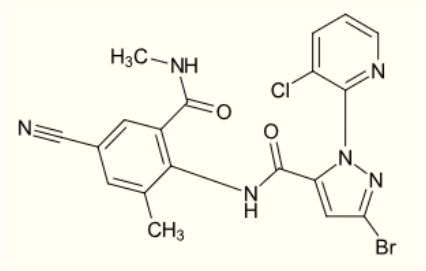
When Health Canada makes its registration decision, it will publish a Registration Decision on cyantraniliprole and Ference Insecticide (based on the Science Evaluation section of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

Cyantraniliprole and Ference Insecticide

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Cyantraniliprole
Function	Insecticide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	3-bromo-1-(3-chloro-2-pyridyl)-4′-cyano-2′-methyl-6′-(methylcarbamoyl)-1*H*-pyrazole-5-carboxanilide
2. Chemical Abstracts Service (CAS)	3-bromo-1-(3-chloro-2-pyridinyl)-*N*-[4-cyano-2-methyl-6-[(methylamino)carbonyl]phenyl]-1*H*-pyrazole-5-carboxamide
CAS number	736994-63-1
Molecular formula	$C_{19}H_{14}BrClN_6O_2$
Molecular weight	473.7
Structural formula	
Purity of the active ingredient	96.7%

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

Technical Product—Cyantraniliprole Technical

Property	Result
Colour and physical state	Off-white fine powder
Odour	No characteristic odour
Melting range	217 – 219 °C
Boiling point or range	Decomposes at 350 °C prior to boiling

Density	1.38 g/cm^{-3}	
Vapour pressure at 20 °C	5×10^{-12} mPa (estimated)	
Ultraviolet (UV)-visible spectrum	pH	λ_{max} (nm)
	Neutral methanol	205, 267
	Acidic methanol	204, 264
	Basic methanol	222, 272, 312
Solubility in water at 20 °C	pH	solubility (mg/L)
	Purified water	14.2
	pH 4 buffer	17.4
	pH 7 buffer	12.3
	pH 9 buffer	5.9
Solubility in organic solvents at 20 °C	Solvent	Solubility (g/ 100 mL)
	Acetone	0.654
	Dichloromethane	0.505
	Methanol	0.473
	Acetonitrile	0.245
	Ethyl Acetate	0.196
	n-Octanol	0.079
	o-Xylene	0.029
	n-Hexane	6.7×10^{-6}
n-Octanol-water partition coefficient (K_{ow})	pH	log K_{ow}
	distilled water	1.97
	pH 4 buffer	1.97
	pH 7 buffer	2.02
	pH 9 buffer	1.74
Dissociation constant (pK_a)	pK_a = 8.80	
Stability (temperature, metal)	Stable at elevated temperatures, and at elevated temperatures in contact with iron and aluminum metal and their acetate salts.	

End-use Product—Ference Insecticide

Property	Result
Colour	White
Odour	Weak aromatic
Physical state	Liquid
Formulation type	Suspension
Label concentration	200 g/L

Container material and description	Fluorinated and non-fluorinated high density polyethylene bottle (HDPE), 1 – 1050 liters
Density	1.089 g/cm^3 at 20 ºC
pH of 1% suspension in water	5 – 7
Oxidizing or reducing action	The product is not classified as oxidizing agent but is considered a reducing agent.
Storage stability	The product is stable in fluorinated and non-fluorinated HDPE bottles when stored for 14 days at 54 ºC.
Corrosion characteristics	The product is not corrosive to its commercial packaging material.
Explodability	This product is not potentially explosive.

1.3 Directions for Use

Ference Insecticide is applied to turf on golf courses and sod farms only at rates between 585 and 1462 mL product/ha (117.0 and 292.4 g a.i./ha) to control annual bluegrass weevil, bill bugs and European crane fly, and to suppress black cutworm, chinch bugs, fall armyworm, and larvae of European chafer, Japanese beetle and June beetles. The rate used depends on the pest. For full details, refer to the product label.

1.4 Mode of Action

Cyantraniliprole is a diamide insecticide in Group 28 of the Insecticide Resistance Action Committee mode of action classification. It modulates the ryanodine receptors of insects causing paralysis and death of the insect. Cyantraniliprole has systemic activity when absorbed by the roots of plants and translaminar activity when absorbed by plant foliage.

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 impurities in the technical product have been validated and assessed to be acceptable.

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.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

Cyantraniliprole belongs to the anthranilic diamide class of pesticides, which control insects through activation of ryanodine receptor channels. This leads to unregulated internal calcium store depletion, resulting in impaired regulation of muscle contraction. Insects exposed to the

anthranilic diamide class of pesticides exhibit general lethargy and muscle paralysis followed ultimately by death. Mammalian ryanodine receptors are substantially less sensitive to the effects of anthranilic diamides than insect ryanodine receptors.

A detailed review of the toxicological database for cyantraniliprole was conducted previously and is summarized in the Proposed Registration Decision, PRD2013-09, *Cyantraniliprole*. The toxicological reference values for use in human health risk assessment that were previously established and published in PRD2013-09 have not changed. The toxicology studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The human health risk assessment also considered information in the published literature. The scientific quality of the data is acceptable and the database is considered adequate to characterize the potential health hazards associated with cyantraniliprole.

Following the original review of the cyantraniliprole toxicity database, two studies (acute oral toxicity and 28-day dietary toxicity studies in rats) were conducted using IN-M2G98, a potential minor environmental transformation product. These studies were required by the European Food Safety Authority. These studies were submitted and reviewed for their potential impact on the human health risk assessment. The findings of these studies, as well as the acute toxicity profile of the new end-use product, Ference Insecticide, are summarized below.

The results of acute toxicity studies conducted with the end-use product Verimark Insecticide (formerly known as DuPont Verimark Insecticide), and summarized in Table 2 of PRD2013-09, were considered adequate to characterize the acute hazards of the end-use product Ference Insecticide. Based on the acute hazard profile of Verimark Insecticide, Ference Insecticide was considered to be of low acute toxicity via the oral, dermal and inhalation routes in rats. In rabbits, Ference Insecticide was considered to be non-irritating to the skin and minimally irritating to the eyes. Negative reactions were documented in a local lymph node assay in mice and a Buehler method in guinea pigs and, therefore, Ference Insecticide is not considered to be a potential dermal sensitizer.

In an acute oral toxicity study in female rats, the environmental transformation product IN-M2G98 was determined to be highly acutely toxic, whereas cyantraniliprole was previously determined to be of low acute oral toxicity in rats. Dietary administration of IN-M2G98 resulted in excessive toxicity which led to the early termination of rats at the two highest dose levels. Light tan feces and decreased body weight and food consumption were observed down to the lowest dose level tested. Nasal effects were also noted at all dose levels and included minimal degeneration of the olfactory epithelium and minimal focal erosion or ulceration of the epithelium. The dose levels resulting in adverse effects in rats after short-term dietary exposure to IN-M2G98 were lower than those for cyantraniliprole. Although the results of these newly submitted studies suggest that IN-M2G98 is more toxic than cyantraniliprole, IN-M2G98 was not identified as a major transformation product of cyantraniliprole in soil or water (PRD2013-09). Based on the location of IN-M2G98 in the transformation pathway of cyantraniliprole and the fact that IN-M2G98 was not formed in environmental fate studies conducted with cyantraniliprole but was only formed late in a study that was conducted with another

transformation product, the amount of IN-M2G98 expected to be present in drinking water in Canada is minimal. Therefore, the results of these newly submitted studies had no impact on the previously determined residue definition for drinking water or on the human health risk assessment for cyantraniliprole.

The toxicological reference values for use in the human health risk assessment for cyantraniliprole are summarized in Appendix I, Table 1. Results of the toxicology studies conducted on laboratory animals with the environmental transformation product IN-M2G98 are summarized in Appendix I, Table 2.

Incident Reports

As of 14 May 2019, one minor human incident involving cyantraniliprole had been submitted to the PMRA. In this incident, an individual experienced a rash at an unknown time when working with soil that was treated with a product containing thiamethoxam and cyantraniliprole. It is not known when the soil was treated with the product or when the individual had contact with the treated soil. Therefore, given the ambiguities in the reported circumstances of exposure, no additional mitigation is proposed.

Aggregate Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from dietary (food and drinking water), residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation). Short- to intermediate-term aggregate exposure to cyantraniliprole from the proposed turf use may be comprised of food, drinking water and residential exposure via the dermal route. No endpoints were selected for short- to intermediate-term aggregate risk assessment, as there was an absence of effects at the limit dose in the repeat-dose dermal toxicity study, no increased susceptibility of the young in reproductive or developmental toxicity studies, and no indications of neurotoxicity. There are no food uses associated with the current expansion of use (turf) for cyantraniliprole. Therefore, the aggregate assessment, which combined dietary exposure from other uses of cyantraniliprole and drinking water, was addressed in PRD2013-09.

Cumulative Assessment

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with a common mechanism of toxicity. Accordingly, an assessment of a potential common mechanism of toxicity with other pesticides was undertaken for cyantraniliprole. Although other pesticides of the same class that are known to target the insect ryanodine receptors are registered in Canada, there is insufficient evidence to link the apical endpoints observed in the toxicology databases for the anthranilic diamide class of pesticides with activation of mammalian ryanodine receptors. Furthermore, the toxicological effects following exposure to anthranilic diamide insecticides are considered indicative of more generalized toxicity, and a common mechanism of toxicity has not been identified. Therefore, a cumulative health risk assessment is not required at this time.

3.2 Occupational and Residential Risk Assessment

3.2.1 Toxicological Reference Values

3.2.1.1 Dermal Absorption

A dermal absorption study was previously submitted but was not required for the current risk assessment as the dermal no observed adverse effect level (NOAEL) was derived from a dermal toxicological study representing the durations of exposure relevant to the proposed end-use product.

3.2.2 Occupational Exposure and Risk

3.2.2.1 Mixer/loader/applicator Exposure and Risk Assessment

Workers have the potential to be exposed to cyantraniliprole during the mixing, loading and application of Ference Insecticide. Exposure is expected to be short- to intermediate-term in duration and occur primarily by the dermal and inhalation routes. No systemic toxicity was identified in a 28-day dermal toxicological study; therefore, no short- to intermediate-term dermal endpoints were established. As a result, only an inhalation risk assessment is required for mixer/loader/applicators.

Inhalation exposure estimates were derived for mixers/loaders/applicators applying cyantraniliprole to turf on sod farms and golf courses using open cab groundbooms and turf gun. Unit exposure values were derived from Agricultural Handlers Exposure Task Force (AHETF) and the Outdoor Residential Exposure Task Force (ORETF) and considered the personal protective equipment (PPE) that is in keeping with label instructions.

Exposure estimates were compared to the NOAEL to obtain the MOE; the target MOE is 300 and risks to workers were not of concern (Appendix I, Table 3).

3.2.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

There is the potential for workers entering treated areas to be exposed to cyantraniliprole after the application to turf to perform activities such as mowing, watering and slab harvesting. Given the nature of activities performed, dermal contact with treated turf is expected to be short- to intermediate-term in duration. However, as no systemic toxicity was identified via the dermal route for the short- to intermediate-term duration, a quantitative risk assessment is not required. Inhalation exposure is not expected to be of concern given the non-volatile nature of cyantraniliprole and restricted-entry interval (REI) of 12 hours for sod farms and until the spray has dried for golf courses.

3.2.3 Residential Exposure and Risk Assessment

3.2.3.1 Handler Exposure and Risk

The proposed end-use product is of the commercial marketing class, therefore a residential applicator risk assessment is not required.

3.2.3.2 Postapplication Exposure and Risk

As Ference Insecticide can be used on turf in golf courses, there is the potential for dermal exposure while golfing. However, as no systemic toxicity was identified via the dermal route for the short- to intermediate-term duration, a quantitative risk assessment is not required. Inhalation exposure is not expected to be of concern given the non-volatile nature of cyantraniliprole.

3.2.3.3 Bystander Exposure and Risk

Bystander exposure should be negligible since the potential for drift is expected to be minimal. Application is limited to when the potential for drift to areas of human habitation and human activity (other than golf courses) is minimal. The applicator must take into consideration wind speed, wind direction, temperature inversions, application equipment, and sprayer settings.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Ference Insecticide will be used on turf (golf courses and sod farms only), greenhouse (including cut flowers) and outdoor ornamentals as a foliar or soil drench application, or by chemigation to control various insect pests.

The fate and environmental behaviour of cyantraniliprole have been previously assessed for use on agricultural crops and greenhouse and outdoor ornamentals. For further details, refer to Proposed Regulatory Decision PRD2013-09, *Cyantraniliprole* and the Regulatory Decision RD2013-25, *Cyantraniliprole*.

4.2 Environmental Risk Characterization

The environmental risk characterisation of cyantraniliprole has been previously assessed for foliar and soil drench use on agricultural crops and greenhouse and outdoor ornamentals. For further details, refer to Proposed Regulatory Decision PRD2013-09, *Cyantraniliprole* and the Regulatory Decision RD2013-25, *Cyantraniliprole*.

The maximum rate of application for turf (450 g a.i./ha) is the same as that currently registered for various terrestrial crops; however, the application scenarios (single maximum rates and application intervals) differ. The proposed use pattern for outdoor and greenhouse ornamentals is similar to that currently registered; however, application to cut flowers is outside of the currently registered use pattern. The difference in application scenario is not expected to impact the estimated environmental concentrations (EECs) calculated under the original submission, as the

maximum cumulative rate remains the same (450 g a.i/ha). The previous assessment for organisms that may be exposed from turf and ornamental uses is considered relevant, and the potential impact on risk quotients (RQs) due to the difference in application scenario will be discussed in the following sections for the various organism groupings.

Additionally, the impact of five new studies with the honeybee and the parasitic wasp, *Aphidius rhopalosiphi*, on the risk assessment will be discussed in the corresponding organism grouping sections.

4.2.1 Risks to Terrestrial Organisms

Terrestrial organisms, such as honeybees, beneficial arthropods, birds, small wild mammals and terrestrial vascular plants, could be exposed to cyantraniliprole through direct contact with spray or spray drift, contact with sprayed surfaces or from ingestion of contaminated food (including systemic transport into plants).

Birds and mammals: The original screening level risk assessment for birds and mammals (PRD2013-09) was conducted using a foliar application at a maximum cumulative rate of 262.5 g a.i./ha (3 × 150 g a.i./ha with 5-d interval and a 5-d foliar half-life). Resulting RQs were all ≤0.14. The proposed turf application scenario results in a maximum cumulative rate of 352.1 g a.i./ha (157.6 g a.i./ha followed by an application of 292.4 g a.i./ha at a 7-d interval and a 5-d foliar half-life). The increase in the cumulative rate results in RQs all ≤0.31 (Appendix I, Table 4); therefore, the use of Ference Insecticide is not expected to pose a risk to birds and mammals.

Soil dwelling arthropods: The original screening level risk assessment for soil dwelling arthropods (PRD2013-09) was conducted using in-field EECs of 0.195 mg a.i./kg soil (foliar application at 3 × 150 g a.i./ha with 5-d interval and a 130-d soil half-life) and 0.13 mg a.i./kg soil (soil drench application at 1 × 300 g a.i./ha and a 130-d soil half-life). The in-field EEC resulting from the proposed turf use is 0.197 mg a.i./kg soil (157.6 g a.i./ha followed by an application of 292.4 g a.i./ha at a 7-d interval and a 130-d soil half-life), which represents a 1% increase in the original foliar EEC. This increase in EEC will not impact the risk conclusions, and the use of cyantraniliprole is not expected to pose a risk to soil dwelling arthropods.

Predators and parasites: Two extended laboratory studies were recently provided under the Incident Reporting program examining the effects of freshly-dried and field-aged residues of cyantraniliprole on with the parasitic wasp, *Aphidius rhopalosiphi*. Significant effects on survival were observed in both studies. These studies represent additional Tier II toxicity studies for cyantraniliprole with the parasitic wasp. Tier I, II, and III tests have already been submitted to the PMRA and assessed for this species. In the original risk assessment for cyantraniliprole (PRD2013-09), a risk to *Aphidius rhopalosiphi* was identified at all tiers (I, II and III), and label statements protective of beneficial insects were required on end-use product labels. The significant effects on mortality of the parasitic wasp observed in these Tier II incident reporting studies do not impact the original risk conclusions, and the use of cyantraniliprole may pose a risk to the parasitic wasp.

Despite the minor differences in application scenarios (single maximum rates and application intervals) for the proposed use of cyantraniliprole on turf and ornamentals, the previous assessment for beneficial arthropods is considered relevant. The original screening level assessment for *Aphidius rhopalosiphi* resulted in RQ values ranging from 284 to 2763 from both in-field and off-field exposure. Higher tiered laboratory studies with residues on foliage (Tier II) and field studies (Tier III) were therefore used to further characterize the risk under more realistic conditions. Cyantraniliprole may pose a risk to beneficial arthropods; therefore, label statements protective of beneficial insects are required on the end-use product label (consistent with the original risk assessment for cyantraniliprole).

Honeybees: In support of these major new use submissions and through PMRA's Incident Reporting Program, three additional studies with the honeybee were made available. The results of these studies represent the first acute larval, chronic larval and adult chronic honeybee toxicity tests for cyantraniliprole. The original (PRD2013-09) Tier I screening risk for contact and oral exposure for adult honeybees was based on a single application rate of 150 g a.i./ha. As well, for oral exposure, a refined Tier I dietary risk assessment was conducted using maximum reported concentrations in pollen and nectar. The potential risk of cyantraniliprole to honeybee brood following acute and chronic oral exposure, and the potential chronic risk to adult honeybees were assessed considering higher tier data including semi-field and field studies.

Although the new use on turf (golf courses and sod farms only) and greenhouse (cut flowers) excludes pollinator exposure, given the availability of the new studies, an additional risk assessment was conducted using both the endpoints from the original Tier I pollinator risk assessment and the newly available studies (Appendix I, Table 5). The screening level risk assessment was conducted using a single maximum application of 292.4 g a.i./ha (proposed turf use) and 150 g a.i./ha (maximum single application rate for all other crops, including ornamentals). A Tier I refined dietary risk assessment was also conducted (Appendix I, Table 6) using maximum reported concentrations in pollen and nectar. Typically, maximum residue levels would be used for an acute risk assessment and mean residue levels would be used for a chronic risk assessment. However, only maximum residues were available for consideration in the current risk assessment (based on the study design of the residue studies submitted for the original submission), and thus were used as a conservative estimate to assess both acute and chronic risk. The application rates for the residue studies were generally close or identical to the proposed rates in Canada with application before and during bloom, and the various crop groups and application scenarios are considered acceptable to also cover the proposed higher turf application rate. Consistent with the original risk assessment for pollinators, a risk was identified at the screening level and tier I refined level. Higher tiered semi-field (Tier II) and field (Tier III) studies were therefore considered to further characterize the risk under more realistic conditions.

The risk conclusions from the original pollinator risk assessment are considered applicable, and cyantraniliprole may pose a risk to honeybees for bee attractive crops. Based on consideration of all of the available data (including acute laboratory studies, Tier I semi-field and Tier II field studies), and a weight of evidence approach, it was concluded that adult bees only exhibited effects (mortality and behavioural) for a short time period, with no lasting effects on the colony. Therefore, hazard and risk based labelling will be required to reduce the potential exposure to bees during active foraging. Cyantraniliprole is systemic and, therefore, can also reach pollen

and nectar through movement inside the plant. Label statements are required for greenhouse ornamentals that may be attractive for bees (which could be moved outside), and also for outdoor ornamentals (consistent with the original risk assessment for cyantraniliprole).

Terrestrial plants: The original screening level risk assessment for seedling emergence and vegetative vigour (PRD2013-09) was based on in-field EECs of 438.3 and 262.5 g a.i./ha, respectively (foliar application at 3 × 150 g a.i./ha with 5-d interval and a 130-d soil or 5-d foliar half-life for seedling emergence and vegetative vigour, respectively). The proposed turf application scenario results in slightly higher seedling emergence and vegetative vigour screening level EECs of 444.2 and 352.1 g a.i./ha (157.6 g a.i./ha followed by an application of 292.4 g a.i./ha at a 7-d interval and a 130-d soil or 5-d foliar half-life for seedling emergence and vegetative vigour, respectively).

Effects on vegetative vigour and seedling emergence have been studied with the end-use product, Cyantraniliprole 100 g/L (formulated with and without codacide oil) at rates up to 150 g a.i./ha, and the results of these studies were used to assess the potential risk from exposure to the Ference Insecticide formulation (200 g a.i./L). Following the screening level risk assessment, it was determined that there was a potential risk to terrestrial plants from the proposed use of Ference Insecticide (Appendix I, Table 7). Thus, in order to mitigate the potential adverse effects of cyantraniliprole on non-target plants, buffer zones and hazard statements will be required on the label (consistent with the original risk assessment for cyantraniliprole).

Overall conclusion about potential risks to terrestrial organisms

Overall, there is no risk of concern for birds and mammals and soil dwelling organisms. Cyantraniliprole may pose a risk of concern to terrestrial plants, beneficial arthropods and bees. As such, preventative measures and use restrictions are required on the label.

4.2.2 Risks to Aquatic Organisms

Aquatic organisms, such as fish, amphibians, invertebrates, algae and vascular plants, could be exposed to cyantraniliprole through contact with spray drift or overland runoff.

Freshwater invertebrates: The original screening level risk assessment for freshwater invertebrates (PRD2013-09) was conducted using a direct application to an 80 cm depth water body EEC of 0.055 mg a.i./L (foliar application at 3 × 150 g a.i./ha with 5-d interval and a 90-d aquatic half-life). The proposed turf application rate results in an EEC of 0.055 mg a.i./L, which is the same as the original risk assessment. Therefore, the risk conclusions from the original risk assessment are considered applicable and there is a potential risk from exposure to spray drift. Mitigative drift reduction statements and buffer zones will be required on the end-use product label (consistent with the original risk assessment for cyantraniliprole). There is also a potential risk for run-off and statements for run-off reduction will be required on the end-use product label.

Fish and amphibians: The original screening level risk assessment for fish and amphibians (PRD2013-09) was conducted using a direct application to 80 and 15 cm depth water body EECs of 0.055 and 0.29 mg a.i./L (foliar application at 3 × 150 g a.i./ha with 5-d interval and a 90-d

aquatic half-life). The proposed turf application rate (157.6 g a.i./ha followed by an application of 292.4 g a.i./ha at a 7-d interval and a 90-d aquatic half-life) results in EECs of 0.055 and 0.29 mg a.i./L in 80 and 15 cm depth water bodies, respectively, which are the same as the original risk assessment. Therefore, the risk conclusions from the original risk assessment are considered applicable, and the use of cyantraniliprole is not expected to pose a risk to fish and amphibians.

Algae and aquatic plants: The original screening level risk assessment for aquatic plants (PRD2013-09) was conducted using a direct application to an 80 cm depth water body EEC of 0.055 mg a.i./L (foliar application at 3 × 150 g a.i./ha with 5-d interval and a 90-d aquatic half-life). The proposed turf application rate results in an EEC of 0.055 mg a.i./L, which is the same as the original risk assessment. Therefore, the risk conclusions from the original risk assessment are considered applicable, and the use of cyantraniliprole is not expected to pose a risk to aquatic plants.

Estuarine/marine species: The original screening level risk assessment for marine species (PRD2013-09) was conducted using a direct application to an 80 cm depth water body EEC of 0.055 mg a.i./L (foliar application at 3 × 150 g a.i./ha with 5-d interval and a 90-d aquatic half-life). The proposed turf application rate results in an EEC of 0.055 mg a.i./L, which is the same as the original risk assessment. Therefore, the risk conclusions from the original risk assessment are considered applicable, and the use of cyantraniliprole is not expected to pose a risk to marine organisms.

Overall conclusion about potential risks to aquatic organisms

Overall, there is no risk of concern for aquatic plants, algae, fish (marine and freshwater), and amphibians. Cyantraniliprole may pose a risk of concern to aquatic invertebrates. As such, drift reduction statements and buffer zones are required on the label.

4.2.3 Incident Reports

Environmental incident reports are obtained from two main sources, the Canadian pesticide incident reporting system (including both mandatory reporting from the registrant and voluntary reporting from the public and other government departments) and the USEPA Ecological Incident Information System (EIIS). Specific information regarding the mandatory reporting system regulations that came into force 26 April 2007, under the *Pest Control Products Act* can be found on the Report a Pesticide Incident page on Canada.ca.

As of 14 May 2019, no environmental incidents involving cyantraniliprole were reported to the PMRA.

5.0 Value

Information submitted demonstrated that the product, when used as directed, controlled annual bluegrass weevil, bill bugs and European crane fly, and suppressed black cutworm, chinch bugs, fall armyworm, and larvae of European chafer, Japanese beetle and June beetles.

Cases of resistance to cyantraniliprole have not been reported for the turf pests listed on the Ference Insecticide label. Resistance management recommendations are included on the product label to decrease the potential for the development of insecticide resistance.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

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

During the review process, cyantraniliprole and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the conclusion that cyantraniliprole and its transformation products do not meet all of the TSMP Track 1 criteria. Please refer to PRD2013-09, *Cyantraniliprole* for further information on the TSMP assessment.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the active ingredient as well as formulants and contaminants in the end-use products are compared against Parts 1 and 3 of the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern.[6] The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations, including the Toxic Substances Management Policy[1] and Formulants Policy,[8] 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 conclusion that cyantraniliprole and its end-use product, Ference Insecticide, do not contain any formulants or contaminants identified in the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

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

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

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

8 DIR2006-02, *Formulants Policy and Implementation Guidance Document*

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

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for cyantraniliprole is adequate to define the majority of toxic effects that may result from exposure. There was no evidence of carcinogenicity in laboratory animals after longer-term dosing. There was no evidence of increased susceptibility of the young in reproductive or developmental toxicity studies. Cyantraniliprole was not neurotoxic or immunotoxic. In short-term and chronic studies on laboratory animals, the primary targets were the liver, the thyroid gland, and the adrenal gland. Evidence indicated that the effects on the thyroid were secondary to liver enzyme activation by cyantraniliprole. The risk assessment protects against the toxic effects noted above by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Mixers, loaders and applicators handling cyantraniliprole and workers entering treated turf are not expected to be exposed to levels of cyantraniliprole that will result in risks of concern when Ference Insecticide is used according to label directions and the required restricted-entry intervals are adhered to. Those mixing, loading and applying Ference Insecticide must wear a long-sleeved shirt, long pants, chemical-resistant gloves, shoes and socks.

Exposure to golfers is not expected to result in risks of concern when Ference Insecticide is used according to label directions. Bystander exposure is not of concern.

7.2 Environmental Risk

Current environmental assessment methodology was used to conduct a risk assessment of the proposed use of the end-use product, Ference Insecticide, on turf (golf courses and sod farms only) and ornamentals (outdoor and greenhouse). Using previously evaluated information, in addition to new bee larvae toxicity, bee adult chronic toxicity and parasitic wasp data, it has been determined that when used according to label directions, cyantraniliprole does not present a risk of concern to soil dwelling organisms, aquatic plants, algae, fish, and amphibians. Cyantraniliprole may pose risks of concern to aquatic invertebrates, terrestrial plants, beneficial arthropods, and bees; therefore, preventative measures and use restrictions are required on the Ference Insecticide label.

7.3 Value

Ference Insecticide is a new tool for use against listed pests of turf on golf courses and sod farms only. It controls or suppresses chinch bugs, black cutworm, fall armyworm, European crane fly and various beetle pests.

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act*, is proposing registration for the sale and use of Cyantraniliprole Technical and Ference Insecticide, containing the technical grade active ingredient cyantraniliprole, to control or supress a variety of insects on turf (golf courses and sod farms only), as well as the currently registered uses on outdoor ornamentals and greenhouse ornamentals.

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

List of Abbreviations

↑	increased
↓	decreased
♂	male
♀	female
λ	wavelength
µg	micrograms
<	lesser than
≤	lesser than or equal to
>	greater than
≥	greater than or equal to
=	equal to
a.i.	active ingredient
AHETF	Agricultural Handlers Exposure Task Force
ATPD	area treated per day
bw	body weight
CAS	Chemical Abstracts Service
CBI	confidential business information
cm	centimetres
d	day(s)
DACO	data code
EDE	estimated daily exposure
EEC	estimated environmental concentration
EIIS	USEPA Ecological incident Information System
ER_{25}	effective rate for 25% of the population
ER_{50}	effective rate for 50% of the population
fc	food consumption
FIR	food ingestion rate
g	gram
h	hour(s)
ha	hectare(s)
HDPE	High Density Polyethylene
HDT	highest dose tested
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOQ	limit of quantitation
mg	milligram
mL	millilitre
MOE	margin of exposure

mPa	milliPascals
M/L/A	mixer/loader/applicators
nm	nanometre
NOAEC	no observed adverse effect concentration
NOED	no observed effect dose
NOAEL	no observed adverse effect level
NOEL	no observed effect level
ORETF	Outdoor Residential Exposure Task Force
pH	measure of the acidity or basicity of an aqueous solution
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppb	parts per billion
PPE	personal protective equipment
PRD	proposed registration decision
RD	registration decision
REI	restricted entry interval
RQ	risk quotient
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet

Appendix I Tables and Figures

Table 1 Toxicological Reference Values for Use in Health Risk Assessment for Cyantraniliprole[1]

Exposure Scenario	Study	Point of Departure and Endpoint	Target MOE[2]
Short- and Intermediate-term dermal	Not required based on the absence of adverse systemic effects in the repeat-dose dermal toxicity study, and no developmental, reproductive, or neurotoxic effects.		
Short-term inhalation	28-day inhalation toxicity in the rat	NOAEC = 0.1 mg/L (HDT) (equivalent to NOAEL = 26 mg/kg bw/day) No adverse effects	100
Intermediate-term inhalation	28-day inhalation toxicity in the rat	NOAEC = 0.1 mg/L (HDT) (equivalent to NOAEL = 26 mg/kg bw/day) No adverse effects	300
Short- and intermediate-term Aggregate	Not required based on the absence of adverse systemic effects in the repeat-dose dermal toxicity study, and no developmental, reproductive, or neurotoxic effects.		
Cancer	Not required as no treatment-related increase in tumour incidence		

[1] Additional details pertaining to the selection of toxicological reference values for cyantraniliprole can be found in PRD2013-09, *Cyantraniliprole*.
[2] MOE refers to a target MOE for occupational and residential assessments.

Table 2 Toxicity Profile of Transformation Product IN-M2G98

Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted. Effects seen above the LOAEL have not been reported in this table for reasons of brevity.

Study Type/Animal/PMRA #	Study Results
Acute Oral Toxicity (Up and Down) Rat (Sprague Dawley) (♀) PMRA 2683503	LD_{50} = 175 mg/kg bw (♀)
28-day oral toxicity (diet) Rat (Sprague Dawley) PMRA 2691218	NOAEL = Not determined LOAEL = 12 mg/kg bw/day (♂/♀) Effects at LOAEL: ↓ bw, fc, minimal degeneration of the olfactory epithelium (♂/♀); minimal focal erosion/ulceration of the olfactory epithelium

Table 3 Mixer/loader/applicator risk assessment for Ference Insecticide on Golf Courses and Sod Farms

Exposure scenario	Inhalation Unit Exposure (µg/kg a.i. handled)[a]	ATPD (ha/day) [c]	Rate (kg a.i./ha)	Inhalation Exposure (mg/kg bw/day) [d]	MOE [e]
PPE: Single layer and CR gloves					
Turf Gun – ORETF (M/L/A)	4.0	2	0.292	0.00002920	894000
Groundboom / Golf Course – AHETF (M/L+A)	2.31[b]	16	0.292	0.0001349	193000
Groundboom / Sod Farm – AHETF (M/L+A)	2.31[b]	30	0.292	0.0002530	103000

[a] All unit exposure values are light inhalation
[b] AHETF open pour mix/load liquids (0.63 µg/kg a.i. handled) + AHETF open cab groundboom (1.68 µg/kg a.i. handled)
[c] Default Area Treated Per Day (ATPD)
[d] Inhalation Exposure = (Unit exposure × ATPD × Rate) / (80 kg bw × 1000 µg/mg)
[e] Based on NOAEL = 26 mg/kg bw/day, target MOE = 300

Table 4 Screening level risk assessment for birds and mammals

	Toxicity (mg a.i./kg bw/d)[a]	Feeding Guild (food item)	EDE (mg a.i./kg bw)[b]	RQ
Small Bird (0.02 kg)				
Acute	225.00	Insectivore (small insects)	28.66	0.13
Reproduction	93.20	Insectivore (small insects)	28.66	0.31
Medium Sized Bird (0.1 kg)				
Acute	225.00	Insectivore (small insects)	22.37	0.10
Reproduction	93.20	Insectivore (small insects)	22.37	0.24
Large Sized Bird (1 kg)				
Acute	225.00	Herbivore (short grass)	14.45	0.06
Reproduction	93.20	Herbivore (short grass)	14.45	0.16
Small Mammal (0.015 kg)				
Acute	500.00	Insectivore (small insects)	16.49	0.03
Reproduction	1352.70	Insectivore (small insects)	16.49	0.01
Medium Sized Mammal (0.035 kg)				
Acute	500.00	Herbivore (short grass)	31.97	0.06
Reproduction	1352.70	Herbivore (short grass)	31.97	0.02
Large Sized Mammal (1 kg)				
Acute	500.00	Herbivore (short grass)	17.08	0.03
Reproduction	1352.70	Herbivore (short grass)	17.08	0.01

[a] Bird endpoints: Acute – 1/10 LC_{50} of 2250 mg a.i./kg bw/day, Reproduction – NOEL of 93.2 mg a.i./kg bw/day
Mammal endpoints: Acute – 1/10 LC_{50} of 5000 mg a.i./kg bw/day, Reproduction – NOEL of 1352.7 mg a.i./kg bw/day
[b] EDE = Estimated dietary exposure; is calculated using the following formula: (FIR/BW) × EEC, where:
FIR: Food Ingestion Rate (Nagy, 1987). For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used; for generic birds with body weight greater than 200 g, the "all birds" equation was used:
Passerine Equation (body weight < or =200 g): FIR (g dry weight/day) = 0.398(BW in g) $^{0.850}$
All birds Equation (body weight > 200 g): FIR (g dry weight/day) = 0.648(BW in g) $^{0.651}$.
For mammals, the "all mammals" equation was used: FIR (g dry weight/day) = 0.235(BW in g) $^{0.822}$
BW: Generic Body Weight
EEC: Concentration of pesticide on food item based on Hoerger and Kenaga (1972) and Kenaga (1973) and modified according to Fletcher et al. (1994). At the screening level, relevant food items representing the most conservative EEC for each feeding

guild are used.
RQ = Risk Quotient = EDE/Toxicity. The RQ is compared to a level of concern (LOC) of 1.

Table 5 Screening level risk assessment for honeybees (*Apis mellifera*)

Exposure	Endpoint (µg a.i./bee)	EEC (µg a.i./bee)[1]	RQ	Level of Concern[2]
72h Acute contact, adult bees	LD_{50} > 0.0934	Max. turf use: 0.70	<7	Exceeded
		Max. all other uses: 0.36	<4	Exceeded
48h Acute oral, adult bees	LD_{50} > 0.1055	Max. turf use: 8.48	<79	Exceeded
		Max. all other uses: 4.35	<41	Exceeded
72h Acute oral, bee larvae	LD_{50} = 0.037	Max. turf use: 3.55	96	Exceeded
		Max. all other uses: 1.82	49	Exceeded
22d Chronic oral, bee larvae	NOED ≥ 0.0025	Max. turf use: 3.55	≤1421	Exceeded
		Max. all other uses: 1.82	≤729	Exceeded
10d Chronic oral, adult bees	NOED = 0.0212	Max. turf use: 8.48	394	Exceeded
		Max. all other uses: 4.35	202	Exceeded

[1] **Contact exposure** = application rate (kg a.i./ha) × adjustment factor (2.4 µg a.i./bee per kg a.i./ha, based on the maximum residue value reported by Koch and Weißer (1997));
Adult oral exposure = application rate (kg a.i./ha) × adjustment factor (29 µg a.i./bee per kg a.i./ha, based on consumption rates primarily derived from Rortais et al. (2005) and Crailsheim et al. (1992 and 1993));
Brood exposure = application rate (kg a.i./ha) × adjustment factor (12 µg a.i./bee per kg a.i./ha, based on consumption rates primarily derived from Rortais et al. (2005) and Crailsheim et al. (1992 and 1993)).
[2] Level of concern = 0.4 for acute risk to pollinators; 1 for chronic risk to pollinators

Table 6 Refined Tier I dietary risk assessment for honeybees (*Apis mellifera*) using maximum reported concentrations in pollen and nectar

Sampled Crop & Considerations	EEC - Maximum residue value in ppb		Did the Acute RQ[1] exceed LOC (0.4)? (RQ)			EEC - Mean residue value in ppb		Did the Chronic RQ[1] exceed LOC (1.0)? (RQ)		
	Pollen	**Nectar**	**Nectar forager**	**Nurse bees**	**Bee larvae**	**Pollen**	**Nectar**	**Nectar forager**	**Nurse bees**	**Bee larvae**
Sunflower Applied at 3 × 150 g a.i./ha Foliar application 3 – 4 weeks **before flowering**, 7 – 10 days apart. Single study rate is below single maximum rate for turf. Cumulative rate is consistent with turf rate. PMRA# 2070718 Considered in the RA because it has the highest pollen residues.	4354	<LOQ (5 µg/kg)	No (<0.02)	**Yes** **(<0.40)**	**Yes** **(0.44)**	4354	<LOQ (5 µg/kg)	No (0.08)	**Yes** **(2)**	**Yes** **(<6.51)**

Sampled Crop & Considerations	EEC - Maximum residue value in ppb		Did the Acute RQ[1] exceed LOC (0.4)? (RQ)			EEC - Mean residue value in ppb		Did the Chronic RQ[1] exceed LOC (1.0)? (RQ)		
	Pollen	**Nectar**	**Nectar forager**	**Nurse bees**	**Bee larvae**	**Pollen**	**Nectar**	**Nectar forager**	**Nurse bees**	**Bee larvae**
Residues may be applicable to bee attractive turf uses.										
Rapeseed Applied at 4 × 100 g a.i./ha Foliar application 7 days apart **during bloom**. Single study rate is below single maximum rate for turf. Cumulative rate is slightly below turf rate. PMRA# 2070733 Considered in the RA because it has the highest combination of pollen/nectar residues (outside of orchard crops). Residues may be applicable to bee attractive turf uses.	1933	38	No (<0.11)	No (<0.23)	No (0.31)	1933	38	No (0.53)	**Yes** **(1.13)**	**Yes** **(<4.61)**
Residues considered in original risk assessment **Pollen (Sunflower):** Foliar application 3 – 4 weeks before flowering, 7 – 10 days apart. PMRA 2070718 **Nectar (Citrus):** 1 × 150 g a.i./ha soil application before bloom to citrus PMRA# 2070736 Considered in the RA because it has the highest combination of pollen/nectar residues (including orchard crops). Residues may be applicable to bee attractive ornamentals. Citrus residues may be applicable to ornamental	4354	837	**Yes** **(2.32)**	**Yes** **(1.51)**	**Yes** **(3.14)**	4354	837	**Yes** **(11.5)**	**Yes** **(7.5)**	**Yes** **(<46.5)**

Sampled Crop & Considerations	EEC - Maximum residue value in ppb		Did the Acute RQ[1] exceed LOC (0.4)? (RQ)			EEC - Mean residue value in ppb		Did the Chronic RQ[1] exceed LOC (1.0)? (RQ)		
	Pollen	Nectar	Nectar forager	Nurse bees	Bee larvae	Pollen	Nectar	Nectar forager	Nurse bees	Bee larvae
shrubs/trees.										

[1]Chronic RQ = Chronic estimated daily dose (EDD)/acute toxicity endpoint
Chronic EDD = nectar dose [nectar consumption rate (mg/day) × maximum nectar residue (µg/kg)/ 1.0 × 10^6] + pollen dose [pollen consumption rate (mg/day) x maximum pollen residue (µg/kg)/1.0 x 10^6]
Daily consumption rate used for adult worker bees foraging for nectar: 292 mg/day nectar; 0.041 mg/day pollen; 292 mg/day total
Daily consumption rate used for adult nurse bees: 140 mg/day nectar; 9.6 mg/day pollen; 149.6 mg/day total
Daily consumption rate used for bee larvae: 120 mg/day nectar; 3.6 mg/day pollen; 124 mg/day total
Adult acute oral **LD_{50} = >0.105 µg a.i./bee for technical grade active ingredient;** bee larvae acute **LD_{50} = 0.037 µg a.i./larva/day for technical grade active ingredient**
Adult chronic oral **NOED = 0.021 µg a.i./bee for technical grade active ingredient;** bee larvae chronic **NOED = >0.0025 µg a.i./larva/day for technical grade active ingredient**

Table 7 Screening level risk assessment for terrestrial plants

Exposure	Endpoint	EEC (g a.i./ha)	RQ	LOC exceeded?
21-d Seedling emergence, Cyantraniliprole 100 g/L OD	ER_{25} > 150 g a.i./ha	In field: 444.2 [a]	< 3.0	Unable to determine; however, unlikely based on limited effects observed in study.
		Off-field: 217.9 [b]	< 1.4	
21-d Seedling emergence, Cyantraniliprole 100 g/L OD *with codacide oil*	ER_{25} =123 g a.i./ha (tomato shoot dry weight) All other species were >150 g a.i./ha	In field: 444.2 [a]	3.6	YES
		Off-field: 217.9 [b]	1.8	YES
21-d Vegetative vigour, Cyantraniliprole 100 g/L OD	ER_{25} and ER_{50} > 150 g a.i./ha Note: onion and ryegrass had shoot dry weight inhibition of 22 and 20%, respectively.	In field: 352.1 [c]	< 2.3	Unable to determine; however, possible based on up to 22% effects following one application.
		Off-field: 153.1 [d]	< 1.0	
21-d Vegetative vigour, Cyantraniliprole 100 g/L OD *with codacide oil*	ER_{25} and ER_{50} > 150 g a.i./ha All effects well below 5%	In field: 352.1 [c]	< 2.3	Unable to determine; however, unlikely based on <5% effects observed in the study.
		Off-field: 153.1 [d]	< 1.0	

[a] Based on a maximum turf rate of 157.6 g a.i./ha followed by an application of 292.4 g a.i./ha at a 7-d interval and a 130-d soil half-life.
[b] Based on off-field exposure from a maximum outdoor ornamental rate of two applications of 150 g a.i./ha at a 7-d interval, a 130-d soil half-life, and a 74% drift value (based on early season airblast application).
[c] Based on maximum turf rate of 157.6 g a.i./ha followed by an application of 292.4 g a.i./ha at a 7-d interval and a 5-d foliar half-life.
[d] Based on off-field exposure from a maximum outdoor ornamental rate of two applications of 150 g a.i./ha at a 7-d interval, a 5-d foliar half-life, and a 74% drift value (based on early season airblast application).

References

PMRA Document Number | References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

2848143 2016, Description of Starting Materials, DACO: 3.2.1,3.3.1 CBI

2848144 2016, Enforcement Analytical Method, DACO: 3.4.1 CBI

2848145 2016, Enforcement Analytical Method, DACO: 3.4.1 CBI

2848146 2016, Enforcement Analytical Method, DACO: 3.4.1 CBI

2848147 2016, Explodability, DACO: 3.5.1,3.5.10,3.5.11,3.5.12,3.5.14,3.5.2,3.5.3,3.5.6,3.5.7,3.5.8,3.5.9,3.7 CBI

2916888 2018, Container Material and Description, DACO: 3.2.2,3.5.5 CBI

2848141 2016, Description of Starting Materials, DACO: 2.2,3.1.2,3.2.1,3.2.2,3.2.3,3.3.1,3.4.2,4.8 CBI

2.0 Human and Animal Health

2683503 2016, IN-M2G98: Acute Oral Toxicity Study in Rats - Up-and-Down Procedure, DACO: 4.2.1

2691218 2016, IN-M2G98: Repeated-Dose Oral Toxicity 28-Day Feeding Study in Rats, DACO: 4.3.3

3.0 Environment

2847654 2018, Cyantraniliprole (SYN545377) - Repeated Exposure to the Honey Bee (*Apis mellifera*) Larvae under laboratory Conditions (until Adult Emergence up to Day 22). BioChem agrar. Study Code 16 10 48 127 B. Study completion date: 08 Jan 2018. 71pp. DACO: 9.2.4.3.

2847655 2018, Cyantraniliprole (SYN545377) - Chronic toxicity to the honey bee *Apis mellifera* L. in a 10 day continuous laboratory feeding study. BioChem agrar. Study Code 17 48 BAC 0038. Study completion date: 05 Jan 2018. 87pp. DACO: 9.2.4.4.

2589314 Cyantraniliprole (DPX-HGW86) 100 g/L OD: Honey Bee (*Apis mellifera* L.) larval toxicity test (single feeding exposure). Eurofins Agroscience Services EcoChem GmbH. Study Code S14-00331. Study completion date: 01 Dec 2014. 46 pp. DACO 9.2.4.3.

2721271 Cyantraniliprole WG (A16971B) - Rate-response extended laboratory bioassays to determine the effects of fresh and field-aged residues on the parasitic wasp *Aphidius rhopalosiphi* (Hymenoptera, Braconidae). Mambo-Tox Ltd. Study Code SYN-14-40. Study completion date: 15 Oct 2015. DACO 9.2.6.

2811604 Cyantraniliprole WG (A16971B) - Rate-response extended laboratory bioassays to determine the effects of fresh and field-aged residues on the parasitic wasp *Aphidius rhopalosiphi* (Hymenoptera, Braconidae). Mambo-Tox Ltd. Study Code SYN-16-39. Study completion date: 9 Nov 2016. DACO 9.2.6.

4.0 Value

2848085 2017, Efficacy summary to register the new product, Ference™ Insecticide, for use on turf and ornamentals in Canada, DACO: 10.1

2848086 2017, Ference (New EUP) Turf Data Summary, DACO: 10.2.3.1

2848088 2006, TUR06-01: Chlorantraniliprole curative treatments for Annual Bluegrass Weevil in Annual, DACO: 10.2.3.3

2848089 2013, TUR13-03: Cyantraniliprole: Efficacy of A20520A and Spinner for control of grubs and billbugs in turf, DACO: 10.2.3.3

2848090 2013, TUR13-04: Cyantraniliprole: Efficacy of A20520A and Spinner for control of grubs and billbugs in turf, DACO: 10.2.3.3

2848091 2015, TUR15-01: Comparitive testing of chlorantraniliprole and cyantraniliprole formulations for billbug control in turfgrass, DACO: 10.2.3.3

2848092 2015, TUR15-02: Comparitive testing of chlorantraniliprole and cyantraniliprole formulations for billbug control in turfgrass, DACO: 10.2.3.3

2848093 2015, TUR15-03: Comparitive testing of chlorantraniliprole and cyantraniliprole formulations for billbug control in turfgrass, DACO: 10.2.3.3

2848094 2005, TUR05-01: Curative cyantraniliprole and chlorantraniliprole applications for control of hairy chinch bugs (*Blissus leucopterus hirta*) in a lawn, DACO: 10.2.3.3

2848095 2014, TUR14-01: Cyantraniliprole: Control of Craneflies in Turf, DACO: 10.2.3.3

2848096 2015, TUR15-04: Comparitive testing of cyantraniliprole formulations for control of lepidopterous pests in turfgrass, DACO: 10.2.3.3

2848097 2016, TUR16-04: Evaluate chlorantraniliprole and cyantraniliprole 200SC formulations for lepidopterous pest control in turf, DACO: 10.2.3.3

2848098 2015, TUR15-05: Comparitive testing of cyantraniliprole formulations for control of lepidopterous pests in turfgrass, DACO: 10.2.3.3

2848099 2008, TUR08-01: Efficacy of Acelepryn, Provaunt, Talstar and DPXHGW86 in a timed trial against annual bluegrass weevil, DACO: 10.2.3.3

2848100 2016, TUR16-05: Evaluate chlorantraniliprole and cyantraniliprole 200SC formulations for lepidopterous pest control in turf, DACO: 10.2.3.3

2848101 2009, TUR09-01: Influence of Application Rate and Post-application Irrigation on Efficacy of Acelepryn and DPX-HGW86 Applied at two Different Timings Against Japanese Beetle Larvae in Turfgrass, DACO: 10.2.3.3

2848102 2013, TUR13-05: Cyantraniliprole: Efficacy of A20520A and Spinner for control of grubs and billbugs in turf, DACO: 10.2.3.3

2848103 2017, TUR17-01: Evaluate cyantraniliprole (CYNT) and chlorantraniliprole (CTPR) formulations for control of white grubs in turfgrass, DACO: 10.2.3.3

2848104 2017, TUR17-02: Evaluate cyantraniliprole (CYNT) and chlorantraniliprole (CTPR) formulations for control of white grubs in turfgrass, DACO: 10.2.3.3

2848105 2015, TUR15-06: Comparitive testing of chlorantraniliprole and cyantraniliprole formulations for annual white grub control in turfgrass, DACO: 10.2.3.3

2848106 2015, TUR15-07: Comparitive testing of chlorantraniliprole and cyantraniliprole formulations for annual white grub control in turfgrass, DACO: 10.2.3.3

2848107 2006, TUR06-02: Comparison of DPX E2Y45 Against Merit and Arena for Preventative control of European Chafer, DACO: 10.2.3.3
2848108 2015, TUR15-08: Comparitive testing of chlorantraniliprole and cyantraniliprole formulations for annual white grub control in turfgrass, DACO: 10.2.3.3
2848109 2016, TUR16-06: Evaluate cyantraniliprole 200SC formulations for white grub control in turf, DACO: 10.2.3.3
2848110 2008, TUR08-02: Efficacy of Provaunt, Dylox and DPX HGW 86 as curative applications against annual bluegrass weevil, DACO: 10.2.3.3
2848121 2010, TUR10-01: Acelepryn, Provaunt and HGW86 Annual Bluegrass Weevil Control in turfgrass, DACO: 10.2.3.3
2848133 2013, TUR13-01: Evaluation of Syngenta insecticides for control of 2nd-3rd generation annual bluegrass weevil adults, DACO: 10.2.3.3
2848137 2016, TUR16-01: Comparison of A20520C and A20520A for annual bluegrass weevil control in cool-season turfgrass, DACO: 10.2.3.3
2848138 2016, TUR16-02: Comparison of A20520C and A20520A for annual bluegrass weevil control in cool-season turfgrass, DACO: 10.2.3.3
2848139 2016, TUR16-03: Comparison of A20520C and A20520A for annual bluegrass weevil control in cool-season turfgrass, DACO: 10.2.3.3
2848140 2013, TUR13-02: Cyantraniliprole: Efficacy of A20520A and Spinner for control of grubs and billbugs in turf, DACO: 10.2.3.3

B. Additional Information Considered

i) Published Information

1.0 Human and Animal Health

3007343 2015, Conclusion on the peer review of the pesticide risk assessment of the active substance cyantraniliprole, EFSA Journal 12 (9): 3814, DACO: 12.5.4